

Nutrición Hospitalaria



Órgano Oficial

Sociedad Española de Nutrición Clínica y Metabolismo | Sociedad Española de Nutrición | Federación Latino Americana de Nutrición Parenteral y Enteral | Federación Española de Sociedades de Nutrición, Alimentación y Dietética

Editorial

Actualización del consenso de codificación hospitalaria según los criterios GLIM: un enfoque adaptado a la complejidad hospitalaria 1137

Trabajos Originales

Paciente crítico

Healthcare resource utilization among critically-ill COVID-19 survivors – Results from the NUTRICOVID study 1139

Associations of body mass index and oxygen saturation with chronic obstructive pulmonary disease grade in patients 1147

Association between length of hospital stay before and after surgery and nutritional risk according to NRE-2017 – A secondary analysis of a cohort study 1153

Nutrición artificial

Gastrostomía radiológica frente a endoscópica en pacientes con esclerosis lateral amiotrófica 1160

Paciente anciano

Criterios GLIM para diagnosticar la desnutrición en adultos mayores institucionalizados 1165

Pediatría

Serum glutathione peroxidase is associated with nonalcoholic fatty liver disease in children and adolescents 1171

Clinical value of vitamin K testing in children aged 1-2 years with vitamin D deficiency rickets 1178

Decision tree model development and *in silico* validation for avoidable hospital readmissions at 30 days in a pediatric population 1186

Obesidad y síndrome metabólico

Prevalence of the genetic variant rs61330082 and serum levels of the visfatin gene in Mexican individuals with metabolic syndrome: a clinical and bioinformatics approach 1194

Differences in the cluster of depressive symptomatology among bariatric surgery candidates, long-term bariatric surgery patients, and subjects with a major depressive disorder without obesity 1202

Cambios metabólicos, clínicos y de composición corporal en adultos mexicanos sometidos a cirugía bariátrica 1209

Weight-adjusted waist index predicts metabolic syndrome in Caucasian patients with obesity 1217

El combate de los análogos de GLP-1: efectos de semaglutida 0,5 mg semanales *versus* liraglutida 3 mg diarios sobre los parámetros antropométricos durante 3 meses en la vida real 1224

Relationship between serum omentin-1 levels and nascent metabolic syndrome in Caucasian patients with obesity 1231

Valoración nutricional

Heuristic evaluation of body mass index with bioimpedance data in the Mexican population 1238

Do nutritional assessment scores have a relationship with transthyretin levels? 1246

Exploring the link between the Naples prognostic score and the cardio-ankle vascular index 1253

Epidemiología y dietética

Adherence to the Mediterranean diet and risk of stroke in a Chilean population: a case-control study 1258

Reliability of the New Index of Global Food Quality and its relationship with sociodemographic variables and physical activity levels in the Chilean population 1265

Hydration profile of the Latin American population and the contribution of total daily pure water. The ELANS study 1274

Otros

Relación entre el consumo de suplementos deportivos y la adicción al deporte en corredores de asfalto y montaña 1286

Adaptation and validation of the Brief Questionnaire for Measuring Disordered Eating Behaviors in Mexican children 1294

Artículo Especial

Dietista-nutricionista interno residente (D-NIR): una necesidad a años luz de producirse en España 1300

Grupo de Trabajo SENPE

Revisión y actualización del documento de consenso SENPE-SEDOM-SEEN sobre la codificación de la desnutrición hospitalaria 1307

Cartas al Director

La importancia de los determinantes sociales en la detección de síntomas depresivos y su relación con el consumo de agua del grifo 1315

Omega-3 y parto pretérmino: descifrando las piezas del rompecabezas para su prevención 1317

La necesaria y compleja mirada biopsicosocial a la alimentación 1319

Relationship between fermented dairy consumption, gut microbiota and type 2 diabetes 1321

Sobre la obesidad en niños de México 1322

Crítica de Libros

Tratado de nutrición (4.ª edición) 1324

Nutrición Hospitalaria



Órgano Oficial

Sociedad Española de Nutrición Clínica y Metabolismo | Sociedad Española de Nutrición | Federación Latino Americana de Nutrición Parenteral y Enteral | Federación Española de Sociedades de Nutrición, Alimentación y Dietética

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Sumario

Vol. 41 Noviembre-Diciembre N.º 6

Editorial

- Actualización del consenso de codificación hospitalaria según los criterios GLIM: un enfoque adaptado a la complejidad hospitalaria
G. Oliveira..... 1137

Trabajos Originales

Paciente crítico

- Uso de recursos sanitarios en pacientes críticos supervivientes de la COVID-19: resultados del estudio NUTRICOID
J. Álvarez-Hernández, P. Matía-Martín, E. Cáncer-Minchot, C. Cuerda; en representación del Grupo de Estudio NUTRICOID de SENDIMAD 1139

- Asociación del índice de masa corporal y la saturación de oxígeno con el grado de enfermedad pulmonar obstructiva crónica en los pacientes
W. Tan, S. Wang, B. Xing, W. Wang, B. Li, Y. Hu 1147

- Asociación entre duración de la estancia hospitalaria antes y después de la cirugía y riesgo nutricional según la NRE-2017: análisis secundario de un estudio de cohortes
A. M. Chacon, M. S. Tarnowski, J. Brito, A. Garcez, M. V. Beretta, C. B. A. Gottschall 1153

Nutrición artificial

- Gastrostomía radiológica frente a endoscópica en pacientes con esclerosis lateral amiotrófica
M. J. Vallejo Herrera, V. Vallejo Herrera, A. del Toro Ortega, M. J. Tapia Guerrero 1160

Paciente anciano

- Criterios GLIM para diagnosticar la desnutrición en adultos mayores institucionalizados
D. Robles-Torres, B. Bea-Mascato, M. Alfonsín-Lara, E. Y. Romero-Ventosa, N. García-Beloso, A. López-López, P. Pérez Castro, N. Martínez-López-de-Castro, N. Lago-Rivero 1165

Pediatría

- La glutatión-peroxidasa sérica se asocia a la enfermedad del hígado graso no alcohólico en niños y adolescentes
P. Q. Santos, R. Rocha, C. H. Dalto, S. C. S. Andrade, H. P. Cotrim..... 1171

- El valor clínico de la determinación de la vitamina K en niños de 1 a 2 años de edad con raquitismo por déficit de vitamina D
L. Jie, L. Niu, T. Lu, Q. Sun..... 1178

- Desarrollo de un modelo de árbol de decisión y validación *in silico* de reingresos hospitalarios evitables a 30 días en una población pediátrica
N. C. Silva, L. R. Amaral, M. S. Gomes, P. L. L. Bertarini, Ma. K. Albertini, A. R. Backes, G. G. Pena 1186

Sumario

Nutrición Hospitalaria

Sumario

Vol. 41

Noviembre-Diciembre

N.º 6

sumario

Obesidad y síndrome metabólico

Prevalencia de la variante genética rs61330082 y niveles séricos del gen de la visfatina en individuos mexicanos con síndrome metabólico: una aproximación clínica y bioinformática

G. D. González-Sánchez, L. A. Martínez-Pérez, Á. Pérez-Reyes, J. M. Guzmán-Flores, M. J. García-Robles 1194

Diferencias en el perfil de síntomas depresivos entre pacientes candidatos a cirugía bariátrica, pacientes intervenidos de cirugía bariátrica a largo plazo y personas con trastorno depresivo sin obesidad

J. Nicolau, P. Sanchis, L. Ayala, S. Pascual, M. I. Tamayo, A. Cifuentes, L. Masmiquel 1202

Cambios metabólicos, clínicos y de composición corporal en adultos mexicanos sometidos a cirugía bariátrica

T. Rivera-Carranza, A. León-Téllez Girón, M. E. Rojano-Rodríguez, L. S. Romero-Loera, E. Zúñiga-León 1209

El índice de cintura ajustado al peso predice el síndrome metabólico en pacientes caucásicos con obesidad

D. de Luis, D. Primo, O. Izaola, D. Rico, J. J. López Gómez 1217

El combate de los análogos de GLP-1: efectos de semaglutida 0,5 mg semanales *versus* liraglutida 3 mg diarios sobre los parámetros antropométricos durante 3 meses en la vida real

A. Pujol, J. Nicolau, A. Gil, J. Blanco 1224

Relación entre los niveles séricos de omentina-1 y el síndrome metabólico incipiente en pacientes caucásicos con obesidad

D. A. de Luis, O. Izaola, D. Primo 1231

Valoración nutricional

Evaluación heurística del índice de masa corporal con datos de bioimpedancia en la población mexicana

A. Ramos-Jiménez, M. A. Hernández Lepe, R. P. Hernández-Torres, M. Murguía-Romero 1238

¿Las puntuaciones de la evaluación nutricional tienen relación con los niveles de transtiretina?

M. A. Linden, R. G. B. O. Nascimento Freitas, L. O. S. Teles, A. Moreno Morcillo, M. T. Ferreira, R. J. N. Nogueira 1246

Explorando el vínculo entre la puntuación pronóstica de Nápoles y el índice vascular cardio-tobillo

E. Aydin, S. Özer, A. Özdeyera, E. Yilmaz, A. Kaya, A. Ösken, G. Yeriikaya, S. Yaylaci 1253

Epidemiología y dietética

Adherencia a la dieta mediterránea y riesgo de infarto cerebral en una población chilena: estudio de casos y controles

L. Hoffmeister, P. Caro, P. Lavados 1258

Confiabilidad del Nuevo Índice de Calidad Global de Alimentación y su relación con variables sociodemográficas y niveles de actividad física en la población chilena

J. F. Aburto González, R. Armstrong, A. Monterrosa Quintero 1265

Perfil de hidratación de la población latinoamericana y el aporte de agua pura total diaria. Estudio ELANS

M. C. Yépez García, M. Villar, G. Gómez, M. J. Mateo, R. Y. Almeida, D. Albuja, I. Kovalskys, R. G. Pareja, M. Fisberg; en representación del Estudio Latinoamericano de Nutrición y Salud (ELANS) 1274

Otros

Relación entre el consumo de suplementos deportivos y la adicción al deporte en corredores de asfalto y montaña

S. Martín Hernández, A. Rivero Santana, A. Tórtola-Navarro, L. I. Perestelo Pérez 1286

Adaptación y validación del Cuestionario Breve para Medir Conductas Alimentarias de Riesgo en niñas y niños mexicanos

C. Unikel Santoncini, I. Castillo Rangel, M. Barajas Márquez, L. A. Rivera Castañeda, A. B. Casillas Arias 1294

Nutrición Hospitalaria

Sumario

Vol. 41

Noviembre-Diciembre

N.º 6

sumario

Artículo Especial

Dietista-nutricionista interno residente (D-NIR): una necesidad a años luz de producirse en España
N. Benítez Brito, B. Pinto Robayna 1300

Grupo de Trabajo SENPE

Revisión y actualización del documento de consenso SENPE-SEDOM-SEEN sobre la codificación de la desnutrición hospitalaria
J. A. Irlés Rocamora, J.-J. Alfaro-Martínez, P. Asensio Villahoz, M. D. Ballesteros Pomar, R. Burgos Peláez, C. Gallego Díaz, T. Martín Folgueras, V. Pulgar Perera, C. Velasco Gimeno, A. Zugasti Murillo, Á. L. Abad-González, J. Álvarez Hernández; en representación de la Sociedad Española de Nutrición Clínica y Metabolismo (SENPE), Sociedad Española de Endocrinología y Nutrición (SEEN) y Sociedad Española de Documentación Médica (SEDOM) 1307

Cartas al Director

La importancia de los determinantes sociales en la detección de síntomas depresivos y su relación con el consumo de agua del grifo
D. García Martínez, I. Morona Mínguez, D. Gómez Rocha, Á. Pousada Fonseca 1315

Omega-3 y parto pretérmino: descifrando las piezas del rompecabezas para su prevención
I. G. Martínez Velasco, M. A. Guillén Román, R. Jiménez López, O. Arciniega Mancilla 1317

La necesaria y compleja mirada biopsicosocial a la alimentación
C. Troncoso-Pantoja 1319

Relación entre consumo de lácteos fermentados, microbiota intestinal y diabetes de tipo 2
S. V. Flores, Á. Roco-Videla 1321

Sobre la obesidad en niños de México
N. Cipatli Ayuzo del Valle, P. Pérez Treviño, R. M. Murillo Torres, A. Heredia Luna, L. A. Ojeda Robledo 1322

Crítica de Libros

Tratado de nutrición (4.ª edición)
A. Gil Hernández 1324

Nutrición Hospitalaria

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Summary

Vol. 41 November-December No. 6

Editorial

- Update on the consensus for hospital coding according to GLIM criteria: an approach adapted to hospital complexity
G. Oliveira..... 1137

Original Papers

Critical patients

- Healthcare resource utilization among critically-ill COVID-19 survivors – Results from the NUTRICOVID study
J. Álvarez-Hernández, P. Matía-Martín, E. Cáncer-Minchot, C. Cuerda; on behalf of the NUTRICOVID Study Group of SENDIMAD* 1139
- Associations of body mass index and oxygen saturation with chronic obstructive pulmonary disease grade in patients
W. Tan, S. Wang, B. Xing, W. Wang, B. Li, Y. Hu 1147
- Association between length of hospital stay before and after surgery and nutritional risk according to NRE-2017 – A secondary analysis of a cohort study
A. M. Chacon, M. S. Tarnowski, J. Brito, A. Garcez, M. V. Beretta, C. B. A. Gottschall 1153

Artificial nutrition

- Radiological versus endoscopic gastrostomy in patients with amyotrophic lateral sclerosis
M. J. Vallejo Herrera, V. Vallejo Herrera, A. del Toro Ortega, M. J. Tapia Guerrero 1160

Elderly patient

- GLIM criteria for diagnosing malnutrition in institutionalized older adults
D. Robles-Torres, B. Bea-Mascato, M. Alfonsín-Lara, E. Y. Romero-Ventosa, N. García-Beloso, A. López-López, P. Pérez Castro, N. Martínez-López-de-Castro, N. Lago-RiveroPediatría..... 1165

Pediatrics

- Serum glutathione peroxidase is associated with nonalcoholic fatty liver disease in children and adolescents
P. Q. Santos, R. Rocha, C. H. Daltro, S. C. S. Andrade, H. P. Cotrim..... 1171
- Clinical value of vitamin K testing in children aged 1-2 years with vitamin D deficiency rickets
L. Jie, L. Niu, T. Lu, Q. Sun..... 1178
- Decision tree model development and *in silico* validation for avoidable hospital readmissions at 30 days in a pediatric population
N. C. Silva, L. R. Amaral, M. S. Gomes, P. L. L. Bertarini, Ma. K. Albertini, An. R. Backes, G. G. Pena 1186

Yearly
Summaries

Nutrición Hospitalaria

Summary

Vol. 41 November-December No. 6

summary

Obesity and metabolics syndrome

Prevalence of the genetic variant rs61330082 and serum levels of the visfatin gene in Mexican individuals with metabolic syndrome: a clinical and bioinformatics approach

G. D. González-Sánchez, L. A. Martínez-Pérez, Á. Pérez-Reyes, J. M. Guzmán-Flores, M. J. García-Robles 1194

Differences in the cluster of depressive symptomatology among bariatric surgery candidates, long-term bariatric surgery patients, and subjects with a major depressive disorder without obesity

J. Nicolau, P. Sanchís, L. Ayala, S. Pascual, M. I. Tamayo, A. Cifuentes, L. Masmiquel 1202

Metabolic, clinical and body composition changes in Mexican adults undergoing bariatric surgery

T. Rivera-Carranza, A. León-Téllez Girón, M. E. Rojano-Rodríguez, L. S. Romero-Loera, E. Zúñiga-León 1209

Weight-adjusted waist index predicts metabolic syndrome in Caucasian patients with obesity

D. de Luis, D. Primo, O. Izaola, D. Rico, J. J. López Gómez 1217

The GLP-1 analogue battle: effects of semaglutide 0,5 mg/weekly versus liraglutide 3 mg/daily on anthropometric parameters after 3 months in a real world-scenario

A. Pujol, J. Nicolau, A. Gil, J. Blanco 1224

Relationship between serum omentin-1 levels and nascent metabolic syndrome in Caucasian patients with obesity

D. A. de Luis, O. Izaola, D. Primo 1231

Nutritional evaluation

Heuristic evaluation of body mass index with bioimpedance data in the Mexican population

A. Ramos-Jiménez, M. A. Hernández Lepe, R. P. Hernández-Torres, M. Murguía-Romero 1238

Do nutritional assessment scores have a relationship with transthyretin levels?

M. A. Linden, R. G. B. O. Nascimento Freitas, L. O. S. Teles, A. Moreno Morcillo, M. T. Ferreira, R. J. N. Nogueira 1246

Exploring the link between the Naples prognostic score and the cardio-ankle vascular index

E. Aydın, S. Özer, A. Özderya, E. Yılmaz, A. Kaya, A. Ösken, G. Yerlikaya, S. Yaylacı 1253

Epidemiology and dietetics

Adherence to the Mediterranean diet and risk of stroke in a Chilean population: a case-control study

L. Hoffmeister, P. Caro, P. Lavados 1258

Reliability of the New Index of Global Food Quality and its relationship with sociodemographic variables and physical activity levels in the Chilean population

J. F. Aburto González, R. Armstrong, A. Monterrosa Quintero 1265

Hydration profile of the Latin American population and the contribution of total daily pure water. The ELANS study

M. C. Yépez García, M. Villar, G. Gómez, M. J. Mateo, R. Y. Almeida, D. Albuja, I. Kovalskys, R. G. Pareja, M. Fisberg; on behalf of the ELANS Study Group 1274

Others

Relationship between consumption of sports supplements and addiction to sport in road and mountain runners

S. Martín Hernández, A. Rivero Santana, A. Tórtola-Navarro, L. I. Perestelo Pérez 1286

Adaptation and validation of the Brief Questionnaire for Measuring Disordered Eating Behaviors in Mexican children

C. Unikel Santoncini, I. Castillo Rangel, M. Barajas Márquez, L. A. Rivera Castañeda, A. B. Casillas Arias 1294

Nutrición Hospitalaria

Summary

Vol. 41 November-December No. 6

summary

Special Article

- Dietitian-nutritionist intern resident (D-NIR) – A need light years away from occurring in Spain
N. Benitez Brito, B. Pinto Robayna 1300

SENPE Working Group

- Review and update of the SENPE-SEDOM-SEEN consensus document on the coding of hospital malnutrition
J. A. Irlés Rocamora, J.-J. Alfaro-Martínez, P. Asensio Villahoz, M. D. Ballesteros Pomar, R. Burgos Peláez, C. Gallego Díaz,
T. Martín Folgueras, V. Pulgar Perera, C. Velasco Gimeno, A. Zugasti Murillo, Á. L. Abad-González, J. Álvarez Hernández;
on behalf of the Sociedad Española de Nutrición Clínica y Metabolismo (SENPE), Sociedad Española
de Endocrinología y Nutrición (SEEN) and Sociedad Española de Documentación Médica (SEDOM) 1307

Letters to the Editor

- The importance of social determinants in the detection of depressive symptoms and their relationship
with tap water consumption
D. García Martínez, I. Morona Mínguez, D. Gómez Rocha, Á. Pousada Fonseca 1315
- Omega-3 and preterm birth: deciphering the pieces of the puzzle for its prevention
I. G. Martínez Velasco, M. A. Guillén Román, R. Jiménez López, O. Arciniega Mancilla 1317
- The necessary and complex biopsychosocial view of food
C. Troncoso-Pantoja 1319
- Relationship between fermented dairy consumption, gut microbiota and type 2 diabetes
S. V. Flores, Á. Roco-Videla 1321
- About obesity in Mexican children
N. Cipatli Ayuzo del Valle, P. Pérez Treviño, R. M. Murillo Torres, A. Heredia Luna, L. A. Ojeda Robledo 1322

Book Review

- Nutrition Teatrise (4th edition)
A. Gil Hernández 1324



Actualización del consenso de codificación hospitalaria según los criterios GLIM: un enfoque adaptado a la complejidad hospitalaria

Update on the consensus for hospital coding according to GLIM criteria: an approach adapted to hospital complexity

En los últimos años, la identificación y codificación precisa de la desnutrición hospitalaria ha cobrado una importancia creciente, no solo por sus implicaciones clínicas, sino también por su impacto en la gestión hospitalaria y en la optimización de los recursos. El reciente consenso elaborado por las sociedades SENPE, SEDOM y SEEN, basado en los criterios GLIM (*Global Leadership Initiative on Malnutrition*), publicado en este número de la revista *Nutrición Hospitalaria*, representa un avance significativo para mejorar la codificación en los hospitales, adaptando los diagnósticos a la realidad actual de los sistemas sanitarios de países desarrollados (1).

Los criterios GLIM proponen un enfoque sistemático para el diagnóstico de la desnutrición hospitalaria, basándose en criterios fenotípicos (como la pérdida de peso, el índice de masa corporal y la reducción de masa muscular) y etiológicos (como la ingesta reducida, la malabsorción y la presencia de inflamación) (2), lo que facilita un registro más acorde con la realidad clínica y asistencial. El consenso de 2019 destacó la importancia de estos criterios para estandarizar la evaluación de la desnutrición en diversos contextos clínicos (2).

La correcta codificación de la desnutrición tiene repercusiones directas en los sistemas de gestión hospitalaria, especialmente en la asignación de grupos relacionados con el diagnóstico (GRD) y el cálculo de los costes asociados. Estudios recientes han demostrado que la falta de codificación adecuada de la DRE puede llevar a una infraestimación de la complejidad del paciente, afectando negativamente a la financiación basada en GRD (3,4). Un ejemplo ilustrativo es un estudio realizado en pacientes oncológicos, donde la correcta codificación de la desnutrición permitiría un aumento significativo en el reembolso hospitalario (4).

Si bien la implementación de los criterios GLIM ha supuesto un avance en la codificación de la DRE, persiste un desafío importante: la rigidez de los actuales códigos de la Clasificación Internacional de Enfermedades (CIE). Los códigos vigentes se enfocan en gran medida en escenarios de desnutrición propios de contextos de hambrunas y pobreza extrema, con una perspectiva más orientada a los problemas de salud pública en países en vías de desarrollo. Sin embargo, esta visión resulta inadecuada y obsoleta cuando se aplica a la realidad de los hospitales en entornos desarrollados, donde la desnutrición hospitalaria presenta características muy distintas (3,5).

En los hospitales de alta complejidad, la DRE no es una mera consecuencia de la falta de acceso a alimentos, sino una condición multifactorial frecuentemente vinculada con la presencia de inflamación aguda o crónica, disminución de la ingesta alimentaria, malabsorción o un aumento en los requerimientos metabólicos debido a la enfermedad subyacente (5). Esta complejidad no se refleja adecuadamente en los códigos CIE actuales, que continúan enfocándose en diagnósticos genéricos que no capturan la verdadera naturaleza de la DRE en el entorno hospitalario.

editorial

Es urgente que los sistemas de codificación internacional evolucionen para integrar diagnósticos que consideren la complejidad clínica de la DRE en contextos hospitalarios, permitiendo registrar no solo la desnutrición por déficit calórico o proteico, sino también las situaciones más frecuentes en nuestros hospitales, como la desnutrición secundaria a estados inflamatorios severos o a enfermedades crónicas reagudizadas (3,6).

La actualización del consenso de codificación basado en los criterios GLIM representa un paso adelante en la optimización de los sistemas de información hospitalaria y en la mejora de la eficiencia en la gestión clínica. Sin embargo, sigue siendo imprescindible una adaptación contextualizada de los códigos de la Clasificación Internacional de Enfermedades que permita reflejar mejor la complejidad.

Conflicto de intereses: los autores declaran no tener conflicto de interés.

Inteligencia artificial: los autores declaran no haber usado inteligencia artificial (IA) ni ninguna herramienta que use IA para la redacción del artículo.

Gabriel Olveira

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Trabajo Original

Paciente crítico

Healthcare resource utilization among critically-ill COVID-19 survivors – Results from the NUTRICOVID study

Uso de recursos sanitarios en pacientes críticos supervivientes de la COVID-19: resultados del estudio NUTRICOVID

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Abstract

Background: critically ill patients admitted to the intensive care unit (ICU) are often associated with malnutrition and nutrition therapy is recommended. Previous studies on COVID-19 focused on the recovery of critically ill patients after hospital discharge; however, there are limited data on healthcare resource utilization (HRU) after discharge.

Aims: to describe and analyze the HRU and nutritional status of COVID-19 patients during hospitalization and one year after discharge.

Methods: during hospitalization and 12-month follow-up after discharge, we collected data on hospital and ICU length of stay, ventilatory support therapies, medical nutrition therapy, and outpatient visits. Factors contributing to outpatient visits and readmissions during the follow-up period were also analyzed.

Results: a total of 199 patients were included, with a median hospital and ICU length of stay of 53.0 and 23.5 days, respectively. During hospitalization, 86.4 % of the patients needed invasive ventilation and 51.5 % non-invasive ventilation; 50.3 % of the patients required parenteral nutrition, while 84.3 % required enteral nutrition and 66.0 % oral nutritional supplements. After discharge a mean number of visits per patient to general practitioner, specialized care, and emergency department of 4.5, 14.7, and 0.8, respectively, were registered, most of them directly or possibly related to COVID-19. Additionally, a better health-related quality of life (HRQoL) at discharge and lower weight loss during hospitalization were associated with lower HRU during follow-up.

Conclusions: our study shows a high HRU among patients with COVID-19 admitted to ICU in the year following discharge and highlights the importance of the nutrition status during admission and its relation to HRU.

Keywords:

Coronavirus disease (COVID-19). Intensive care. Nutritional therapy. Malnutrition. Healthcare resource utilization.

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Resumen

Introducción: los pacientes críticos ingresados en la unidad de cuidados intensivos (UCI) suelen presentar desnutrición, siendo recomendable la terapia nutricional. Estudios previos sobre la COVID-19 se centraron en la recuperación de los pacientes críticos tras el alta hospitalaria; sin embargo, existen pocos datos sobre el uso de recursos sanitarios (URS) tras el alta.

Objetivos: describir y analizar el URS y el estado nutricional de pacientes con COVID-19 durante la hospitalización y un año después del alta.

Métodos: durante la hospitalización y el seguimiento de 12 meses se recogieron la duración de la estancia hospitalaria y, en la UCI, las terapias de soporte ventilatorio, la terapia médica nutricional y las visitas ambulatorias. Se analizaron los factores que contribuyeron a las visitas ambulatorias y a los reingresos durante el período de seguimiento.

Resultados: se incluyeron 199 pacientes, con una mediana de estancia hospitalaria y en UCI de 53,0 y 23,5 días, respectivamente. Durante la hospitalización, el 86,4 % de los pacientes necesitó ventilación invasiva y el 51,5 % ventilación no invasiva; el 50,3 % precisó nutrición parenteral, mientras que el 84,3 % nutrición enteral y el 66,0 % suplementos nutricionales orales. Tras el alta se registró una media de visitas por paciente al médico general, la atención especializada y urgencias de 4,5, 14,7 y 0,8, respectivamente, la mayoría relacionadas directa o posiblemente con la COVID-19. Una mejor calidad de vida relacionada con la salud (CVRS) en el momento del alta y una menor pérdida de peso durante la hospitalización se asociaron a menor URS durante el seguimiento.

Conclusiones: nuestro estudio muestra un elevado URS entre los pacientes con COVID-19 ingresados en UCI en el año siguiente al alta y destaca la importancia del estado nutricional durante el ingreso y su relación con el URS.

Palabras clave:

Enfermedad por coronavirus (COVID-19).
Cuidados intensivos.
Terapia nutricional.
Desnutrición. Uso de recursos sanitarios.

INTRODUCTION

The coronavirus disease-19 (COVID-19) was caused by the emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus (1). March 2020 represents a hallmark as the World Health Organization declared the outbreak as a pandemic (1,2). At that time, SARS-CoV-2 spread rapidly and, together with the lack of knowledge about the incipient disease, specific treatments and vaccines, led to a large number of patients admitted to the hospital or the intensive care unit (ICU) (3), which overloaded the healthcare system.

Patients with critical illness are often admitted to the ICU and associated with malnutrition (4). In fact, the prevalence of malnutrition in the ICU can be up to 78 % (5). In these patients, loss of muscle mass, a known indicator of malnutrition, is frequently observed (4). In this context, the guidelines recommend implementing a nutritional intervention within 24-48 hours of ICU admission in critically ill COVID-19 patients (6-8), as previous studies have shown that the prevalence of malnutrition in critically ill COVID-19 patients admitted to an ICU was 18-60 % (9,10), and that approximately 40 % of them had reduced muscle mass (11).

Additionally, during ICU stay patients often require mechanical ventilation; throughout the duration of mechanical ventilation, patients may receive inadequate protein and energy levels and some still present malnutrition to some extent after ICU discharge (4).

Previous studies have reported a median length of stay in the ICU of 8-12 days (12-14). Such values might lead to a rapid reduction of ICU capacity and resources (12), and are associated with increased medical costs (15). In this context, studies on other pathologies revealed that malnutrition is associated with longer hospital lengths of stay and increased risk of readmission and costs (16,17).

Most of the studies on COVID-19 focus on patient recovery after hospital discharge and describe persistent symptoms (18). However, data on healthcare resource utilization (HRU) after hospital discharge and on factors that may increase HRU are scarce.

The aim of this work was to describe HRU, including nutritional treatment, in the NUTRICOVID study cohort during hospitalization and at one year after hospital discharge, and to analyze the sociodemographic and clinical factors that may lead to high HRU.

METHODS

STUDY DESIGN AND PATIENTS

Details of the NUTRICOVID study design and population have been published previously (19). Briefly, this multicentric, observational, ambispective cohort study was carried out in adult (≥ 18 years old) patients with confirmed COVID-19 and admitted to an ICU from March 1st to June 30th, 2020. Patients were followed up for 12 months after hospital discharge.

The study protocol was approved by the Ethics Committee of Hospital Clínico San Carlos (Madrid, Spain), and was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. A written informed consent was obtained from all patients.

DATA COLLECTION

Eligible patients were invited to participate voluntarily in the study after discharge from hospital. Sociodemographic characteristics, patient nutritional status, patient use of healthcare resources, medical nutrition therapy (MNT) received, duration of MNT, functional status, and health-related quality of life (HRQoL) were collected. Full details have been previously published (19).

Healthcare resource utilization

Data on HRU during hospitalization and for a 12-month period post-discharge were retrospectively collected from electronic medical records.

The following variables were collected: hospital and ICU length of stay, ventilatory support therapies (including invasive or non-invasive ventilation) and tracheostomy, MNT during hospitalization (use of oral nutritional supplements [ONS], enteral or parenteral nutrition [EN or PN]) and MNT prescribed after discharge and in readmissions, number of outpatient

(visit date, service [general practitioner (GP), specialist]) and emergency department (ED) visits, and number and length of readmissions were recorded. The researchers consulted the patients' health records to establish the motive for each consultation and determined whether it was directly or possibly related to COVID-19, or the motive was not determined. Mean number of visits per patient and visit frequency according to each motive were estimated.

STATISTICAL ANALYSIS

Measures of centrality and dispersion (mean, standard deviation [SD], interquartile range [IQR], minimum, and maximum) for quantitative variables, and absolute and relative frequencies for qualitative variables were estimated for the study outcomes.

A regression was performed using a generalized linear model in order to assess the factors that contributed to the number of outpatient visits during the follow-up period. The following, previously published (20) characteristics of the patients at hospital discharge were used as explanatory variables (factors): age, sex, risk of malnutrition, risk of sarcopenia, level of dependency, EQ-VAS score (EuroQoL-Visual Analogue Scale), EuroQoL-5D dimensions (mobility issues, personal care, daily activities, discomfort/pain, anxiety/depression), utility value, and weight loss during hospitalization. To determine factors that contributed to readmissions a logistic regression was performed using the same variables. In both models a multivariate analysis using the stepwise method (21) was carried out.

All statistical analyses were performed using the software STATA v.14 (Stata Corp. College Station, TX, USA). The level of statistical significance was set at $p = 0.05$.

RESULTS

HOSPITALIZATION AND VENTILATORY SUPPORT THERAPIES

A total of 199 patients were included in the study. Of these, 188 (94.5 %) patients were followed-up throughout the study. Of the remaining eleven patients, six were lost to follow-up after three months and did not complete the study, and in five cases the patients had to be withdrawn from the study because they had not complied with any of the established procedures. Mean (SD) age of the patients completed was 60.7 (10.1) and most of them were men ($n = 140, 70.4 \%$).

The median (IQR) hospital length of stay was 53.0 (27.0-85.0) days, while the median (IQR) ICU length of stay was 23.5 (11.0-43.0) days.

During hospitalization, 172 (86.4 %) patients needed invasive ventilation, while 101 (51.5 %) needed non-invasive ventilation. In addition, 106 (53.5 %) patients underwent a tracheostomy (Table I).

Table I. Support therapies requirement for the included patients during hospitalization

Support therapies	Hospitalization
<i>Invasive ventilation, n (%)</i>	
Yes	172 (86.4)
No	16 (8.0)
Unknown	11 (5.5)
Missing data	0
<i>Non-invasive ventilation, n (%)</i>	
Yes	101 (51.5)
No	82 (41.8)
Unknown	13 (6.6)
Missing data	3 (1.5)
<i>Tracheostomy, n (%)</i>	
Yes	106 (53.5)
No	87 (43.9)
Unknown	5 (2.5)
Missing data	1 (0.5)

NUTRITIONAL SUPPORT

Most of the patients required some kind of MNT during hospitalization ($n = 177; 94.1 \%$). A total of 100 (50.3 %) patients required PN, with a mean (SD) duration of 15.8 (14.0) days, with values ranging from 1.0 to 97.0 days. In addition, 166 (84.3 %) patients required EN during a mean (SD) of 25.6 (23.9) days (ranging from 1.0 to 123.0 days), while 130 (66.0 %) patients needed ONS during a mean (SD) of 22.0 (21.4) days (ranging from 2.0 to 118.0 days) (Table II).

At hospital discharge, only two patients (1.0 %) required EN (Table II). The mean (SD) duration of EN after discharge was 62.5 (38.9) days, ranging from 35.0 to 90.0 days. As of the 3-month visit, no patient required EN.

Additionally, 69 patients (34.7 %) still required ONS after discharge, with a mean (SD) duration of 85.6 (41.1) days and values ranging from 6.0 to 180.0 days. The number of patients requiring ONS decreased with follow-up time. In fact, at the 12-month visit only 12 patients (6.4 %) still continued treatment with ONS.

CONSULTATION VISITS AFTER DISCHARGE

Data regarding resource utilization from 198 patients was collected during the following 12 months after hospital discharge.

General practitioner visits

A total of 889 visits to GP during the 12-month period after discharge were registered. Of these, 529 (59.5 %) were related to COVID-19, 107 (12.0 %) were not directly related, and for 253 (28.5 %) the relation to COVID-19 was unknown.

Table II. Medical nutrition therapy requirement by the included patients during hospitalization and after discharge

Medical nutrition therapy	Hospitalization	After discharge
<i>Parenteral nutrition, n (%)</i>		
Yes	100 (50.3)	0
No	94 (47.2)	199 (100)
Unknown	5 (2.5)	0
Missing data	0	0
<i>Enteral nutrition, n (%)</i>		
Yes	166 (84.3)	2 (1.0)
No	28 (14.2)	197 (99.0)
Unknown	3 (1.5)	0
Missing data	0	0
<i>Oral nutritional supplements, n (%)</i>		
Yes	130 (66.0)	69 (34.7)
No	61 (31.0)	127 (63.8)
Unknown	6 (3.0)	3 (1.5)
Missing data	2 (1.0)	0

The mean (SD) number of total visits to GP per patient was 4.5 (4.7), with values ranging from 0 to 24 visits. Of these, a mean (SD) of 2.7 (3.7) visits were directly or possibly related to COVID-19.

Specialized care visits

Of the total 2906 visits to specialized care registered during the follow-up period, 2312 (79.6 %) were related to COVID-19,

while 414 (14.0 %) were not related. Only 180 (6.2 %) of these visits were of unknown relation to the disease. Data on medical specialties could only be registered for 945 visits. Of these, most of the visits were in Pneumology ($n = 142, 15.0 \%$), Physical Medicine and Rehabilitation ($n = 109, 11.5 \%$) and Endocrinology and Nutrition ($n = 80, 8.5 \%$) departments (Fig. 1).

The mean (SD) number of total visits to specialized departments per patient was 14.7 (13.0), with values ranging from 0 to 81 visits. A mean (SD) of 11.6 (11.7) visits were directly related to COVID-19.

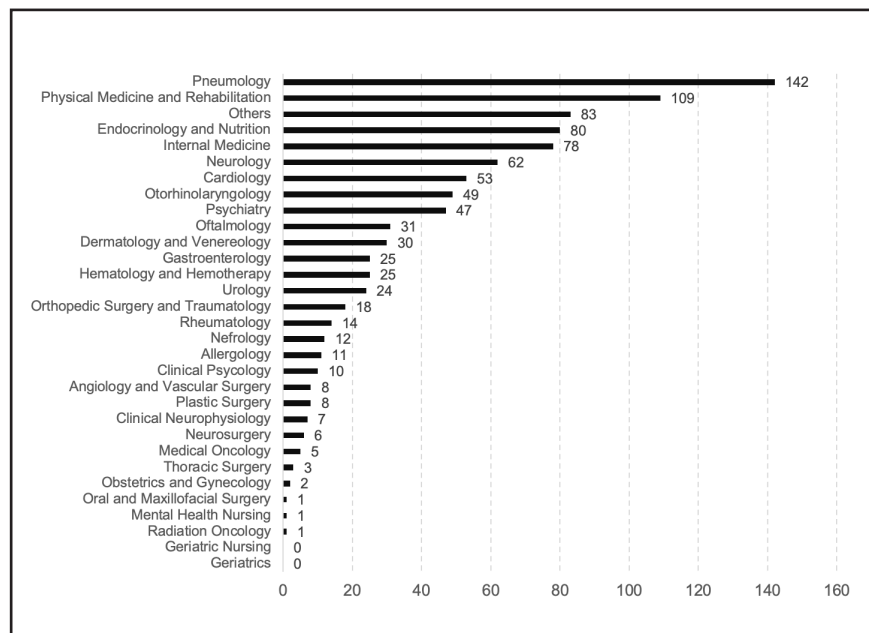


Figure 1. Number of visits registered to the different departments of specialized care ($n = 945$ visits).

Emergency department visits

One hundred and fifty visits to ED were registered. Approximately half of those ($n = 79$, 52.7 %) were related to COVID-19, while 15 (10.0 %) were not related to the disease. A high number of visits ($n = 56$, 37.3 %) did not provide information regarding their relation to COVID-19. Of the total visits to ED, only 19 (12.7 %) required further hospitalization.

The mean (SD) number of total visits to ED per patient was 0.8 (1.3), with values ranging from 0 to 8 visits. Of these, a mean (SD) of 0.4 (0.9) visits were related to the disease.

HOSPITAL READMISSIONS

A mean (SD) of 0.2 (0.5) hospital readmission per patient was registered, with readmission values ranging from 0 to 2.

During the 12-month follow-up period 33 (16.7 %) patients were readmitted corresponding to a total of 38 registered readmissions. Of these, invasive and non-invasive ventilation was required in one (2.6 %) and two occasions (5.3 %), respectively. Moreover, ONS was required in eight (21.1 %) readmissions, while parenteral nutrition was required in only one (2.6 %) occasion.

FACTORS ASSOCIATED WITH CONSULTATIONS

Finally, we evaluated which factors (20) could be involved in more frequent consultations during the 12-month follow-up period after discharge. The analysis revealed that patients with self-care issues, anxiety, and problems with daily activities according to EuroQoL-5D questionnaire at discharge were significantly associated with a higher number of total visits (GP, specialized care, and ED) during 12 months after discharge compared with those patients with no reported issues in neither of these domains (Table III). In addition, a better HRQoL (higher score in the EQ-VAS) and a lower weight loss during hospitalization were significantly associated with a lower number of total visits during follow-up (Table III).

Regarding hospital readmission, the analysis showed that neither of these factors was significantly associated with a higher probability of readmission.

DISCUSSION

Our study evaluated the use of nutritional treatment and HRU in COVID-19 patients admitted to the ICU during the first wave of the pandemic and in the 12-month period after hospital discharge.

Patients included in the study were hospitalized for a median of 53.0 days. For those who were admitted to the ICU, a median length of stay of 23.5 days was registered.

The length of hospitalization observed in the NUTRICOVID cohort, although high, was similar to that reported previously. However, the length of ICU stay observed in our cohort was higher than those reported during the first wave in other populations. A systematic review of studies (most of them carried out in China) reporting COVID-19 length of hospital stay showed a median of hospital and ICU stay ranging from 4 to 53 days and 5 to 19 days, respectively (14). In a cohort of patients admitted to ICU in a region of Italy the reported median ICU length of stay ranged from 5 to 13 days (13), while the estimated mean of ICU stay in England reported by Shryane and colleagues was over 16 days (12). These observed differences could be explained as during the first wave Madrid was severely hit by the SARS-CoV-2, being the most affected city in Spain. Indeed, it was reported to have one of the highest COVID-19 mortality in Europe (22).

During hospitalization, 172 (86.4 %) patients needed invasive ventilation, while 101 (51.5 %) needed non-invasive ventilation. In addition, 106 (53.5 %) patients underwent a tracheostomy. Grasselli and colleagues reported similar data regarding patients requiring invasive ventilation (88 %) (13). However, the percentage of patients requiring invasive ventilation in our cohort and Grasselli's was higher than that reported in ICU populations from the United States and China (30 %-71 %) (23-26). Data on the use of non-invasive ventilation is heterogeneous; the NUTRICOVID cohort showed a higher proportion of patients who required non-invasive ventilation compared with some of these populations (11 %-42 %) (13,23,24), while it was lower than in others (56 % and 62 %) (25,26).

Previous studies have reported that nutritional risk is highly prevalent in patients with COVID-19 (27). Moreover, a worse nutritional status of patients admitted to the ICU leads to an elevated weight loss and longer stays (27,28), which results in higher HRU. Additionally, at discharge, these patients report malnutrition,

Table III. Factors significantly associated with the number of visits

Factors	Coefficient	SD	p-value
Self-care issues	2.19	0.82	< 0.01
Anxiety/Depression	1.88	0.73	0.01
Daily activities	2.9	0.90	< 0.01
EQ-VAS score	-0.06	0.02	< 0.01
Weight loss during hospitalization	-0.09	0.04	0.023

EQ-VAS: EuroQoL Visual Analogue Scale; SD: standard deviation.

loss of functionality for daily activities and show a poor HRQoL (20). Thus, clinicians should consider the risks of malnutrition in patients in the ICU, with focus on those with a longer stay (28,29). Given the importance of ICU occupancy, attention should be paid the nutrition therapy as a proper nutritional status could reduce length of stay. Furthermore, this would impact positively on patient's HRQoL and HRU after hospital discharge.

A further analysis revealed that some factors were significantly associated with the number of visits, and therefore, with HRU. In this regard, we have published that almost all patients had lost weight at discharge compared with their weight at hospital admission (20). However, patients showing a lower weight loss and a better HRQoL during hospitalization were less likely to need further consultations during the 12-months period after discharge. This highlights the importance of the nutritional status during ICU stay and at discharge and its relation to HRU.

One year after discharge, HRU associated to COVID-19 was still high; of the total registered visits to GP, specialized care, and ED, 59.5 %, 79.6 % and 53.7 %, respectively, were directly related to the disease, and 16.7 % of the patients were readmitted.

Our data on readmission were similar to those previously published on COVID survivors one year after discharge (30). This population showed the same proportion of patients readmitted after two years of follow-up (31).

Even though in our cohort most of the patients required nutritional support during hospitalization, including PN, EN, and ONS, the proportion of patients requiring MNT drastically reduced after discharge. In this regard, our results are consistent with those previously observed in patients with COVID-19 (29) and in popu-

lations with other conditions admitted to the ICU (32). In addition, it has been reported that patients who required intubation during ICU stay showed lower appetite and swallowing difficulties (4), which could explain the need for MNT after discharge.

Our study has several strengths and limitations. The main strength was the period of follow-up after discharge, which is long enough to draw conclusions and is higher than length showed in other studies. Even though our study sample is smaller compared with other studies, 16 different hospitals participated in study. Thereby, we believe our cohort is representative of the most populated city in the country. However, the study has some limitations. Due to the pandemic situation and the consequent healthcare system saturation, a prospective follow-up could not be carried out and part of the data were retrospectively collected through electronic medical records. Nevertheless, information was precisely registered and there was little loss of data for the main variables. Finally, some data regarding visits to specialized care could not be collected and the relation of the visit to COVID-19 was established based on doctor's appreciation, not following specific diagnostic tools due to overload and saturation of the different departments caused by the pandemic.

CONCLUSION

In conclusion, HRU is high among patients with COVID-19 admitted to ICU even one year after discharge. Special attention should be paid to patients' nutritional status as it directly affects HRU after discharge.

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Trabajo Original

Paciente crítico

Associations of body mass index and oxygen saturation with chronic obstructive pulmonary disease grade in patients

Asociación del índice de masa corporal y la saturación de oxígeno con el grado de enfermedad pulmonar obstructiva crónica en los pacientes

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Abstract

Introduction: we aimed to investigate the associations of body mass index (BMI) and oxygen saturation with chronic obstructive pulmonary disease (COPD) grade in COPD patients.

Materials and methods: the clinical data of 105 COPD patients admitted to and treated in our hospital during January 2021 and January 2022 were acquired for a retrospective analysis, and grade 1 group [$n = 15$, subjects presenting forced expiratory volume in one second (FEV1) $\geq 80\%$ of the predicted value], grade 2 group ($n = 32$, those with FEV1 $\geq 50\%$ and $< 80\%$ of the predicted value), grade 3 group ($n = 34$, those with FEV1 $\geq 30\%$ and $< 50\%$ of the predicted value), and grade 4 group ($n = 24$, those with FEV1 $< 30\%$ of the predicted value or with FEV1 $< 50\%$ of the predicted value and concomitant respiratory failure) were set up based on COPD grade.

Results and conclusion: the BMI of the 105 patients was 20.39 ± 3.31 kg/m² on average, and it showed differences of statistical significance regarding the subjects with varying COPD grades ($p < 0.05$). The oxygen saturation was 89.98 ± 4.04 on average in the 105 patients, and it also displayed statistically significant differences among patients with different grades of COPD ($p < 0.05$). According to pairwise comparison, grade 1 group exhibited the highest oxygen saturation, followed by grade 2, 3, and 4 groups in turn ($p < 0.05$). Both BMI and oxygen saturation had negative correlations with COPD grade ($p < 0.05$). In COPD patients, COPD grade is negatively correlated with BMI and oxygen saturation.

Keywords:

Chronic obstructive pulmonary disease. Body mass index. Grade. Oxygen saturation.

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Resumen

Introducción: nuestro objetivo fue investigar las asociaciones del índice de masa corporal (IMC) y la saturación de oxígeno con el grado de enfermedad pulmonar obstructiva crónica EPOC en pacientes con EPOC.

Materiales y métodos: se recogieron para un análisis retrospectivo los datos clínicos de 105 pacientes con EPOC ingresados y tratados en nuestro hospital durante los meses de enero de 2021 y enero de 2022, grupo grado 1 [$n = 15$, sujetos con volumen espiratorio forzado en un segundo (FEV1) $\geq 80\%$ del valor previsto], grupo grado 2 ($n = 32$, aquellos con FEV1 $\geq 50\%$ y $< 80\%$ del valor previsto), grupo grado 3 ($n = 34$, aquellos con FEV1 $\geq 30\%$ y $< 50\%$ del valor previsto) y grupo grado 4 ($n = 24$, aquellos con FEV1 $< 30\%$ del valor predicho o con FEV1 $< 50\%$ del valor predicho e insuficiencia respiratoria concomitante) se configuraron en función del grado de EPOC.

Resultados y conclusión: el IMC de los 105 pacientes fue $20,39 \pm 3,31$ kg/m² en promedio, y mostró diferencias de significación estadística con respecto a los sujetos con grados variables de EPOC ($p < 0,05$). La saturación de oxígeno fue $89,98 \pm 4,04$ de media en los 105 pacientes y también mostró diferencias estadísticamente significativas entre los pacientes con diferentes grados de EPOC ($p < 0,05$). De acuerdo con la comparación de pares, el grupo de grado 1 presentó la mayor saturación de oxígeno, seguido por los grupos de grado 2, 3 y 4 a su vez ($p < 0,05$). Tanto el índice de masa corporal como la saturación de oxígeno tuvieron correlaciones negativas con el grado de EPOC ($p < 0,05$). En pacientes con EPOC, el grado de EPOC está negativamente correlacionado con el índice de masa corporal y la saturación de oxígeno.

Palabras clave:

Enfermedad pulmonar obstructiva crónica. Índice de masa corporal. Grado. Saturación de oxígeno.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) refers to a preventable and remediable morbid state, with the feature of airway limitation, which, however, cannot be completely reversed. Usually, airway limitation is progressive and has an association with the aberrant inflammatory reactions in the lungs to toxic particles or gases, which is mainly attributed to smoking. COPD acts as the primary cause of morbidity and disability in the world. The mortality rate and prevalence rate of COPD rose by nearly 11 % and 44 %, respectively, from 1990 to 2015 (1). COPD manifests pulmonary elastic recoil loss and/or airway stenosis-induced airway limitation (2). COPD not only has an effect upon pulmonary function but also leads to malnutrition, weight loss, peripheral muscle dysfunction and other severe systemic consequences (3). Such severe systemic consequences are also considered as important clinical characteristics of COPD since they have been found to easily result in exercise intolerance, decreased health status and increased mortality rate along with the deepening of the research on COPD (4). Besides, with pulmonary function deterioration plus disease progression, the risks of alveolar hypoxia and hypoxemia induced therefrom are on the rise. COPD subjects with oxygen saturation levels below 90 % are more likely to suffer from severe dyspnea, impaired quality of life, raised risks of cardiovascular disease and death, and decreased exercise tolerance (5,6). In COPD patients, the low body weight shows a relation to increased mortality rate, and it is independent of pulmonary function (7).

In the present study, the correlations of oxygen saturation and body mass index (BMI) with COPD severity were determined. The correlations between COPD grade and the two indicators can serve as a supplementary index for the disease severity, conducive to the cognition and management of COPD.

METHODS

GENERAL DATA

Totally 105 COPD sufferers, who were hospitalized for treatment from January 2021 to January 2022 were enrolled for retrospective analysis of clinical data. The inclusion criteria in-

cluded: 1) patients meeting the clinical diagnostic criteria for COPD (8); 2) those with an age of ≥ 18 years old, and 3) those possessing completely recorded clinical data. The exclusion criteria included 1) patients with acute COPD exacerbation within 4 weeks before enrollment; 2) those undergoing oral steroid therapy or home oxygen therapy, or 3) those suffering active pulmonary tuberculosis, heart failure or malignant tumor. The 105 COPD patients were assigned to grade 1 group [$n = 15$, patients whose forced expiratory volume in one second (FEV1) was more than or equal to 80 % of the predicted value], grade 2 group ($n = 32$, patients whose FEV1 was more than or equal to 50 % and less than 80 % of the predicted value), grade 3 group ($n = 34$, patients whose FEV1 was more than or equal to 30 % and less than 50 % of the predicted value), and grade 4 group ($n = 24$, patients whose FEV1 was more than or equal to 30 % of the predicted value or those with FEV1 below 50 % of the predicted value and suffered from respiratory failure) based on COPD grade. The present study was implemented as per the Declaration of Helsinki.

MEASUREMENT OF BMI

The body weight and height of patients were measured by a specially assigned person using 813 digital weight scale (Seca, Germany) and 217 portable stadiometer (Seca, Germany) at admission, and then BMI was obtained from the formula as follows: BMI = body weight / height² (kg/m²).

OXYGEN SATURATION

The oxygen saturation of patients was measured by a fingertip pulse oximeter (MD300C, Beijing Choice Electronic Tech Co., Ltd., China) after patients did not inhale oxygen for 30 min.

STATISTICAL ANALYSIS

The SPSS 23.0 software was adopted for data analysis. The continuous variables such as age, BMI and oxygen saturation

were expressed by mean \pm standard deviation ($x \pm s$) and subjected to normality test and homogeneity test for variance. The t -test and analysis of variance were adopted to assess the significant differences in the aforementioned variables among groups. The classified variables including gender, education level, occupation and marital status were expressed as percentage [n (%)], and their significant differences among groups were evaluated by the chi-square test. Pearson's correlation analysis was employed to probe into the correlations involving COPD grade, BMI and oxygen saturation. The difference of statistical significance was denoted with $p < 0.05$.

RESULTS

BASELINE DATA

Among the 105 COPD patients enrolled in the present study, 75 were males and 30 were females, with an age of 47-80 years and 62.36 ± 6.54 years on average. As to the education level, 55 cases of primary school or below, 36 cases of junior high school, and 14 cases of senior high school or above were recorded. In terms of occupation, there were 21, 61 and 23 cases of light, moderate and heavy work, respectively. For marital status, 92 patients were married, 11 patients were widowed, 1 patient was unmarried, and 1 patient was divorced. No statistically significant differences were found in age and gender distribution among grade 1, 2, 3 and 4 groups ($p > 0.05$) (Table I).

BMI OF SUBJECTS PRESENTING DIVERSE COPD GRADES

The mean BMI of the 105 patients was 20.39 ± 3.31 kg/m². For the patients with varied COPD grades, the BMI was statistically significantly different ($p < 0.05$). The results of pairwise comparison uncovered that the BMI was the largest in grade 1 group, followed by that in grade 2, 3, and 4 groups in turn ($p < 0.05$) (Table II).

OXYGEN SATURATION IN PATIENTS DISPLAYING DIVERSIFIED COPD GRADES

The average oxygen saturation was 89.98 ± 4.04 in the 105 patients. The difference in oxygen saturation among patients with varying COPD grades was statistically significant ($p < 0.05$). It was found by pairwise comparison that grade 1 group manifested the highest oxygen saturation, followed by grade 2, 3, and 4 groups in turn ($p < 0.05$) (Table III).

CORRELATIONS OF COPD GRADE WITH OXYGEN SATURATION PLUS BMI

The Pearson correlation analysis was performed with BMI and oxygen saturation as the dependent variables and COPD grade as the independent variable. The results revealed that both BMI and oxygen saturation were negatively correlated with COPD grade ($r = -0.617$ and -0.926 , $p < 0.001$) (Table IV).

Table I. Baseline data [n (%), ($x \pm s$)]

Group	n	Age (year)	Gender	
			Male	Female
Grade 1 group	15	61.45 ± 4.28	11 (73.33 %)	4 (26.67 %)
Grade 2 group	32	61.96 ± 4.32	22 (68.75 %)	10 (31.25 %)
Grade 3 group	34	62.78 ± 5.89	23 (67.65 %)	11 (32.35 %)
Grade 4 group	24	62.11 ± 5.69	19 (79.17 %)	5 (20.83 %)
F/χ^2		0.270	1.081	
p		0.845	0.781	

Table II. BMI in patients with different COPD grades ($x \pm s$)

Group	n	BMI (kg/m ²)
Grade 1 group	15	24.52 ± 3.37^{abc}
Grade 2 group	32	21.15 ± 2.64^{bc}
Grade 3 group	34	19.82 ± 2.68^c
Grade 4 group	24	17.61 ± 1.59
F/χ^2		23.689
p		< 0.001

^a $p < 0.05$ vs. Grade 2 group, ^b $p < 0.05$ vs. Grade 3 group, ^c $p < 0.05$ vs. Grade 4 group.

Table III. Oxygen saturation in patients with different COPD grades ($x \pm s$)

Group	n	Oxygen saturation (%)
Grade 1 group	15	95.89 \pm 1.34 ^{abc}
Grade 2 group	32	92.48 \pm 1.86 ^{bc}
Grade 3 group	34	88.71 \pm 1.47 ^c
Grade 4 group	24	84.76 \pm 1.64
F/ χ^2		181.854
p		< 0.001

^ap < 0.05 vs. grade 2 group, ^bp < 0.05 vs. grade 3 group, ^cp < 0.05 vs. grade 4 group.

Table IV. Pearson's correlation analysis of BMI and oxygen saturation with COPD grade

Variable	Correlation coefficient (r)	p
BMI vs. COPD grade	-0.617	< 0.001
Oxygen saturation vs. COPD grade	-0.926	< 0.001

DISCUSSION

As a common chronic progressive disease in the elderly, COPD displays rapidly elevated morbidity and mortality rates in recent years. In addition, COPD has a high risk of disability, severely affecting the physical and mental health as well as the quality of life of patients. Currently, there are controversies about the pathogenesis of COPD, and exploring biomarkers related to the progression of COPD is of vital significance.

In case of COPD, the inflammatory lesions are distributed in all levels of trachea in the lungs, which, however, can also lead to systemic diseases, with malnutrition and skeletal muscle dysfunction as the most common ones. Some researchers have noticed that COPD patients often experience different degrees of body weight loss, and low body weight is observed in 24 % of patients in the stable stage and 54-60 % of patients in the acute exacerbation stage (9). BMI, a crucial physiological indicator to assess the nutritional status of human body, is a neutral and reliable statistical index, which balances the interaction between height and body weight when determining overweight and underweight. The identification of different metabolic phenotypes in COPD patients is essential for assessing nutritional risk profiles. Two well-characterized phenotypes are the emphysematous "pink puffer" with a BMI and the chronic bronchitis "blue bloater" with a high BMI (10). Nutritional interventions are particularly beneficial for undernourished patients, especially when combined with exercise programs (11).

In this study, the increase in COPD severity had an association with the prominently reduced average oxygen saturation ($p < 0.01$), in line with the findings of Kumar et al. (12), that is, the mean oxygen saturation gradually declined with the increase

in COPD severity. One possible explanation for such a decline is that the ventilation/perfusion mismatch is gradually aggravated as the disease progresses (13). Another vital factor for hypoxemia in COPD patients is the change of ventilation control (14). Similarly, pulmonary function will deteriorate with the progression of the disease, which increases the risks of alveolar hypoxia and hypoxemia, resulting in decreased oxygen saturation. As COPD progresses, hypoxemia and decreased oxygen saturation serve as important manifestations since they will give rise to decreased quality of life, neurocognitive function and exercise tolerance, as well as elevated risks of aggravation along with death (15). Therefore, there is a negative correlation between COPD grade and oxygen saturation, and thus the latter can become a marker hinting COPD severity, particularly in cases that the resources are limited and pulmonary function tests are unavailable.

In the present study, the subjects having grade 4 COPD exhibited the smallest BMI, while those with grade 1 COPD displayed the largest BMI, similar to the study conclusions of Schols et al. (16), that is, weight loss occurred in about 50 % of COPD participants. Besides, research performed by Gupta et al. (17) in India denoted that the malnutrition degree dropped in grade 1 COPD sufferers compared with that in grade 4 COPD sufferers (25 % vs. 80 %). The present study yielded consistent results with previous studies. However, a study carried out by Cochrane et al. (18) reported that in 103 COPD patients in Britain, the change in COPD severity had no impact on the BMI of patients. In this study, BMI of COPD patients was found to have a negative correlation with COPD grade, and it was obviously affected by the change of the illness. This is inconsistent with the conclusion of the previous study, which may be ascribed to the disparities between the two countries in terms of dietary intake patterns besides geographical distribution. In clinical practice, nutritional management should be strengthened for severe COPD patients because low BMI may be a vital and independent risk factor for the death and attack of such patients.

It was uncovered in the present study that the BMI of subjects decreased continuously as the COPD grade rose, similar to the findings reported by Steuten et al. (19). The nutritional status of COPD patients deteriorates with the aggravation of the disease. Likewise, Montes de Oca et al. discovered that patients with a higher BMI presented lower COPD grades, and they forecast the potential role of low BMI as an indicator for mortality rate of COPD patients (20).

Moreover, many cross-sectional or cohort studies have also proved the association between COPD and low BMI. For instance, as manifested by the PLATINO study in Latin America, COPD patients were composed of higher proportions of underweight (< 20 kg/m²) and normal weight (20-24.9 kg/m²) subjects but lower proportions of overweight and obese (≥ 25 kg/m²) subjects by contrast to subjects without COPD (18). In addition, it that low BMI was reported to serve as an independent risk factor for the death of COPD patients (21), and it exhibits the strongest correlation in patients having serious COPD. Patients presenting a higher BODE (BMI [B], airflow obstruction [O], dyspnea [D] and exercise capacity [E]) score suffer a raised death risk. For every

1-point increase in BODE score, the hazard ratios of all-cause death and respiratory death are 1.34 [95 % confidence interval (95 % CI): 1.26-1.42, $p < 0.05$] and 1.62 (95 % CI: 1.48-1.77, $p < 0.05$), respectively (22).

Malnutrition in COPD patients, reflected in an BMI indicating underweight, has a relationship with the imbalance between energy intake and energy consumption. Food intake is reduced in COPD patients since they have such symptoms as dyspnea, early satiety, fatigue, and loss of appetite after meals (23). Besides, energy consumption increases because of enhanced work of breathing, systemic inflammation, as well as thermogenic action of bronchodilators. Additionally, the weight loss of COPD patients is also possibly attributed to the role of corticosteroids in negatively affecting skeletal muscle function. From the microscopic perspective, the increased COPD severity has a relation to muscle fiber atrophy, muscle fiber change and mitochondrial function loss (24). Based on the aforementioned results, COPD damages the cellular metabolic function, thereby inducing weight loss that leads to a low BMI. The low BMI has a correlation with the mortality rate of COPD patients.

The progression of COPD is closely linked to a decrease in BMI, particularly in advanced stages of the disease. As COPD severity increases, patients often experience a negative energy balance due to elevated resting energy expenditure and reduced caloric intake. This imbalance is driven by the increased work of breathing, systemic inflammation, and altered nutrient metabolism. Additionally, chronic inflammation and elevated levels of pro-inflammatory cytokines, such as TNF- α and IL-6, contribute to skeletal muscle wasting and reduced appetite, exacerbating weight loss and decreasing BMI (25). The loss of muscle mass is a critical factor in the decline of BMI in COPD patients, as muscle atrophy is a direct consequence of oxidative stress, hypoxia, and impaired protein metabolism (26). Addressing these metabolic alterations through nutritional interventions and personalized treatment strategies is crucial for improving the management of COPD and mitigating the risk of severe weight loss in affected individuals (27).

The present study has some limitations. For example, the sample size was small, so the effect of a moderate sample size should be taken into account when interpreting results. Furthermore, BMI may fail to function as an ideal tool for body weight measurement of all COPD subjects given that some COPD patients may suffer from edema due to pulmonary arterial hypertension, so the results of these patients should be discreetly interpreted.

In conclusion, in COPD patients, the disease grade is negatively correlated with BMI plus oxygen saturation, i.e., the BMI and oxygen saturation decline with the increase in COPD grade. This finding may be conducive to the prediction of the severity of the illness in such patients, rendering some reference for clinic practice.

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Trabajo Original

Paciente crítico

Association between length of hospital stay before and after surgery and nutritional risk according to NRE-2017 – A secondary analysis of a cohort study

Asociación entre duración de la estancia hospitalaria antes y después de la cirugía y riesgo nutricional según la NRE-2017: análisis secundario de un estudio de cohortes

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Abstract

Aim: to evaluate the predictive ability of the Nutritional Risk Emergency - 2017 (NRE) to predict prolonged length of stay, ICU admission intra-mortality and readmission, severe postoperative complications.

Methods: a prospective cohort was conducted with surgical patients admitted in a public tertiary hospital. The NRE-2017 tool was applied for detecting malnutrition risk in hospitalized patients. Surgical complications were assessed by Clavien-Dindo. Patients were followed during hospitalization to identify length of stay as well as stay after surgery in the Intensive Care Unit (ICU). Regression analysis was performed to assess the association between risk of malnutrition and clinical outcomes.

Results: we included 162 elective surgery patients; 79 patients were identified with nutritional risk using the NRE-2017 (≥ 1.5) tool and 83 without nutritional risk. Patients with nutritional risk were at higher risk of prolonged hospitalization [18 (10-36) days vs. 13 (7-23) days; p : 0.006] and ICU hospitalization [6 (2-14) days vs. 3.5 (1-7) days; p : 0.020]. There was an association between surgical complications and nutritional risk independently, but the significance was lost when adjusting the analysis. There was no association with mortality and readmission in this sample of patients.

Conclusion: the NRE-2017 tool was associated with hospital stay in those patients at nutritional risk, however there was no association with mortality and readmission.

Keywords:

Nutritional risk. Nutritional screening. Mortality. Surgical patients.

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Resumen

Objetivo: evaluar la capacidad predictiva de la herramienta Emergencia de Riesgo Nutricional-2017 (NRE) para predecir la estancia prolongada, la mortalidad y el reingreso en la UCI, y las complicaciones postoperatorias graves.

Métodos: se estudió una cohorte prospectiva con pacientes quirúrgicos ingresados en un hospital público terciario. Se aplicó la herramienta NRE-2017 para la detección del riesgo de desnutrición en pacientes hospitalizados. El Clavien-Dindo evaluó las complicaciones quirúrgicas. Los pacientes fueron seguidos durante la hospitalización para identificar la duración de la estancia, así como la estancia después de la cirugía en la Unidad de Cuidados Intensivos (UCI). Se realizó un análisis de regresión para evaluar la asociación entre el riesgo de desnutrición y los resultados clínicos.

Resultados: se incluyeron 162 pacientes de cirugía electiva; se identificaron 79 pacientes con riesgo nutricional mediante la herramienta NRE-2017 ($\geq 1,5$) y 83 sin riesgo nutricional. Los pacientes con riesgo nutricional tuvieron mayor riesgo de hospitalización prolongada [18 (10-36) días vs. 13 (7-23 días); $p: 0,006$] y hospitalización en la UCI [6 (2-14 días vs. 3,5 (1-7 días); $p: 0,020$]. Hubo asociación entre complicaciones quirúrgicas y riesgo nutricional de forma independiente, pero se perdió la significancia al ajustar el análisis. No hubo asociación con la mortalidad y el reingreso en esta muestra de pacientes.

Conclusión: la herramienta NRE-2017 se asoció con la estancia hospitalaria en aquellos pacientes con riesgo nutricional; sin embargo, no hubo asociación con la mortalidad y el reingreso.

Palabras claves:

Riesgo nutricional. Cribado nutricional. Mortalidad. Pacientes quirúrgicos.

INTRODUCTION

Malnutrition in surgical patients is prevalent and represents a risk for the development of complications (1-3). In Western Europe, approximately 25 % to 30 % of preoperative surgical patients are at nutritional risk, with a consequent increase in postoperative complications, mortality, prolonged hospitalization, and higher costs (4-7). A multicenter study identified the presence of malnutrition in 55 % of surgical patients, and 19 % of patients were severely malnourished (8).

In fact, malnutrition has been associated with humoral depression, reduced cellular immune function, changes in the inflammatory response system, and delayed or failed surgical wound healing (6). Consequently, these patients have a high incidence of severe complications in the immediate postoperative period (6). Surgical procedures induce metabolic stress and, as a result, a series of trauma responses are activated by the metabolic and endocrine pathways that are the center of the body's compensatory return to surgical trauma (9). In addition, these responses mobilize energy substrates, conserve volume, homeostasis, and induce the inflammatory response (10).

Several malnutrition screening tools have been applied in hospitals, some more sophisticated and others simpler, but these have few validations in clinical results (11). Although there is no consensus on the best instrument to be applied in the elderly and surgical patients to detect malnutrition in hospitalized patients in general, the American Society for Parenteral and Enteral Nutrition (ASPEN) suggests the use of the Subjective Global Assessment (SGA). There is well-established evidence for the ability of SGA to predict survival in adult and elderly patients, with well-nourished patients having longer survival than malnourished patients (12,13). An ideal nutritional screening instrument should be easy and quick to apply, in addition to having a good performance in detecting nutritional risk (14).

In this sense, in 2017, a new easy-to-apply tool for nutritional screening was proposed and validated, the Nutritional Risk Emergency-2017 (NRE-2017), which showed good accuracy when compared to NRS-2002 in 748 patients in the emergency department (15). The NRE-2017 was performed to screen hospitalized patients and considers unintentional weight loss

in the last 6 months, reduction in food intake in the last two weeks, metabolic demand of the underlying disease, age, and loss of muscle mass (15). The NRE-2017 score of 1.5 was discriminatory in identifying the risk of malnutrition. On the other hand, considering the higher sensitivity (91.7 %) and acceptable specificity (68.5 %), a score NRE2017 1.0 was able to detect the risk of malnutrition (15).

According to the European Society of Clinical Nutrition and Metabolism (ESPEN), screening, nutritional assessment and nutritional intervention of surgical patients can prevent weight loss, as well as preserve the intestinal microbiota and improve functional performance (16).

In view of the above, the present study aimed to evaluate the relationship of the nutritional screening tool (NRE-2017) in predicting postoperative outcomes, such as prolonged hospitalization, ICU admission, postoperative complications, readmission, and death in patients undergoing elective surgeries.

MATERIALS AND METHODS

This is a secondary analysis of a prospective cohort study (17) (unpublished), conducted between July 2018 and May 2019, including patients admitted for elective surgery at a tertiary public hospital. The study protocol was approved by the Research Ethics Committee of the hospital (approval number 3,461,904) and all patients signed an informed consent form prior to data collection.

The sampling process considered the inclusion of adult patients aged 18 years or older who were hospitalized with indication for elective surgery. Among the hospitalized patients, patients with edema or amputation of the lower limbs, inability to walk or unable to respond to detailed nutritional anamnesis were excluded.

The sample size calculation was based on a study conducted by Garcia et al. (18), considering the association between nutritional risk and length of hospital stay in patients undergoing elective surgeries at a teaching hospital in southern Brazil. The length of hospital stay was evaluated among patients with medium and high nutritional risk (33.1 %) and low nutritional

risk (66.9 %), with a power of 80 % and losses and refusals of 10 %, and a sample of 162 individuals was estimated to be necessary.

The information was obtained through a secondary database from a survey conducted between 2018 and 2019 and the analysis of medical records. The variables investigated were: data from the NRE-2017 and SGA; sociodemographic (age, sex, ethnicity) and anthropometric data; clinical history; length of hospital stay; postoperative complications; and hospitalization outcome. Data collection was performed within the first 48 hours after hospital admission by a trained nutritionist and three nutrition students. A standardized form was used, filled out based on data obtained from medical records and anamnesis performed at the bedside, along with anthropometric evaluation. Clinical data regarding the reason for hospitalization and previous medical history were obtained from electronic medical records.

Nutritional risk screening was performed using the NRE-2017 tool, including six dichotomous variables (with score ranging from 0.25 to 1.0) related to advanced age, metabolic stress of the disease, decreased appetite, change in food consistency, unintentional weight loss, and loss of muscle mass. Patients were considered at nutritional risk when NRE-2017 was ≥ 1.5 points (15).

Nutritional anamnesis was performed through the Subjective Global Assessment (SGA) (19), considering the percentage of weight loss, presence of gastrointestinal symptoms and changes in food intake, functional capacity, metabolic stress of the disease and loss of muscle mass, subcutaneous fat, edema, and ascites according to physical examination. Patients were classified as well-nourished (SGA-A), moderately or suspected malnutrition (SGA-B) and severely malnourished (SGA-C) (19).

Anthropometric data included body weight and height measured on a scale with an attached Filizola® stadiometer. The patient's usual weight (6 months) was asked and used to calculate the percentage of weight loss considering the measured weight.

Postoperative complications were evaluated using the Clavien-Dindo classification, classified by grades (I, II, III-IIIa, IIIb, IV-IVa, IVb and V) in ascending order according to the severity of the complication and based on the type of treatment used to correct it (20,21). Grade I corresponds to — Any deviation from the ideal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Grade II — Requires pharmacological treatment with drugs other than those allowed for complications Grade I; blood transfusion and total parenteral nutrition are also included. Grade III — Requires surgical, endoscopic, or radiological intervention (where III a. Intervention without general anesthesia; III b. Intervention under general anaesthesia). Grade IV — Life-threatening complication (including CNS): brain hemorrhage, ischemic stroke, subarachnoid hemorrhage, but excludes transient ischemic attacks or ICU need (IV a. Single-organ dysfunction (including dialysis); IV b. Multi-organ dysfunction). Grade IV: death (20,21).

Information regarding the surgery performed, surgical size (small, medium or large) (21), the duration of the surgery, and the classification of the physical status according to the Ameri-

can Association of Anaesthesia (ASA) score (22) were collected from the patient's medical records, and were recorded by the surgical team as routine care. ASA I: normal, ASA II: mild systemic disease (e.g., hypertension, diabetes); ASA III: Severe non-disabling systemic disease; ASA IV: severe, disabling, life-threatening systemic disease; ASA V: minimum life expectancy, regardless of surgery. For data analysis, the reason for hospitalization was grouped according to medical specialty.

The outcomes investigated were length of hospital stay, postoperative intensive care unit stay, postoperative complications (Clavien-Dindo classification), in-hospital mortality, and readmission. The length of hospital stay and post-surgical ICU stay were calculated by subtracting the date of hospital discharge (or death) and the date of admission or surgery, respectively. Patients were followed up through the electronic medical record until hospital discharge for evaluation of postoperative complications, readmission, and mortality. The complications, according to Clavien-Dindo, were identified as severe (yes/no) complications.

Quantitative variables were expressed as mean and standard deviation (parametric distribution) or median and interquartile range (non-parametric distribution) and categorical variables were expressed as absolute and relative frequencies. The NRE-2017 was stratified according to nutritional risk. Comparisons between patients at and without risk of malnutrition were performed using the Student's t-test, Man-Whitney test, Chi-square/Fisher's exact test, as appropriate. Poisson regression and binary logistics were used to evaluate the association between risk of malnutrition and clinical outcomes (ICU admission, severe postoperative complications, and death) to obtain the measures of association (relative risk) and their respective 95 % confidence intervals (95 % CI). Two models of analysis were considered: unadjusted and adjusted. We considered adjustment for age, sex, presence of cancer, and ASA classification. All analyses were performed in the software SPSS version 21.0 and $p < 0.05$ values were considered statistically significant.

RESULTS

Table I shows the general characteristics of the sample. The study included 162 patients, with a mean age of 59.7 years (± 14 years) and most of whom were male — 51.9 % ($n = 84$); 74.7 % ($n = 121$) were of white ethnicity. Most patients (54.9 %, $n = 89$) had oncology as their medical specialty. Regarding surgery, 52.8 % ($n = 84$) underwent minor surgery and 60.8 % ($n = 76$) had ASA II classification (mild systemic disease). Regarding nutritional risk, 48.8 % ($n = 79$) of hospitalized patients presented nutritional risk according to NRE-2017 (≥ 1.5 points). The median length of hospital stay and ICU stay were 14 and 4 days, respectively. The frequency of complications (Clavien-Dindo) among patients was 11.1 % ($n = 18$), and the incidence of in-hospital death was 4.3 % ($n = 7$).

The relationship between clinical variables and nutritional risk is shown in table II. Patients at nutritional risk (NRE ≥ 1.5 points) ($n = 79$) were older (mean age, 65.1 vs. 54.4 years, $p < 0.001$),

mostly male (60.8 % vs. 39.2 % female). In addition, in the group with nutritional risk by NRE (NRE \geq 1.5 points) there was a higher prevalence of cancer patients ($n = 53$ [67 %]), longer hospitalization time (18 days vs. 13, $p = 0.006$), and had more days in the intensive care unit (6 vs. 3.5 days, $p: 0.020$) when compared to patients without risk for NRE.

Table I. General characteristics of the sample of hospitalized surgical patients

Variables	$n = 162$
Age (years)	59.7 \pm 14.0
Gender	
Male	84 (51.9)
Marital status	
Married/Stable union	90 (55.6)
Ethnics, n (%)	
White	121 (74.7)
NRE-2017 – n (%)	
Without risk	83 (51.2)
At risk	79 (48.8)
SGA – n (%)	
Well nourished	89 (54.9)
Moderate malnutrition	55 (34.0)
Severe malnutrition	18 (11.1)
Types of surgeries	
Oncology	89 (54.9)
Gastroenterology	29 (17.9)
Nephrology	10 (6.2)
ASA classification ($n = 125$)	
I	11 (8.8)
II	76 (60.8)
III	36 (28.8)
IVB	2 (1.6)
Surgery	
Minor surgery	84 (52.8)
Middle surgery	36 (22.6)
Major surgery	39 (24.5)
Admission in ICU	7 (4.5)
Complication after surgery	
No	144 (88.9)
Yes	18 (11.1)
LOS (days)	14 (8-26)*
LOS after surgery (days)	4 (1.5-8)*
Mortality in hospital	7 (4.3)

*Median (P25-P75). NRE: Nutritional Risk in Emergency; SGA: subjective global assessment; LOS: length of stay; ASA: American Society of Anesthesiology; ICU: intensive care unit.

The association between NRE-2017 and outcomes is shown in table III. NRE \geq 1.5, indicating nutritional risk, was an independent predictor of prolonged length of hospital stay (> 14 days) [RR: 1.60, 95 % CI (1.49-1.71), $p < 0.001$], length of stay in UTI [RR: 2.0, 95 % CI (1.80-2.27), $p < 0.001$] and complications after surgery [RR: 3.16, 95 % CI (1.07-9.31), $p: 0.037$].

After adjusting for confounding factors, NRE \geq 1.5 maintained an association with length of stay (> 14 days) and length of ICU stay (after surgery), with RR: 1.41 (95 % CI, 1.28-1.55) and RR: 1.87 (95 % CI, 1.62-2.16), respectively. In this sample of patients, there was no significant association with readmissions and mortality.

DISCUSSION

This study aimed to evaluate the association of the NRE-2017 tool in predicting clinical outcomes after elective surgery. The results pointed to a high prevalence of nutritional risk in surgical patients (48.8 %); a higher risk for cancer patients and older patients. NRE \geq 1.5, indicating nutritional risk, was associated with longer hospital stay and ICU stay (post-surgery).

It is well established in the literature that malnutrition in surgical patients is prevalent and carries a serious risk for the development of complications (1-6,17). In our sample of surgical patients, the nutritional risk according to the NRE-2017 tool (≥ 1.5 points) was 48.8 %. Like the original validation study of the tool, in which the prevalence of nutritional risk in a sample of 748 hospitalized adults was 38.8 % (95 % CI, 35.4 %-42.5 %). Similarly, a study including 601 hospitalized patients identified nutritional risk by NRE-2017 in 24 % of the sample (23).

It is recommended that individuals at risk of malnutrition be identified by validated screening tools and should be evaluated and treated according to the necessary interventions (24,25). The NRE-2017 is a recent nutritional screening tool, and most studies use the diagnosis of SGA as an exclusive tool at hospital admission (19). The impact of nutritional risk on postoperative outcomes was demonstrated in a meta-analysis that evaluated the nutritional risk and postoperative outcomes of patients undergoing abdominal surgery, and was strongly correlated with increased rates of general and infectious complications, increased mortality, and prolonged hospital stay (26). Other studies have pointed to a linear increase in mortality as nutritional risk increases (18,24).

In our study, the nutritional risk identified by the NRE-2017 tool ≥ 1.5 , was associated with longer hospital stays. Patients with NRE ≥ 1.5 remained hospitalized for 18 days (vs. 13 days in the non-risk group) and 6 days in the ICU (after surgery) (vs. 3.5 days compared to patients without nutritional risk for NRE).

Prolonged hospitalization in surgical patients may be related to the nutritional status prior to surgery, complications related to the underlying disease, postoperative complications, and the patient's age. A study with 565 surgical individuals identified that the length of hospital stay had a linear increase according to the increase in nutritional risk.

Table II. Associations between nutritional risk and clinical variables, and validity of the NRE-2017 in predicting in-hospital outcomes in a cohort of surgical patients (*n* = 162)

Variables	Without nutritional risk (<i>n</i> = 83)	With nutritional risk (≥ 1.5 points) (<i>n</i> = 79)	<i>p</i>
Age (years)	54.4 ± 13.8	65,1 ± 12,1	< 0.001
Gender, <i>n</i> (%)			
Men	36 (43.4)	48 (60.8)	0.040
Women	47 (56.6)	31 (39.2)	
Oncology, <i>n</i> (%)			0.004
Yes	36 (43.4)	53 (67.1)	
No	47 (56.6)	26 (32.9)	
ASA classification, <i>n</i> (%) (<i>n</i> = 125)			0.001
I/II	56 (83.6)	31 (53.4)	
III/IV	11 (16.4)	27 (46.6)	
Surgery, <i>n</i> (%)			0.114 0.060
Minor surgery	37 (45.7)	47 (60.3)	
Middle surgery	19 (23.5)	17 (21.8)	
Major surgery	25 (30.9)	14 (17.9)	
LOS in ICU, <i>n</i> (%)	1 (1.3)	6 (7.8)	
Complications, <i>n</i> (%)			0.063
No	78 (94.0)	66 (83.5)	
Yes	5 (6.0)	13 (16.5)	
LOS (days)	13 (7-23)	18 (10-36)	0.006
LOS > 14 days, <i>n</i> (%)	39 (43.4)	46 (55.7)	0.075
LOS after surgery in ICU (days)	3.5 (1-7)	6 (2-14)	0.020
LOS after surgery > 4 days, <i>n</i> (%)	33 (40.2)	46 (58.2)	0.034
Situation after discharge (%)			0.194
Loss	15 (18.1)	17 (21.5)	
Readmission (no)	36 (43.4)	26 (32.9)	
Readmission (yes)	23 (27.7)	19 (24.1)	
Mortality, <i>n</i> (%)	9 (10.8)	16 (20.3)	

ASA: American Association of Anaesthesia; LOS = length of stay. *Adjusted for the variables that entered the model: age, sex, oncology, ASA classification and surgical size.

Table III. Association between nutritional risk assessed by NRE-2017 and outcomes

Outcome	Variable	RR crude (95 % CI)	<i>p</i> -value	RR adjusted (95 % CI)*	<i>p</i> -value	RR adjusted (95 % CI)†	<i>p</i> -value
LOS	NRE ≥ 1.5 (NUTRITION RISK)	1.60 (1.49-1.71)	< 0.001	1.68 (1.55-1.81)	< 0.001	1.41 (1.28-1.55)	< 0.001
	NRE- without risk						
LOS ICU	NRE ≥ 1.5 (NUTRITION RISK)	2.030 (1.80-2.27)	< 0.001	2.10 (1.87-2.37)	< 0.001	1.87 (1.62-2.16)	< 0.001
	NRE- without risk						
Readmission	NRE ≥ 1.5 (NUTRITION RISK)	0.84 (0.33-2.19)	0.73	---	---	---	---
	NRE- without risk						
Mortality	NRE ≥ 1.5 (NUTRITION RISK)	0.78 (2.72-2.28)	0.66	---	---	---	---
	NRE- without risk						
Complications	NRE ≥ 1.5 (NUTRITION RISK)	3.16 (1.07-9.31)	0.037	2.85 (0.89-9.12)	0.078		
	NRE- without risk						

*Adjusted for age and gender; †Adjusted for age, gender, ASA, oncology. LOS: length of stay.

Patients at high nutritional risk remained hospitalized for four times longer than patients at low risk, reaching a median of 12 days of hospitalization, while patients at medium risk had a median hospitalization time of 6.5 days (18).

In our study, patients with NRE ≥ 1.5 had a 1.4 times higher risk of prolonged hospitalization, as well as a 1.87 times higher risk of ICU stay after surgery, when compared to patients without nutritional risk (15,24), corroborating data from the original NRE-2017 study, in which patients at risk of malnutrition had a two-fold higher relative risk of a prolonged hospital stay (15).

Older patients were associated with higher nutritional risk, corroborating other studies using different screening tools (22,25,26). Similarly, oncology was the medical specialty most associated with nutritional risk, like other previous studies that also listed cancer patients among those with higher nutritional risk, since both the disease and the treatments threaten their nutritional status (28-30). The other clinical outcomes investigated, such as severe postoperative complications, readmission, and death, were significantly higher in the group with nutritional risk by NRE-2017, but it was not associated with mortality alone, with a trend towards an increase in the risk of mortality in those with nutritional risk.

The NRE-2017 nutritional risk screening tool is simple, fast, valid, and low-cost, and can be used to identify nutritional risk in hospitalized surgical patients (15). As a positive aspect, it is easy not to require objective data for implementation, which makes it more practical in situations where the patient does not have the mobility to perform anthropometric measurements or when such information is not included in the patient's records. To confirm its applicability, further studies with surgical and non-surgical hospitalized patients are needed. It is believed that such an instrument can be a component in the routine nutritional care of hospitalized patients, because from the identification of nutritional risk, interventions such as a more detailed assessment or early nutritional therapy can be instituted to minimize the negative consequences of malnutrition. In view of this situation, identifying nutritional risk in a simple and safe way can accelerate nutritional support with the aim of improving the outcomes of surgical patients.

Among the limitations of this study, we highlight the limited sample size, which probably influenced the analysis of negative outcomes when adjusted for gender, age, oncology and ASA, and mortality in isolation. Another point was the heterogeneous sample and the loss of some variables, which may have influenced the results of the study. However, it is important to evaluate the validity of the NRE-2017 nutritional risk screening in predicting clinical outcomes in hospitalized surgical patients.

Nutritional risk is prevalent in hospitalized surgical patients evaluated with the NRE-2017 screening tool and was significantly associated with length of hospital stay (on average 5 days longer) and clinical outcomes in those patients with nutritional risk, however there was no association with mortality. Further studies are needed in different populations.

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Trabajo Original

Nutrición artificial

Gastrostomía radiológica frente a endoscópica en pacientes con esclerosis lateral amiotrófica

Radiological versus endoscopic gastrostomy in patients with amyotrophic lateral sclerosis

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Resumen

Introducción: los pacientes con esclerosis lateral amiotrófica (ELA) precisan tratamiento nutricional, en la mayoría de casos mediante nutrición enteral por gastrostomía, ya sea endoscópica (PEG) o radiológica (PRG).

Objetivos: analizar las características de los pacientes con ELA en el momento de la colocación de la PEG/PRG y comparar la eficacia y seguridad de la PRG frente a la PEG, así como su efecto sobre la supervivencia y la función respiratoria.

Métodos: estudio descriptivo retrospectivo. Se reclutan todos los pacientes con ELA que han requerido gastrostomía en los últimos 3 años (2021-2023) en nuestro hospital (4 PEG y 6 PRG). Se analizan los parámetros demográficos y nutricionales.

Resultados: se incluyeron 10 pacientes con una edad media de 57 años. Todos los pacientes presentaban disfagia y recibían suplementos orales o por sonda antes de la colocación de la gastrostomía. La duración media de la nutrición enteral fue de aproximadamente 50 meses, con una mortalidad total del 30 % a los 12 meses desde la gastrostomía. La tasa de éxito de la PEG y la PRG fue similar, sin complicaciones. Todos los pacientes desarrollaron deterioro de la función respiratoria (necesidad de VMNI/BIPAP), que disminuyó con la evolución de la enfermedad, incluso tras el tratamiento nutricional.

Conclusión: la supervivencia después de la colocación de la gastrostomía fue similar en los pacientes con inicio bulbar e inicio espinal. La edad avanzada en el momento del inicio de la enfermedad y una CVF baja se asociaron a un mayor riesgo de mortalidad a corto plazo. A pesar de que está bien establecido el beneficio a nivel nutricional de la gastrostomía, en la actualidad se evidencia una demora entre el diagnóstico y la colocación de la gastrostomía. La PRG es preferible frente a la PEG en aquellos pacientes que presentan deterioro respiratorio avanzado y en los que esta técnica es técnicamente difícil o está contraindicada, con aumento en la supervivencia y mejoría del estado respiratorio. Ambas técnicas son seguras y tienen baja mortalidad, siendo procedimientos idóneos para el tratamiento nutricional a largo plazo de los pacientes afectados de ELA. La supervivencia está ligada a la evolución de la ELA y no a la elección de la colocación de una PRG o una PEG, y debe basarse principalmente en las instalaciones y la experiencia de cada hospital.

Palabras clave:

Esclerosis lateral amiotrófica. Gastrostomía. Radiológica. Endoscópica. Nutrición.

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Abstract

Introduction: patients with amyotrophic lateral sclerosis (ALS) require nutritional support, in most cases with enteral nutrition through gastrostomy, either endoscopic (PEG) or radiological (PRG).

Objectives: to analyze the characteristics of patients with ALS at the time of PEG/PRG placement, and to compare the efficacy and safety of PRG versus PEG.

Methods: a retrospective descriptive study. All patients with ALS who required gastrostomy in the last 3 years (2021-2023) in our hospital were recruited (4 PEG and 6 PRG). Demographic and nutritional parameters were analyzed.

Results: ten patients were included, with an average age of 57 years. All patients presented with dysphagia and received oral or tube supplements prior to gastrostomy placement. The average duration of enteral nutrition was approximately 50 months, with a mortality rate of 30 % at 12 months after gastrostomy. The success rate of PEG and PRG was similar, with no complications. All patients developed deterioration of respiratory function, even after nutritional support.

Conclusion: gastrostomy should be indicated as soon as a patient is at risk of aspiration pneumonia or when weight loss begins. Although the nutritional benefit of gastrostomy is well established, there is currently a delay between diagnosis and placement of approximately 4 years. PRG appears to be safer than PEG in patients with ALS and respiratory failure.

Keywords:

Amyotrophic lateral sclerosis. Gastrostomy. Radiological. Endoscopic. Nutrition.

INTRODUCCIÓN

La “esclerosis lateral amiotrófica (ELA)” es una enfermedad neurodegenerativa que afecta a la primera motoneurona provocando debilidad y atrofia muscular generalizada, insuficiencia respiratoria y disfagia, con riesgo de desnutrición y muerte de los pacientes en pocos años.

La prevalencia de la desnutrición depende de la forma de presentación (espinal o bulbar) y del estadio de la enfermedad. Son múltiples los factores que influyen en el deterioro nutricional: disfagia por afectación de la musculatura, atrofia y pérdida muscular, alteraciones del estado de ánimo e hipermetabolismo secundario a un incremento del trabajo respiratorio (1). La desnutrición es un factor pronóstico de supervivencia, por lo que debe realizarse una evaluación precoz. Una pérdida de peso > 10 % en los últimos 6 meses o un IMC < 18,5 kg/m² son factores predictivos de mortalidad. La CVF baja y la edad avanzada en el momento del inicio de la enfermedad también se asocian a mayor mortalidad (1,2).

El tratamiento nutricional debe instaurarse de forma individualizada, dependiendo del estadio de la enfermedad, para asegurar un adecuado aporte calórico. Este puede ofrecerse en forma de dieta personalizada con empleo de espesantes/suplementos orales o con nutrición enteral por sonda nasogástrica o gastrostomía, endoscópica (PEG) o radiológica (PRG). En casos excepcionales, como las complicaciones después de la gastrostomía, se puede utilizar la nutrición parenteral. Asimismo, en estos pacientes existe un deterioro respiratorio que requiere el uso de soporte respiratorio en forma de ventilación mecánica no invasiva (VMNI): BIPAP (1,2).

La PEG requiere sedación y anestesia durante el procedimiento. Por el contrario, la PRG se realiza mediante insuflación de aire en la cámara gástrica e inserción de la sonda guiada por fluoroscopia mediante anestesia local, sin precisar sedación durante el procedimiento. Ambas son técnicas seguras y con una tasa baja de complicaciones.

La PEG no se recomienda en los pacientes con ELA que presentan insuficiencia respiratoria con capacidad vital forzada (CVF) < 50 % y no se puede realizar en los pacientes con espasticidad facial importante, en los que la PRG supone una estupenda alternativa (2).

Se ha realizado un estudio en nuestro centro para comparar ambas técnicas (PEG *versus* PRG) en pacientes afectados de ELA. El objetivo de nuestro estudio fue comparar la PEG con la PRG en pacientes con ELA en relación con el tiempo hasta su indicación, la situación nutricional, las complicaciones asociadas y la duración del tratamiento.

MATERIAL Y MÉTODOS

Estudio descriptivo retrospectivo, con intención analítica, donde incluimos “mediante información extraída de los registros de la historia clínica electrónica” a todos los pacientes con ELA de nuestro centro que habían precisado la realización de una gastrostomía (4 PEG y 6 PRG,) en los últimos 3 años (2021-2023) por disfagia severa. Analizamos las variables demográficas (edad, sexo, tipo de ELA, tiempo desde el diagnóstico hasta la colocación de la gastrostomía) y los parámetros nutricionales (IMC < 18,5/pérdida de peso > 10 %, prealbúmina, necesidad de suplementos) y respiratorios (CVF, % pacientes que requieren VMNI) (Tabla I).

Se realizó el seguimiento de los pacientes en las consultas de endocrinología según el “protocolo ELA”, que consiste en un circuito hospitalario de atención multidisciplinar en el que la gestora de casos programa en un mismo día, en acto único, todas las consultas que el paciente y el cuidador deben recorrer (neurología, endocrinología y nutrición, neumología y rehabilitación). La indicación de la gastrostomía la realizó el endocrinólogo en la consulta de nutrición tras la valoración del caso de forma individualizada mediante analítica y exploración física. El criterio para indicar la gastrostomía por vía endoscópica y no radiológica fue que no se pudiera realizar la PRG por algún motivo (*p. ej.*, por tener un “asa interpuesta”). El objetivo principal de nuestro estudio fue comparar dos procedimientos de colocación de gastrostomías para nutrición enteral en pacientes con ELA. Se compararon los pacientes con realización de PEG frente a la PRG y se evaluaron las indicaciones de cada una de ellas, las complicaciones posprocedimiento, la duración del soporte nutricional y el porcentaje de éxitos en cada grupo.

Tabla I. Características de 10 pacientes con ELA y necesidad de gastrostomía en nuestro centro (PEG vs. PRG)

	PEG1	PEG2	PEG3	PEG4	PRG1	PRG2	PRG3	PRG4	PRG5	PRG6
Sexo/edad	Mujer 54	Varón 27	Varón 31	Mujer 48	Varón 71	Varón 54	Varón 53	Mujer 67	Varón 53	Mujer 77
Bulbar/espinal	Bulbar	Espinal	Espinal	Espinal	Espinal	Espinal	Espinal	Bulbar	Espinal	Bulbar
Distagia Tiempo Colocación, años	Distagia 4	Distagia 8	Distagia 2	Distagia 13	Distagia 4	Distagia 1	Distagia 3	Distagia 1	Distagia 1	Distagia 1
Tratamiento nutricional previo	SNO	SNO	SNO	SNO	SNG	SNO	SNO	SNG	SNG	SNG
Parámetros nutricionales previos	No PP > 10 % No IMC < 18,5 kg/m ² Prealb. 19,2 mg/dl	No PP > 10 % No IMC < 18,5 kg/m ² Prealb. 19,7 mg/dl	No PP > 10 % No IMC < 18,5 kg/m ² Prealb. 20 mg/dl	No PP > 10 % No IMC < 18,5 kg/m ² Prealb. 29 mg/dl	SI PP > 10 % SI IMC < 18,5 kg/m ² Prealb. 11,6 mg/dl	No PP > 10 % No IMC < 18,5 kg/m ² Prealb. 29 mg/dl	No PP > 10 % No IMC < 18,5 kg/m ² Prealb. 17,2 mg/dl	No PP > 10 % No IMC < 18,5 kg/m ² Prealb. 16,3 mg/dl	SI PP > 10 % SI IMC < 18,5 kg/m ² Prealb. 18,6 mg/dl	SI PP > 10 % No IMC < 18,5 kg/m ² Prealb. 12,4 mg/dl
Situación respiratoria previa CVF en gastri	BIPAP CVF 81 %	BIPAP CVF 57 %	BIPAP CVF 60 %	BIPAP CVF 59 %	BIPAP CVF 29 %	BIPAP CVF 47 % CVF 25 %	BIPAP CVF 50 %	BIPAP CVF 33 %	BIPAP CVF 30 %	NO BIPAP
Complicaciones registradas	No	No	No	No	No	No	No	No	No	No
Mortalidad	No	No	No	No	SI 1 mes ITU/	No	No	SI 4 meses Inclusion Paliativos	SI 2 meses Sección paliativa /Domante	No
Tiempo de seguimiento	60 meses	108 meses	108 meses	108 meses	Hemorragia digestiva 12 meses	36 meses	48 meses	12 meses	4 meses	5 meses
		Asa interpuesta	Asa interpuesta	Se retrasó por deseo de la paciente						

PEG: gastrostomía endoscópica; PRG: gastrostomía radiológica; SNO: suplementos; PP %: pérdida de peso; SNG: sonda nasogástrica; BIPAP: presión positiva en la vía aérea; CVF: capacidad vital forzada; ITU: infección del tracto urinario.

RESULTADOS

Se incluyeron 10 pacientes (6 hombres y 4 mujeres) con una edad media de 57 años (rango de 33 a 78 años). El 70 % de los casos padecían ELA espinal y un 30 % ELA bulbar. Todos los pacientes presentaban disfagia severa y recibían suplementos orales o por sonda antes de la colocación de la gastrostomía (70 % suplementos orales/30 % nutrición por sonda nasogástrica).

En nuestro centro se usó como primera opción la PRG (60 %) frente a la PEG (40 %) ya que disponemos de un equipo de radiología intervencionista especializado y la primera parece ser una técnica más segura que la PEG, ya que no requiere anestesia ni soporte ventilatorio durante el procedimiento, es rápida y accesible y nos permite realizarla en los pacientes con ELA de mayor edad que presentan deterioro de la función respiratoria. En nuestra serie se realizó la PEG únicamente en 4 pacientes, uno de ellos que sí lo permitía por buena dinámica respiratoria, con CVF > 50 %, y dos de ellos en los que era imposible la realización de la PRG por tener un asa interpuesta. Los pacientes del grupo de PEG eran más jóvenes (27-54 años) que los del grupo de PRG (53-77 años).

Un 40 % de los pacientes presentaban datos de desnutrición severa (30 %, pérdida de peso > 10 %; 10 %, IMC < 18,5 kg/m²). Entre los parámetros analíticos destacaron un valor medio de prealbúmina de 17 mg/dl (rango: 11-19), sin diferencias por tipo de gastrostomía.

Todos los pacientes presentaron deterioro de la función respiratoria (necesidad de VMNI/BIPAP), que disminuyó con la evolución de la enfermedad, incluso tras el tratamiento nutricional. La CVF% media en la consulta inicial de neumología fue del 50 % (rango: 29-81 %), siendo superior en el grupo de PEG y reduciéndose a la mitad, aproximadamente un CVF del 25 %, en el momento de la gastrostomía.

El tiempo mediano desde el diagnóstico hasta la colocación de la gastrostomía fue de 4 años (Ri: 1-13 años). En el grupo de PEG se realizó de forma más tardía a partir de los 2 años, con un retardo de hasta 13 años en una paciente, mientras que en el grupo de PRG apenas hubo retraso y la mayoría se realizaron en el periodo de 1 año (máximo de 3-4 años).

Se realizaron 4 gastrostomías PEG y 6 PRG. La tasa de éxito "rápido, mínimamente invasivo y sin complicaciones" de la PEG y la PRG fue del 100 %, similar en ambos grupos, y no se registraron complicaciones posprocedimiento en ninguno de los casos.

Durante la valoración y el seguimiento del tratamiento nutricional en la consulta observamos el beneficio a nivel nutricional de la gastrostomía, presentando una mejor evolución de los parámetros antropométricos como la dinamometría (incremento medio de 11 a 19) y los parámetros analíticos como la prealbúmina, con un marcado ascenso hasta aproximadamente 23 (rango de 19-32) en ambos grupos.

La duración media de la nutrición enteral durante el seguimiento en la consulta fue de 50 meses, mayor para el grupo de PEG (108 meses) y menor para el grupo de PRG (4-48 meses), con una mortalidad total del 30 % durante el seguimiento a los 12 meses desde la gastrostomía (50 % en el grupo de PRG y 0 % en el grupo de PEG). Los 3 pacientes que fallecieron (2 con ELA espinal, 1 con ELA bulbar) lo hicieron por complicaciones no relacionadas con la gastrostomía

(uno al mes por infección urinaria/hemorragia digestiva y los otros dos por la propia evolución de la enfermedad), produciéndose los éxitos a los 2 y 4 meses de la realización de la PEG/PRG.

DISCUSIÓN

El tratamiento nutricional de los pacientes con ELA que presentan disfagia se encuentra dentro del manejo multidisciplinar de esta patología, precisando suplementos orales en los casos leves y de nutrición enteral con sonda nasogástrica/gastrostomía en los casos avanzados. Factores como la disfagia, la pérdida del apetito, la depresión, la disnea y el hipermetabolismo contribuyen al deterioro nutricional. La gastrostomía se puede realizar vía endoscópica por el Servicio de Digestivo (PEG) o por vía radiológica (PRG) por Radiología Intervencionista, con escasa necesidad de gastrostomías quirúrgicas (alto coste).

Queremos resaltar la importancia de la valoración nutricional y de la función respiratoria de estos pacientes en la indicación de la inserción de la gastrostomía, dado que su inserción puede provocar una mayor morbimortalidad en caso de existir desnutrición y cuando la insuficiencia respiratoria es mayor. La PEG y la PRG se asocian a un aumento de la supervivencia debido a la mejora del estado nutricional de estos pacientes (1,2).

Presentamos un estudio descriptivo retrospectivo donde incluimos a 10 pacientes con ELA y gastrostomía seguidos en nuestro centro. Se realizó un seguimiento de los pacientes en las consultas de endocrinología según el "protocolo ELA", donde los pacientes con ELA se atienden en un circuito multidisciplinar que incluye neurólogos, endocrinólogos, neumólogos, rehabilitadores y radiólogos. Este tipo de asistencia permite coordinar todo el tratamiento de soporte. El criterio para indicar la gastrostomía fue: pacientes con disfagia grave, atragantamientos y riesgo de broncoaspiración o pérdida de peso significativa.

El objetivo principal de nuestro estudio fue comparar los dos procedimientos de colocación de gastrostomías para nutrición enteral en pacientes con ELA (PEG frente a PRG).

En los pacientes con ELA que presentan un deterioro respiratorio importante, con CVF < 50 %, la PEG está limitada ya que, como hemos comentado, para su realización requiere sedación. La PRG constituye una alternativa segura a la PEG en este tipo de pacientes, incluso sin el uso concomitante de ventilación, ya que se realiza bajo anestesia local, con menor duración de la técnica y ausencia de sedación. También está indicada en los casos que la PEG no ha sido posible por otros motivos. Esta técnica presenta una baja tasa de complicaciones (sangrados autolimitados, obstrucción, malposición) (3-6).

La PEG se indica en los pacientes con menor deterioro respiratorio (CVF > 50 %) o imposibilidad de realización de una PRG, como ocurre en nuestros casos, por asa interpuesta y riesgo de perforación (7-10).

Todos nuestros pacientes requirieron soporte nutricional por disfagia, datos de desnutrición (pérdida de peso > 10 %, IMC < 18,5) o deterioro respiratorio (CVF < 50 %), y se realizó la PEG solo en caso de imposibilidad de realizar la PRG por algún motivo (*p. ej.*, tener una "asa interpuesta") o menor deterioro

respiratorio. No hubo complicaciones posprocedimiento en ningún grupo, con una duración media global de la nutrición enteral mayor para el grupo de PEG.

A pesar de que está establecido el beneficio del tratamiento nutricional en los pacientes con ELA (evidenciado en la mejora de los parámetros nutricionales) con mejora en la supervivencia, en nuestro hospital continúa existiendo una demora desde el diagnóstico hasta la realización de la gastrostomía (mayor en grupo de PEG).

La tasa de mortalidad es de aproximadamente un 30 % a 50 % con la PRG a los 12 meses en nuestra serie, mortalidad similar a la descrita en la literatura para la PEG (50 %), lo que se relaciona con el estadio avanzado de la enfermedad que presentan estos pacientes en el momento de la colocación de la gastrostomía, con desnutrición severa y deterioro respiratorio, más que por la técnica usada en sí misma (7).

En la literatura existen muy pocas publicaciones que comparen ambas técnicas de gastrostomía (PEG versus PRG) en estos pacientes (12,13). Algunos autores han resaltado la importancia de la edad, la CVF y la hospitalización previa como factores independientes de morbimortalidad coincidiendo con lo descrito en nuestra serie. Una variable que sí parece jugar algún papel en la aparición de complicaciones es la sedación durante el procedimiento en el caso de la PEG. También afirman que la colocación más precoz de la gastrostomía en estos enfermos podría aumentar la supervivencia ya que mejora los parámetros nutricionales (11). Los datos analizados sugieren que ambas técnicas son seguras con una baja mortalidad, siendo procedimientos idóneos para el tratamiento nutricional a largo plazo de los pacientes afectados de ELA. Otros afirman que se debe preferir la PRG en los casos de ELA ya que esta es más eficaz y se tolera mejor que la PEG, pues evita la descompensación respiratoria que puede ocurrir con la PEG y se asocia a menos aspiraciones. La supervivencia está ligada a la evolución de la ELA y no a la elección de la colocación de una PRG o PEG (14,15).

CONCLUSIONES

La atención multidisciplinar, el uso oportuno del soporte respiratorio y la gastrostomía son aspectos fundamentales para la supervivencia de los pacientes con ELA en nuestra población de estudio. La colocación de sondas de gastrostomía, ya sea por vía endoscópica o radiológica, es relativamente segura y efectiva. La PRG es un procedimiento idóneo para el tratamiento nutricional de los pacientes con ELA, siendo preferible frente a la PEG en aquellos pacientes que presentan deterioro respiratorio avanzado en los que esta es técnicamente difícil o está contraindicada, con aumento de la supervivencia y mejoría del estado respiratorio. La supervivencia después de la colocación de la gastrostomía fue similar en los pacientes con inicio bulbar y espinal. La edad avanzada en el momento del inicio de la enfermedad, la desnutrición y una CVF baja se asociaron a un mayor riesgo de mortalidad a corto plazo. Los pacientes más jóvenes con CVF conservada son los que más se beneficiaron de la PEG.

En la actualidad, a pesar de que esta patología presenta circuitos para una evaluación multidisciplinar, continúa existiendo un retraso entre el diagnóstico y la realización de la gastrostomía,

que coincide con el deterioro respiratorio, precisándose en gran parte de los casos la realización simultánea de una traqueostomía para la ventilación. Por lo tanto, la elección entre PEG y PRG debe basarse principalmente en las instalaciones y la experiencia de cada hospital. En nuestro caso, la PRG es más accesible y disponemos de un equipo especializado en radiología intervencionista que realiza la técnica con éxito y sin complicaciones.

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Trabajo Original

Paciente anciano

Crterios GLIM para diagnosticar la desnutrición en adultos mayores institucionalizados *GLIM criteria for diagnosing malnutrition in institutionalized older adults*

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Resumen

Introducción: la Iniciativa de Liderazgo Global sobre Desnutrición (GLIM) surgió con el propósito de unificar el diagnóstico de la desnutrición a nivel mundial. El objetivo principal de este trabajo es evaluar la validez de los criterios GLIM para diagnosticar la desnutrición en una población mayor de 65 años que vive en un centro sociosanitario. Además, se analizó el orden de importancia de los criterios GLIM para diagnosticar la desnutrición.

Material y métodos: se realizó un estudio transversal con 130 ancianos institucionalizados en un centro sociosanitario. Para estudiar la validez de los criterios GLIM se calcularon la sensibilidad y la especificidad, y se construyó una curva característica operativa del receptor (ROC) utilizando como método diagnóstico de referencia el cuestionario MNA. Para conocer cuál es el orden de importancia de los criterios se utilizó un modelo de regresión Lasso.

Resultados: según los GLIM y el MNA, la prevalencia de la desnutrición fue del 26,2 % y del 18,5 %, respectivamente. Los criterios GLIM resultaron tener una sensibilidad del 100 %, una especificidad del 91 % y un muy buen nivel de precisión (AUC = 0,95). El orden de importancia de los criterios, de mayor a menor, es: pérdida de masa muscular, pérdida de peso, presencia de inflamación, IMC bajo y disminución de la ingesta o la asimilación de nutrientes.

Conclusiones: los criterios GLIM presentaron un nivel de validez satisfactorio y, por lo tanto, son un método aceptable para diagnosticar la desnutrición en una población mayor que reside en un centro sociosanitario.

Palabras clave:

Criterios GLIM.
Desnutrición. Adultos mayores.

Abstract

Introduction: the Global Leadership Initiative on Malnutrition (GLIM) was created to unify the diagnosis of malnutrition worldwide. The main objective of this work is to evaluate the validity of the GLIM criteria for diagnosing malnutrition in a population over 65 years of age living in a nursing home. In addition, the order of importance of the GLIM criteria for diagnosing malnutrition was also analyzed.

Material and methods: a cross-sectional study was carried out with 130 older adults institutionalized in a nursing home. To study the validity of the GLIM criteria, sensitivity and specificity were calculated and a Receiver Operating Characteristic (ROC) curve was calculated using the MNA questionnaire as the reference diagnostic method. A Lasso regression model was used to determine the order of importance of the criteria.

Results: according to GLIM and MNA the prevalence of malnutrition was 26.2 % and 18.5 %, respectively. The GLIM criteria were found to have a sensitivity of 100 %, a specificity of 91 % and a very good level of precision (AUC = 0.95). The order of importance of the criteria from highest to lowest are loss of muscle mass, weight loss, presence of inflammation, low BMI and decreased nutrient intake or assimilation.

Conclusions: the GLIM criteria presented a satisfactory level of validity and are therefore an acceptable method to diagnose malnutrition in institutionalized older adults.

Keywords:

GLIM criteria. Malnutrition.
Older adults.

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INTRODUCCIÓN

La desnutrición relacionada con la enfermedad es un problema sanitario de elevada prevalencia y de gran repercusión clínica debido a que se asocia con un aumento de la morbilidad, una prolongación de la estancia hospitalaria, un aumento de la tasa de reingresos, un aumento de la mortalidad y un aumento de los costes asociados (1,2).

El proceso de envejecimiento provoca importantes cambios fisiológicos y funcionales en el anciano que están relacionados con la nutrición, como cambios en la composición corporal, disminución de la masa muscular, pérdida del gusto y el olfato, disfagia, pérdida del apetito, factores sociales o presencia de comorbilidades (3,4). Además, los ancianos institucionalizados suelen tener un mayor grado de dependencia funcional y psicológica que los ancianos que viven en la comunidad, lo que convierte a esta población en un colectivo especialmente vulnerable de sufrir desnutrición (5).

Para diagnosticar la desnutrición existen multitud de cuestionarios validados para diferentes situaciones clínicas y, a pesar de que esta patología constituye una de las grandes preocupaciones a nivel mundial, no existe un consenso único para su diagnóstico y definición (6). Hasta el momento actual, el cuestionario de referencia recomendado por la ESPEN (Sociedad Europea de Nutrición Clínica y Metabolismo) (7) para diagnosticar la desnutrición en la población mayor de 65 años es el MNA (*Mini Nutritional Assessment*) (8). El MNA consta de dos partes, una primera parte es de cribado nutricional que contiene 6 preguntas, si el cribado es positivo se pasa a realizar el cuestionario completo que contiene en total 18 preguntas, obteniendo así una valoración nutricional completa que clasifica a los pacientes en pacientes desnutridos, en riesgo de desnutrición y en no desnutridos. Este cuestionario ha demostrado su viabilidad mediante su uso en una gran cantidad de estudios (9), incluida la población anciana (10).

Con el objetivo de unificar el diagnóstico de desnutrición, las principales sociedades mundiales de la nutrición clínica, que incluye a la ASPEN (Sociedad Americana de Nutrición Enteral y Parenteral), la ESPEN (Sociedad Europea de Nutrición Clínica y Metabolismo), la FELANPE (Federación Latinoamericana de Terapia Nutricional, Nutrición Clínica y Metabolismo) y la PENSA (Sociedad Asiática de Nutrición Parenteral y Enteral), se reunieron y finalmente publicaron en el año 2018 los criterios GLIM (*Global Leadership Initiative on Malnutrition*) (11). Este nuevo método de diagnóstico se basa en un consenso teórico y, por este motivo, los autores pidieron a la comunidad científica la realización de estudios de validación para demostrar su efectividad y viabilidad en la práctica clínica real (12). El objetivo principal de este trabajo es evaluar la validez de los criterios GLIM en una población mayor de 65 años institucionalizada en centros sociosanitarios. Además, buscamos analizar el orden de importancia de los cinco criterios que componen la GLIM para darse el diagnóstico de desnutrición.

MATERIAL Y MÉTODOS

DISEÑO DEL ESTUDIO

Estudio transversal realizado en un centro sociosanitario del Área Sanitaria de Vigo entre febrero de 2022 y febrero de 2023. Los criterios de inclusión fueron personas mayores de 65 años que viven en el centro y que firmaron el consentimiento informado (o tutor legal en su caso), previa explicación del estudio y entrega de la hoja de información. Los criterios de exclusión fueron los residentes en situación terminal o de extrema gravedad y los que no aceptaron participar en el estudio. Se obtuvo el consentimiento informado de los participantes y se les identificó con un código ficticio (seudonimización) para garantizar la confidencialidad de los datos en todo momento. Este estudio fue llevado para su evaluación al Comité de Ética de la investigación de Pontevedra-Vigo-Ourense, con fecha de 01 de mayo de 2021 (código de registro: 2021/165) y con resolución positiva.

EVALUACIÓN DEL ESTADO NUTRICIONAL

Se realizó la valoración nutricional a cada participante mediante el cuestionario MNA. Según la puntuación obtenida se clasificó a los participantes en estado nutricional normal (de 24 a 30 puntos), en riesgo de desnutrición (de 17 a 23,5 puntos) y con desnutrición (menos de 17 puntos) (8).

Se realizó la valoración nutricional de cada participante mediante los criterios GLIM y se clasificó a los participantes en buen estado nutricional o con desnutrición. Los criterios GLIM incluyen cinco criterios diferentes para evaluar la desnutrición, tres de ellos son aspectos fenotípicos (pérdida de peso involuntaria, bajo índice de masa corporal y masa muscular reducida) y dos de ellos son aspectos etiológicos (ingesta o asimilación de alimentos reducida y carga inflamatoria). Para darse el diagnóstico de desnutrición se deben cumplir al menos un criterio fenotípico y un criterio etiológico (11). Se puede clasificar la gravedad de la desnutrición según los criterios fenotípicos aunque, en este estudio, los pacientes desnutridos se agruparon en una sola categoría y no se distinguieron por gravedad de la desnutrición. Se consideró que se cumplen los criterios fenotípicos cuando la pérdida de peso fue $> 5\%$ en los últimos 6 meses o $> 10\%$ en más de 6 meses; cuando el IMC < 20 para la población menor de 70 años o IMC < 22 para la población mayor de 70 años; cuando se identificó una reducción en la masa muscular según el índice de masa del músculo esquelético apendicular (ASMI) (13), para el cual el valor de corte para hombres es $< 7 \text{ kg/m}^2$ y para las mujeres $< 5,5 \text{ kg/m}^2$ (14). En cuanto a los criterios etiológicos, el criterio "reducción en la ingesta o asimilación de nutrientes" se consideró positivo si se mantuvieron requerimientos energéticos inferiores al 50 % durante más de una semana o cualquier reducción que se presentara durante más de dos semanas. Se consideró que se produjo una reducción de la asimilación de nutrientes cuando hubo presencia de patologías gastrointestinales crónicas que cursaran con un proceso de malabsorción

de nutrientes (síndrome del intestino corto, insuficiencia pancreática o diarrea). El criterio "presencia de inflamación" se consideró positivo si hubo inflamación aguda (infecciones graves, quemaduras o traumatismos) o inflamación crónica (patologías que cursan con un grado de inflamación como: insuficiencia cardíaca congestiva, enfermedad pulmonar obstructiva crónica, artritis reumatoide, enfermedad renal crónica, enfermedad hepática crónica, enfermedad inflamatoria intestinal, cáncer y obesidad).

Para validar los criterios GLIM, que son un consenso teórico, los hemos aplicado a nuestra muestra real de pacientes (prueba diagnóstica). Posteriormente, se compararon sus resultados con los resultados del cuestionario MNA en la misma muestra, considerado en la actualidad como el método de referencia para diagnosticar la desnutrición en este tipo de población (diagnóstico certero) (7). Los pacientes que fueron clasificados por el MNA como estado nutricional normal y los que presentan riesgo de desnutrición se consideraron pacientes no desnutridos a la hora de compararlos con GLIM.

ANÁLISIS ESTADÍSTICO

Se elaboró una tabla de confusión que es una matriz que muestra la relación entre las predicciones de un modelo o resultado de una prueba diagnóstica (GLIM) y las clases reales de datos (MNA) y se calcularon la sensibilidad (S), la especificidad (E), el valor predictivo positivo (VPP) y el valor predictivo negativo (VPN) (15,16). También se construyó una curva característica operativa del receptor, "ROC", que es una herramienta estadística que sirve para evaluar la capacidad discriminativa o rendimiento de una prueba diagnóstica dicotómica. Cuanto más cerca esté la curva del vértice superior izquierdo del gráfico, mejor será el rendimiento del modelo. La interpretación se realiza mediante el área bajo la curva (AUC) de ambas pruebas. Esta área posee un valor comprendido entre 0,5 y 1, donde 1 representa un valor diagnóstico perfecto y 0,5 es una prueba sin capacidad discriminativa diagnóstica (17). Para conocer cuál de las cinco variables que utilizan los GLIM es la más importante o la que mayor peso tiene a la hora de darse el diagnóstico de desnutrición, se utilizó un modelo de regresión Lasso (*least absolute shrinkage and selection operator*) (18), donde un coeficiente más grande implica una mayor influencia de la variable en la predicción del diagnóstico.

RESULTADOS

CARACTERÍSTICAS DE LA MUESTRA

De un total de 130 participantes, 92 fueron mujeres (70,8 %) y 38 hombres (29,2 %). La edad media fue de $84,1 \pm 9,1$ años (rango: 65-100), el peso medio fue $66,5 \pm 13,8$ kg (rango: 40-103,8) y el IMC medio fue de $26,9 \pm 5,1$ kg/m² (rango: 17,1-43,1).

Las principales comorbilidades de la muestra se detallan en la tabla I.

Tabla I. Principales comorbilidades de la muestra

Comorbilidad	Prevalencia (n, %)
Demencia	92 (70,8 %)
Diabetes	29 (22,3 %)
Hipertensión arterial	71 (54,6 %)
Dislipemia	53 (40,8 %)
Polimedicado (> 5 fármacos)	112 (86,2 %)
Disfagia	22 (16,9 %)
Úlceras por presión	10 (7,7 %)

VALORACIÓN NUTRICIONAL

En las tablas II y III se presentan los resultados de la valoración nutricional por el cuestionario MNA y los criterios GLIM. En la figura 1 se representa gráficamente el porcentaje de pacientes desnutridos y no desnutridos por MNA y GLIM.

Tabla II. Resultados del cuestionario MNA

Cuestionario MNA	
Clasificación	Pacientes, n (%)
Bien nutridos	35 (26,9 %)
Riesgo nutricional	71 (54,6 %)
Desnutrición	24 (18,5 %)

Tabla III. Resultados de los criterios GLIM

Criterios GLIM	
Clasificación	Pacientes, n (%)
Bien nutridos	96 (73,8 %)
Desnutrición	34 (26,2 %)

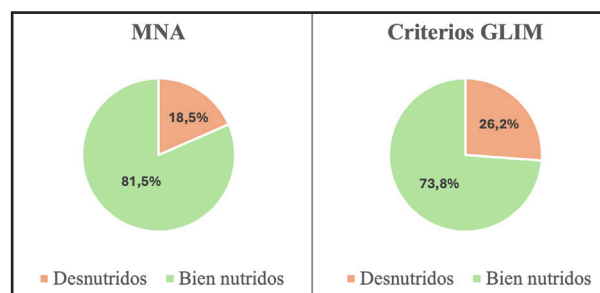


Figura 1.

Porcentaje de pacientes desnutridos según el MNA y los criterios GLIM.

VALIDEZ DE LOS CRITERIOS GLIM

En la tabla IV se muestra la matriz de confusión a partir de la cual se calculan la sensibilidad, la especificidad y los valores predictivos positivo y negativo.

$$Sensibilidad = \frac{VP}{total\ de\ enfermos} = \frac{VP}{VP+FN} = \frac{24}{24+0} = 1$$

GLIM diagnosticó correctamente como desnutridos al 100 % de los pacientes desnutridos.

$$Especificidad = \frac{VN}{total\ de\ sanos} = \frac{VN}{VN+FP} = \frac{96}{96+10} = 0,91$$

GLIM diagnosticó correctamente como bien nutridos al 91 % de los pacientes del estudio que realmente estaban bien nutridos.

$$Valor\ predictivo\ positivo = \frac{VP}{total\ de\ pruebas\ +} = \frac{VP}{VP+FP} = \frac{24}{24+10} = 0,71$$

GLIM tuvo un 71 % de probabilidades de acertar al dar un diagnóstico de desnutrición.

$$Valor\ predictivo\ negativo = \frac{VN}{total\ de\ pruebas\ -} = \frac{VN}{VN+FN} = \frac{96}{96+0} = 1$$

GLIM tuvo un 100 % de probabilidades de acertar al dar un diagnóstico de bien nutrido.

En la figura 2 se representa la curva ROC que tiene un AUC = 0,95, lo que significa que existe un 95 % de probabilidad de que el diagnóstico de desnutrición con los criterios GLIM realizado a un paciente desnutrido sea más correcto que el de una persona sana escogida al azar. Estaríamos ante una prueba diagnóstica con una muy buena precisión por estar el AUC comprendido entre 0,9 y 0,97.

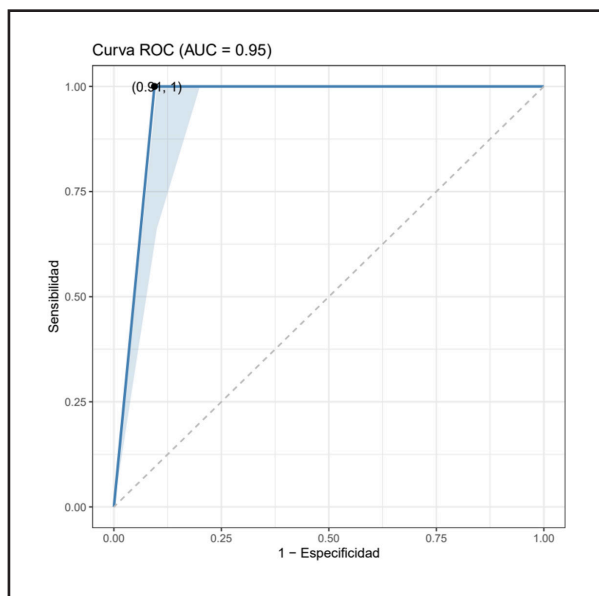


Figura 2. Resultado de la curva ROC para estudiar la validez de los criterios GLIM.

Tabla IV. Matriz de confusión

		MNA	
		Bien nutrido	Desnutrido
Criterios GLIM	Bien nutrido	96 (VN = verdaderos negativos)	0 (FN = falsos negativos)
	Desnutrido	10 (FP = falsos positivos)	24 (VP = verdaderos positivos)

Tabla V. Modelo de regresión Lasso para ordenar los criterios GLIM por importancia

Criterio GLIM	Valor del coeficiente
Pérdida de peso	12,7
Bajo IMC	11,4
Pérdida de masa muscular	13,6
Reducción en la ingesta o asimilación de nutrientes	2,1
Inflamación	12,2

CLASIFICACIÓN DE LOS CRITERIOS SEGÚN ORDEN DE IMPORTANCIA PARA CUMPLIRSE CON EL DIAGNÓSTICO DE DESNUTRICIÓN

El resultado del modelo de regresión Lasso para ordenar los criterios según importancia se expresa en la tabla V.

Los resultados expresados en coeficiente absoluto ordenan por importancia de mayor a menor las variables GLIM para el diagnóstico de la desnutrición de la siguiente forma:

Pérdida de masa muscular > pérdida de peso > presencia de inflamación > bajo IMC > disminución en la ingesta o asimilación de nutrientes.

DISCUSIÓN

La prevalencia de la desnutrición obtenida en nuestro trabajo por el cuestionario MNA es del 18,5 %. Aunque la prevalencia de la desnutrición calculada por el MNA para la población mayor de 65 años institucionalizada es diferente según el estudio, nuestro valor corresponde en gran medida al reportado en la bibliografía. Autores como Kaiser MJ y cols. (19) afirman que es del 13,8 %, mientras que Cereda y cols. (20) dicen que es del 17,5 % y según Milà Villarroel R y cols. (21) es del 20,8 %.

En cuanto a la validez de los criterios GLIM, los resultados indican que este método de diagnóstico tiene una sensibilidad del 100 % y una especificidad del 91 %. Esto significa que si GLIM da un resultado negativo, este es muy fiable y descarta por completo el diagnóstico de desnutrición, mientras que en el caso de que el resultado sea positivo deberíamos tener cierta precaución y pensar en la posibilidad de que sea un falso positivo. GLIM identificó a todos los pacientes desnutridos según el cuestionario MNA (24 pacientes), pero también incluyó a algún paciente como desnutrido que estaba bien nutrido según el MNA (10 pacientes). Es interesante mencionar que estos 10 pacientes considerados falsos positivos estaban todos clasificados como en "riesgo de desnutrición" por el MNA, es decir: no hubo ningún paciente diagnosticado por GLIM como desnutrido que al menos no estuviera en riesgo de desnutrición por el MNA. Por lo que, en el caso de producirse un falso positivo, podría tratarse de un paciente en riesgo de desnutrición porque GLIM no es capaz de detectar este tipo de pacientes y los considera sanos. La desnutrición no es una patología traumática ni que requiera tratamientos agresivos por lo que, en el caso de darse un falso positivo e instaurarse un plan de intervención nutricional, este no tendría grandes consecuencias para el paciente. Sin embargo, en el caso de darse un falso negativo y de que un paciente desnutrido no fuera correctamente diagnosticado, sí que podría haber consecuencias nefastas en términos de salud. Esto confirma la importancia de contar con un método de diagnóstico de la desnutrición que tenga una muy alta sensibilidad.

Las principales limitaciones de los criterios GLIM son que la evaluación de la pérdida de masa muscular y la presencia de inflamación no están claramente definidas, lo que podría dar lugar a ambigüedad de los resultados y dificultar la comparación entre estudios realizados con este método de diagnóstico. Esta falta de precisión inicial en la definición debe sugerirnos la enor-

me dificultad que conlleva definir esta patología. La ecuación ASMI, utilizada en este trabajo, nos permite evaluar la pérdida de masa muscular de una forma viable en la práctica clínica real con tan solo medir la circunferencia de la pantorrilla, por lo que podría ser un sustituto de otras técnicas de medición más sofisticadas y complejas propuestas por los autores, como la tomografía computarizada, la resonancia magnética o el análisis de bioimpedancia, que no suelen estar disponibles en el entorno de los centros sociosanitarios (11). La dinamometría es otra técnica relativamente sencilla para evaluar la pérdida de masa muscular que consiste en medir la fuerza de agarre mediante un dinamómetro, pero esta técnica puede no ser adecuada para la población mayor institucionalizada ya que, a menudo, presentan comorbilidades como demencia o artrosis que provocan que no se pueda realizar correctamente la técnica.

Los criterios GLIM son un método de valoración nutricional rápido y sencillo. Además, son únicos en cuanto a que proporcionan por primera vez un consenso mundial para categorizar la desnutrición (aunque se reconoce que pueden llegar modificaciones con las versiones actualizadas en el futuro). En este trabajo se han demostrado la aplicabilidad de los criterios GLIM y su validez como método de diagnóstico de la desnutrición en personas mayores de 65 años que viven en un centro sociosanitario, reafirmando la idea de que los criterios GLIM son el camino para alcanzar el consenso mundial del diagnóstico de desnutrición. Es necesario realizar estudios de validación de los criterios GLIM en otros ámbitos asistenciales y en poblaciones específicas.

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Trabajo Original

Serum glutathione peroxidase is associated with nonalcoholic fatty liver disease in children and adolescents

La glutatión-peroxidasa sérica se asocia a la enfermedad del hígado graso no alcohólico en niños y adolescentes

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Abstract

Background and aims: oxidative stress is an important factor in the pathophysiology of non-alcoholic fatty liver disease (NAFLD). This study aimed to compare the serum levels of malondialdehyde (MDA), glutathione peroxidase (GPx) and antioxidant micronutrients in children and adolescents with and without NAFLD.

Methods: a cross-sectional study with patients between 8-18 years old, of both sexes. Diagnosis of NAFLD: presence of steatosis on ultrasound and absence of history of ethanol consumption and other liver diseases. Anthropometric measures, MDA, GPx, Interleukin-6, serum levels of vitamins A, C and E, selenium, zinc, and copper were evaluated.

Results: eighty-nine children with mean age of 12 (3) years, 57.3 % female and 24 % with NAFLD were evaluated. Those with NAFLD had more frequent abdominal obesity (high waist-height ratio: 81.0 % x 48.5 %; $p = 0.009$). After logistic regression NAFLD was associated with high body mass index/age (p -adjusted = 0.021) and with reduced serum GPx (p -adjusted = 0.034). There was a positive correlation between MDA and copper ($r = 0.288$; $p = 0.006$), IL-6 ($r = 0.357$; $p = 0.003$) and a negative one with vitamin A ($r = -0.270$; $p = 0.011$).

Conclusions: oxidative stress is present in children with NAFLD and non-invasive markers such as GPx and BMI can be used in clinical practice and help in the early screening of NAFLD.

Keywords:

Non-alcoholic fatty liver disease. Malondialdehyde. Glutathione peroxidase. Antioxidant micronutrients. Children. Adolescents.

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Institutional Review Board statement: the study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the Federal University of Bahia under number 1.471.817, on March 30, 2016. Informed consent was obtained from all subjects involved in the study.

Data availability statement: the data is private because it belongs to human beings. However, if needed, databases can be made available in the future.

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Resumen

Antecedentes y objetivos: el estrés oxidativo es un factor importante en la fisiopatología de la enfermedad del hígado graso no alcohólico (EHGNA). Este estudio tuvo como objetivo comparar los niveles séricos de malondialdehído (MDA), glutatión-peroxidasa (GPx) y micronutrientes antioxidantes en niños y adolescentes con y sin NAFLD.

Métodos: estudio transversal con pacientes de 8-18 años de ambos sexos. Diagnóstico de NAFLD: presencia de esteatosis en la ecografía y ausencia de antecedentes de consumo de etanol y otras enfermedades hepáticas. Se evaluaron medidas antropométricas, MDA, GPx, interleucina-6, niveles séricos de vitaminas A, C y E, selenio, zinc y cobre.

Resultados: se evaluaron 89 niños con edad media de 12 (3) años, 57,3 % del sexo femenino y 24 % con EHGNA. Aquellos con EHGNA tuvieron obesidad abdominal con mayor frecuencia (relación cintura-altura alta: 81,0 % x 48,5 %; $p = 0,009$). Después de la regresión logística, la EHGNA se asoció con un índice de masa corporal/edad elevado (p ajustado = 0,021) y con una GPx sérica reducida (p ajustado = 0,034). Hubo correlación positiva entre MDA y cobre ($r = 0,288$; $p = 0,006$), IL-6 ($r = 0,357$; $p = 0,003$) y negativa con vitamina A ($r = -0,270$; $p = 0,011$).

Conclusiones: el estrés oxidativo está presente en niños con NAFLD y los marcadores no invasivos como GPx e IMC pueden usarse en la práctica clínica y ayudar en la detección temprana de NAFLD.

Palabras clave:

Enfermedad del hígado graso no alcohólico.
Malondialdehído.
Peróxido de glutatión.
Micronutrientes antioxidantes. Niños. Adolescentes.

INTRODUCTION

Non-alcoholic fatty liver disease is characterized by the accumulation of fat in the hepatocytes of individuals without a history of chronic ethanol consumption or other liver diseases (1,2).

Considered the most common chronic liver condition today, it has also become the target of investigation in the child population, as it has a growing and estimated prevalence among children and adolescents at 3 % to 11 %, ranging from 46 % to 80 % in obese children (3).

In this population, of children and adolescents, the disease is usually asymptomatic, being diagnosed by an incidental evaluation of liver enzymes, evidence of steatosis on routine ultrasound or the occurrence of some extrahepatic manifestation (4).

Obesity, especially central obesity, and insulin resistance are risk factors for NAFLD, which is considered a hepatic manifestation of the metabolic syndrome and is associated with oxidative stress (OxS) and important cardiometabolic burden in childhood (5).

The pathogenesis of NAFLD is not fully understood, but it is known that important factors such as OxS induced inflammation with lipid peroxidation, cytokine activation and excessive production of reactive oxygen species (ROS) are associated with the progression of the disease in adults and children (6).

Oxidative stress occurs when there is an imbalance between the concentrations of pro and antioxidant species. In individuals with NAFLD, there may be an increase in serum OxS byproducts such as the malondialdehyde (MDA) marker, or impaired redox balance, also demonstrated by a decrease in glutathione peroxidase (GPx) levels and possibly stores of antioxidant micronutrients, of which vitamins C and E seem to act as protectors against OxS (7-9).

The pediatric population deserves special attention. Due to their life expectancy, they have a longer exposure to risk factors for NAFLD and consequently a greater probability of developing steatohepatitis, liver fibrosis, cirrhosis, and even hepatocellular carcinoma. Early diagnosis and the adoption of measures to prevent the progression of the disease will reduce damage in the future (7,8).

So, the objective of the present study was to compare the serum levels of MDA, GPx and antioxidant micronutrients in children and adolescents with and without NAFLD.

MATERIALS AND METHODS

STUDY DESIGN AND POPULATION

Cross-sectional study with children and adolescents followed up at a pediatric out clinic. The study was approved by the Research Ethics Committee under process number 1.471.817.

Patients of both sexes and aged between 8 and 18 years were included. Children under 8 years of age were not included because in the literature there are reports of liver diseases in this group associated with liver syndromes or autoimmune diseases. The non-inclusion criteria were patients with thinness according to body mass index (BMI)/age; consumption > 140 g of ethanol/week for males and > 70 g of ethanol/week for females; syndromic obesity, pubertal abnormalities; use of drugs that interfere with hepatic and glycemic metabolism such as corticosteroids, sulfa drugs, antipsychotics or amphetamines, antioxidant supplementation. Patients with hypothyroidism, other liver diseases (viral hepatitis A, B and C, autoimmune diseases, Wilson's disease, and hemochromatosis), presence of systemic infectious process in and/or acute in the last 10 days also were not included.

CLINICAL EVALUATION

Sociodemographic variables (age, sex, and family income), lifestyle habits (practice of physical activity (10)) and clinical data such as pubertal stage (11) and presence of acanthosis nigricans (12) were collected using a structured questionnaire and classified according to the references cited.

NAFLD CRITERIA DIAGNOSIS

Presence of hepatic steatosis on ultrasound of the upper abdomen, associated with alcohol consumption ≤ 140 g of ethanol/week for men and ≤ 70 g of ethanol/week for women, and in the absence of liver diseases such as B and C viruses, autoimmune, metabolic, and toxic (2). Abdominal ultrasonography was performed by a single evaluator.

ANTHROPOMETRIC ASSESSMENT

Anthropometric measurements were standardized and tested to determine statistical similarity. The value used was the average of 2 evaluators, and the maximum difference accepted between them was 0.5 cm. Weight was measured on a LD 1050 digital scale[®], and height was measured on an LD 1050 stadiometer[®], with a scale at 0.1 cm intervals. Anthropometric nutritional status was assessed according to the BMI/age and sex indicator, (13) using the WHO AnthroPlus, 2011 version 16. To classify body weight adequacy, patients were divided into two groups: adequate weight for age when $-2 < z \text{ score} < +1$ and overweight when $z \text{ score} > +1$. Waist circumference (WC), measured at the minimum circumference between the iliac crest and ribcage (14) and neck circumference (NC), measured at the midpoint of the neck (15), were measured and evaluated. Waist/height ratio (WHR) was considered normal when ≤ 0.5 (16). The Conicity Index (CI) ranged from 1.14 to 1.16 for children younger than 9 years and from 1.06 to 1.12 for children older than 10 years (17). The conicity index was calculated as follows:

$$\text{Conicity index} = \text{waist circumference} / (0.109 \times \text{square root of weight} / \text{height})$$

where waist circumference and height were measured in meters and weight in kg.

BIOCHEMICAL ASSESSMENT

Biochemical tests were performed after an 8-hour fast. Alanine aminotransferase (ALT), aspartate transaminase (AST) and gamma glutamyl transpeptidase (GGT) were analyzed using the dry chemistry method and had their suitability assessed according to reference values suggested by NASPGHAN (2017) (9). Fasting blood glucose and serum insulin values were evaluated according to the recommendations of the Brazilian Society of Diabetes, 2019-2020 (18). The HOMA-IR (Homeostatic Model Assessment) was analyzed based on the suggested value for insulin resistance (IR) ≤ 3.0 , by Yan et al. 2013 (19). And the lipid profile, total cholesterol and fractions and triglycerides were based on the normality values of the Brazilian Society of Cardiology, 2019-2020 (20).

MDA was evaluated by thiobarbituric acid calorimetry and spectrophotometry, and GPx was evaluated by spectrophotometry, with reference values of 2.3-4.0 $\mu\text{mol/L}$ and 4171-10881 U/L, respectively. IL-6 was evaluated by chemiluminescence and with a normal value $< 3.4 \text{ pg/ml}$.

Vitamins C, E and A, selenium, zinc, and copper levels were measured in the blood and for the analysis of the adequacy of these markers the values considered acceptable were those suggested by the laboratory, being 4.6-15.0 mg/dl, 3-10, 0 mg/dl, 0.3-0.7 mg/dl, 20.0-190.0 $\mu\text{g/dl}$, 70.0-120.0 $\mu\text{g/dl}$ and 80.0-160.0 $\mu\text{g/dl}$, respectively.

STATISTICAL ANALYSIS

The statistical program Statistical Package for the Social Science[®] (SPSS) version 17.0 was used for data analysis.

To calculate the sample size, it was considered a difference of 6 % (21) in the prevalence of oxidative stress in the groups with and without NAFLD, a power of 80 % and alpha of 5 %. Thus, the number needed to answer the objective of the study was eighty-six patients.

Categorical variables were expressed as absolute and relative frequency, and quantitative variables as mean and standard deviation (SD). The sample was divided in two groups with and without NAFLD. The following statistical tests were used to compare groups: t-test for independent samples to compare quantitative variables and chi-square and Fisher's exact test to compare categorical variables. Correlations tests of Pearson and Spearman were used to test linear association between the variables. P values < 0.05 were considered statistically significant. It was performed a logistic regression analysis to investigate confounding. The variables included in the model were those that showed a p -value ≤ 0.20 in bivariate analysis (high BMI/age, elevated MDA, reduced GPx and low copper).

RESULTS

Eighty-nine children and adolescents were included in the study aged between 8 to 18 years and 50 (56 %) were female. For comparison purposes the sample was divided into two groups with (24 %) and without (76 %) non-alcoholic fatty liver disease. It was observed that the group with NAFLD had a higher percentage of individuals with high body mass index/age, high neck circumference and high waist height ratio (Table I).

As for laboratory findings the group with NAFLD had a higher frequency of high total cholesterol and low-density lipoprotein cholesterol, but when all types of dyslipidemias were analyzed together, there was no differences between the groups. There were also no differences between them regarding liver enzymes, micronutrients, and vitamins. However, it was observed that individuals with NAFLD had more frequently reduced levels of GPx (23.8 % \times 2.9 %; $p = 0.007$) and elevated levels of MDA (19.0 % \times 5.9 %; $p = 0.085$), although this last difference did not reach statistical significance (Table II).

To assess confounding variables, it was performed a logistic regression analysis with the variables: high BMI/age, elevated MDA, reduced GPx and low copper. After adjustment, the associations between NAFLD and high BMI/age (p adjusted = 0.021) and reduced glutathione peroxidase (p adjusted = 0.034) remained, however the same did not happen with the associations between elevated malondialdehyde (p adjusted = 0.205) and low copper (p adjusted = 0.118).

Table III shows the correlations between serum levels of malondialdehyde, glutathione peroxidase and antioxidant micronutrients and vitamins. There were positive and statistically significant correlations between serum levels of MDA and copper ($r = 0.288$; $p = 0.006$) and IL-6 ($r = 0.357$; $p = 0.003$) and negative with vitamin A ($r = -0.270$; $p = 0.011$) and GPx ($r = -0.250$; $p = 0.018$). There were no statistically significant correlations between GPx, antioxidant micronutrients and vitamins.

Table I. Demographic and anthropometric characteristics of children and adolescents with and without non-alcoholic fatty liver disease followed up at the Pediatrics Outpatient Clinic, 2021

Characteristics	NAFLD		p-value
	Yes 21 (24 %)	No 68 (76 %)	
Age (years)*	12 (2)	12 (3)	0.924
Male sex	11 (52.4 %)	28 (41.2 %)	0.366
Physical activity practice	9 (42.9 %)	20 (29.4 %)	0.251
Presence of acanthosis nigricans	12 (57.1 %)	40 (58.8 %)	0.891
<i>Pubertal stage</i>			NA
Pre-puberty	3 (14.3 %)	17 (25.0 %)	
Pubescent	16 (76.2 %)	45 (66.2 %)	
Post pubescent	2 (9.5 %)	6 (8.8 %)	
High body mass index/age	20 (95.2 %)	39 (57.4 %)	0.001
High neck circumference	17 (81.0 %)	26 (38.2 %)	0.001
High waist-height ratio	17 (81.0 %)	33 (48.5 %)	0.009
High waist circumference	18 (85.7 %)	45 (66.2 %)	0.085
High conicity index	20 (95.2 %)	67 (98.5 %)	0.418

*Mean (standard deviation); NA: not applicable.

Table II. Laboratorial characteristics of children and adolescents with and without non-alcoholic fatty liver disease followed up at the Pediatrics Outpatient Clinic, 2021

Characteristics	NAFLD		p-value
	Yes 21 (24 %)	No 68 (76 %)	
Elevated ALT	0 (0.0 %)	2 (2.9 %)	1.000
Elevated AST	1 (4.8 %)	2 (2.9 %)	0.559
Elevated GGT	1 (4.8 %)	0 (0.0 %)	0.236
High total cholesterol	11 (52.4 %)	17 (25.0 %)	0.018
High LDL- cholesterol	9 (42.9 %)	14 (20.6 %)	0.042
Low HDL- cholesterol	12 (57.1 %)	23 (33.8 %)	0.056
Elevated triglycerides	14 (66.7 %)	33 (48.5 %)	0.146
Dyslipidemia	16 (76.2 %)	48 (70.6 %)	0.618
High fasting glucose	1 (4.8 %)	3 (4.4 %)	1.000
HOMA-IR elevated	10 (47.6 %)	24 (35.5 %)	0.310
Elevated MDA	4 (19.0 %)	4 (5.9 %)	0.085
Reduced GPx	5 (23.8 %)	2 (2.9 %)	0.007
Elevated IL-6*	3 (27.3 %)	16 (27.6 %)	1.000
Low copper	2 (9.5 %)	1 (1.5 %)	0.137
Low zinc	0 (0.0 %)	1 (1.5 %)	1.000
Low selenium	3 (14.3 %)	6 (8.8 %)	0.435
Low vitamin A	3 (14.3 %)	6 (8.8 %)	0.435
Low vitamin C	15 (71.4 %)	47 (69.1 %)	0.840
Low vitamin E	3 (14.3 %)	9 (13.2 %)	1.000

*Data referring to 69 patients. ALT: alanine aminotransferase; AST: aspartate transaminase; GGT: gamma glutamyl transpeptidase; LDL-cholesterol: low density lipoprotein cholesterol; HDL-cholesterol: high density lipoprotein cholesterol; HOMA-IR: Homeostatic Model Assessment; MDA: malondialdehyde; GPx: glutathione peroxidase; Interleukin-6: IL-6.

Table III. Correlation between serum levels of malondialdehyde, glutathione peroxidase and antioxidant micronutrients in children and adolescents followed up at the Pediatrics Outpatient Clinic, 2021

Antioxidant micronutrients	Malondialdehyde r (p-value)	Glutathione peroxidase r (p-value)
Serum copper	0.288 (0.006)	-0.051 (0.636)
Serum zinc	-0.115 (0.284)	0.054 (0.615)
Serum selenium	0.001 (0.994)	-0.063 (0.560)
Vitamin A	-0.270 (0.011)	-0.013 (0.903)
Vitamin C	-0.179 (0.093)	0.109 (0.309)
Vitamin E	0.085 (0.429)	-0.061 (0.569)
Interleukin-6*	0.357 (0.003)	-0.169 (0.166)

DISCUSSION

Our results showed that children and adolescents with non-alcoholic fatty liver disease more often have higher body mass index for age, increased neck circumference and waist-to-height ratio and low levels of glutathione peroxidase when compared to those without NAFLD. This study also showed a positive correlation between malondialdehyde and serum levels of copper and IL-6 and a negative correlation with vitamin A and glutathione peroxidase.

The interrelationship between genetic, epigenetic, and environmental factors supports the pathogenesis and progressive liver damage of NAFLD in children, which has aroused interest due to its relationship with cardiovascular and metabolic impairment in childhood or even in adulthood (22,23).

Obesity is directly and independently associated with NAFLD and its increased prevalence and severity. Consequently, obesity also appears to increase liver-specific mortality, even in children (24). It seems that this connection occurs when hepatocytes store excess lipids, mainly in the form of triglycerides, initiating hepatic steatosis. That is, the excess of circulating free fatty acids resulting from exacerbated lipolysis and the decrease in the uptake of these free fatty acids by the subcutaneous adipose tissue, promotes the accumulation of fat, including in the liver (24).

Thus, high BMI status is recognized as a risk factor for NAFLD and the prevalence of NAFLD is 10 to 20 times higher in obese children and adolescents compared to lean ones (8). However, it is known that central obesity is more associated with NAFLD than

total body fat (25). In one study, where obese children aged 10 to 18 years were evaluated, NAFLD was more frequent in patients with high weight and neck circumference, which in turn evaluate central fat accumulation and can even be used as predictors of NAFLD (25). In our sample, the increase in BMI, WHR and NC were associated with NAFLD, pointing to the high presence of total body fat and the increase in central body fat as an associated factor for the disease.

The explanation for central body fat being more associated with NAFLD seems to lie in the fact that visceral adipocytes, which are more lipolytic than subcutaneous ones, store and mobilize triglycerides faster than those in other regions, increasing the supply of free fatty acids in the portal system, which stimulate gluconeogenesis and inhibit hepatic insulin clearance, contributing to elevated blood glucose and insulin levels and thus the development of insulin resistance (IR) (26,27).

Thus, obesity and IR seem to compose the first steps in the development of non-alcoholic fatty liver disease, without, however, all the pathogenesis and evolution of NAFLD to steatohepatitis, liver fibrosis, cirrhosis, and even hepatocellular carcinoma, with the possible absence of cirrhosis in children, being completely established (28).

What has been widely presented and discussed is that in the presence of obesity and alterations in the mitochondria, there is an increase in oxidative stress and in the production of pro-inflammatory cytokines in patients with liver disease (29).

The greatest production of reactive oxygen species occurs in the mitochondria and for this 1-2 % of the oxygen existing there is consumed. Under normal conditions and amounts, ROS act as signaling molecules and their unnecessary production is minimized through non-enzymatic and enzymatic antioxidant mechanisms (30).

In the persistent presence of hepatic steatosis, there may be triggering of the oxidative stress process that is characterized in NAFLD by mitochondrial dysfunction, increased release of inflammatory mediators, increased production of oxidative stress byproducts, such as the MDA marker, or impaired redox balance, as well demonstrated by a decrease in GPx levels, or even by impaired inactivation of ROS by deficient reserves of antioxidant nutrients (4,22).

Glutathione peroxidase is one of the most potent parts of the enzymatic defense system against free radical accumulation. Its action takes place by controlling the levels of hydrogen peroxide and lipid hydroperoxides, reducing them to alcohols and water, respectively, which can be subsequently detoxified and removed from the body or, in the case of water, used in other processes (30). Compromised GPx metabolism and activities of antioxidant enzymes in the blood were also observed in the present study. According to the findings of our study, patients with NAFLD showed an increased state of OxS, evidenced in lower serum levels of GPx, when compared to the values of individuals without NAFLD.

In a study developed by Nobili et al. (2005) (31), carried out with children with and without NAFLD, where the blood profile of various forms of glutathione and the presence of systemic oxidative stress were evaluated, there was impairment of glutathione metabolism

and activity of antioxidant enzymes, according to observed serum values in patients with NAFLD. A similar result was observed when comparing children with and without NAFLD in a study that tested GPx as a marker of oxidative stress (32).

Our results showed that the evaluation of the decrease in GPx was significantly associated with NAFLD, ie, patients with NAFLD had an increased state of OxS, evidenced in lower serum levels of GPx, when compared to the values of individuals without NAFLD. These findings reinforce the existence of a decline in the enzymatic antioxidant defense system and the possibility that GPx is a marker, regardless of the degree of steatosis and disease progression (33).

The presence of hepatic steatosis and oxidative stress trigger an increase in the reserve of MDA, which can be used as a standard measure to determine the degree of cellular oxidation (8,34). MDA is a secondary product of lipid peroxidation, derived from the interruption of the endocyclization of polyunsaturated fatty acids, such as linoleic, arachidonic, and docosahexaenoic acids (35).

Although we found a trend towards higher MDA values in children with NAFLD, showing that there may be evidence of changes in the degree of cellular oxidation in this sample, the assessment of the adequacy of this marker was not associated with the disease. This result was contrary to the study published by Bell et al. (2011) (34), where there was a significant increase in hepatic MDA in children with NAFLD when compared with control children or children with chronic hepatitis C virus. According to another study with a similar objective, MDA increases with the severity of NAFLD (30), which may explain our results, since most of our sample had mild cases of the disease.

In the present study, a negative correlation between MDA and GPx was observed. That is, in case of increased levels of MDA, due to the exacerbation of OxS, there is a decrease in the levels of the antioxidant enzyme GPx, portraying the body's attempt to promote defense against the accumulation of free radicals (30).

The pathogenesis of NAFLD has an inflammatory factor characterized mainly by an increase in tumor necrosis factor alpha (TNF- α) and a decrease in adiponectin. TNF- α increases the formation of reactive oxygen species and promotes hepatocyte apoptosis and liver inflammation, while adiponectin decreases the accumulation of hepatic triglycerides (36). TNF- α is also responsible for the increase in lipolysis and consequent increase in the flow of free fatty acids and their accumulation in the liver by suppressing insulin kinase receptor activity and decreasing glucose uptake causing hyperinsulinemia and by promoting IL-6 expression which reduces insulin receptor substrate expression (36).

In the sample studied here, we found a positive correlation between levels of MDA and IL-6. Literature suggests that IL-6 is increased in patients with NAFLD (3,29); however, this expression seems to be higher in individuals with increased OxS process, with NASH or more severe liver disease (37). Ahadi et al. (2021) (38), in a review on NAFLD in obese and non-obese individuals, states that the increase in IL-6 in this population is more linked to the degree of visceral fat accumulation than to the accumulation of subcutaneous fat. If we consider that our sample seems to have a higher degree of OxS, represented by the consumption of glutathione peroxidase, we can explain the existence of this correlation.

Through their lipoprotective, antioxidant, antifibrotic and immunomodulatory functions, vitamins and minerals play a role in the pathogenesis of NAFLD (28).

Micronutrients such as vitamin A, C and E, copper, selenium, and zinc, exert their function as non-enzymatic antioxidants, inhibit the oxidation of biomolecules, neutralizing the harmful effects of oxidation caused by free radicals, thus ensuring redox homeostasis (8).

Our analyzes showed that the decrease in serum levels of copper, selenium, vitamins A and C was more frequent in those with NAFLD, but without statistical significance. It is noteworthy that, despite the absence of statistical significance, this result is interesting because there is a possibility that the disease is related, either as a cause or effect, with suspension of detoxification in the liver in the absence of non-enzymatic antioxidants (8,35,36).

Also, among the correlation analyzes, a negative correlation was identified between MDA and vitamin A. This result can be corroborated by the fact that carotenoids, once converted into vitamin A, can benefit the liver through its antioxidant function and in regulating the expression of genes involved in inflammation and lipid metabolism. Or even because, if in the presence or elevation of oxidative stress, this same serum concentration of vitamin A can be reduced (28).

In addition to the previous correlations, a positive correlation was also seen between MDA and serum copper reserves. According to Mendonza et al. (2017) (39), which determined whether lower tissue copper is associated with increased NAFLD severity in children, & Antonucci et al. (2017) (40), who described the role of copper and copper-binding antioxidant compounds against NAFLD in the development and progression of NAFLD, patients with NAFLD had lower serum levels of copper and this deficiency promotes changes in lipid metabolism, insulin resistance and negative regulation of mitochondrial beta-oxidation, alterations related to increased oxidative stress and the pathophysiology of the disease under study.

Limitations of this work were the measurement of only two markers of oxidative stress and the use of ultrasound. Performing a biopsy for diagnosing NAFLD in this study would be unethical, as this is an invasive test. The use of ultrasound is justified, therefore, as it is a non-invasive, inexpensive, accessible, and widely used method to assess the presence of NAFLD in children. As a strong point of the research, we can mention the public of children and adolescents, and the fact that patients with and without overweight or obesity were evaluated, characteristics that are not frequent in previous studies.

In conclusion, when comparing children with NAFLD and without NAFLD, it was observed that the first group showed an association between the studied disease and a higher body mass index/age, higher neck circumference, and higher waist/height ratio. There was also an association between NAFLD and lower adequacy of serum levels of glutathione peroxidase. The results also showed an impairment of the defence process against oxidative stress in the body of children and adolescents with NAFLD and that non-invasive markers, such as GPx and BMI, can be used in clinical practice and help in the early screening of the disease.

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Trabajo Original

Clinical value of vitamin K testing in children aged 1-2 years with vitamin D deficiency rickets

El valor clínico de la determinación de la vitamina K en niños de 1 a 2 años de edad con raquitismo por déficit de vitamina D

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Abstract

Objective: to investigate the clinical value of vitamin K testing in children with vitamin D deficiency rickets.

Methods: fifty children with vitamin D deficiency rickets admitted to our hospital from March 2021 to March 2022 were recruited as the case group using convenience sampling; and an additional 50 children without bone health diseases during the same period of health checkup were selected as the control group. The relevant indexes between the two groups were compared.

Results: there were statistically significant differences between the two groups in the level of 25 hydroxyvitamin D3 [25-(OH)D3], the proportion of breastfeeding, and the proportion of preterm birth ($p < 0.001$). The levels of vitamin K1 and K2 were lower in the case group than in the control group, and the proportion of those with vitamin K1 deficiency and vitamin K2 deficiency were higher than the control group ($p < 0.001$). Positive correlations were found between vitamins K1 and K2 and 25-(OH)D3, blood calcium, and blood phosphorus ($p < 0.05$); artificial feeding, preterm birth, vitamin K1 deficiency, and vitamin K2 deficiency were risk factors for the development of vitamin D deficiency rickets, and the highest AUC of the combination of each index in predicting the occurrence of vitamin D deficiency rickets was 0.951 (95 % CI: 0.910-0.991).

Conclusion: preterm birth, artificial feeding, and vitamin K1 and K2 deficiency are independent risk factors for bone metabolism in children with vitamin D-deficiency rickets. And these risk factors have predictive and diagnostic value in the diagnosis and management of vitamin D deficiency rickets.

Keywords:

Vitamin D deficiency rickets. Vitamin K. Bone mineral density. Carboxylated osteocalcin.

Resumen

Objetivo: investigar el valor clínico de la determinación de vitamina K en niños con raquitismo por deficiencia de vitamina D.

Métodos: cincuenta niños con raquitismo por deficiencia de vitamina D admitidos en nuestro hospital desde marzo de 2021 hasta marzo de 2022 se reclutaron como grupo de casos mediante muestreo de conveniencia y se seleccionaron adicionalmente 50 niños sin enfermedades óseas durante el mismo período de revisión de la salud como grupo de control. Se compararon los índices relevantes entre los dos grupos.

Resultados: existían diferencias estadísticamente significativas entre los dos grupos en los niveles de 25 hidroxivitamina D3 [25-(OH)D3], la proporción de lactancias maternas y la proporción de nacimientos prematuros ($p < 0,001$). Los niveles de vitaminas K1 y K2 eran inferiores en el grupo de casos que en el grupo de control, y la proporción de aquellos con deficiencia de vitamina K1 y vitamina K2 era mayor que en el grupo de control ($p < 0,001$). Se encontraron correlaciones positivas entre las vitaminas K1 y K2 y la 25-(OH)D3, el calcio sanguíneo y el fósforo sanguíneo ($p < 0,05$); la alimentación artificial, el nacimiento prematuro, la deficiencia de vitamina K1 y la deficiencia de vitamina K2 son factores de riesgo para el desarrollo de raquitismo por deficiencia de vitamina D, y el AUC más alto de la combinación de cada índice en la predicción del raquitismo por deficiencia de vitamina D fue de 0,951 (IC 95 %: 0,910-0,991).

Conclusión: el nacimiento prematuro, la alimentación artificial y la deficiencia de vitaminas K1 y K2 son factores de riesgo independientes para el metabolismo óseo en niños con raquitismo por deficiencia de vitamina D. Y estos factores de riesgo tienen valor predictivo y diagnóstico en el diagnóstico y manejo del raquitismo por deficiencia de vitamina D.

Palabras clave:

Raquitismo por deficiencia de vitamina D. Vitamina K. Densidad mineral ósea. Osteocalcina carboxilada.

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INTRODUCTION

Nutritional vitamin D deficiency rickets is a systemic chronic nutritional disease featuring bone lesions resulting from disorders of calcium and phosphorus metabolism due to vitamin D deficiency in children. Epidemiologic surveys (1) show that the incidence of nutritional vitamin D deficiency rickets decreases yearly in response to the improvement of socio-economic and cultural levels. However, preterm and twin-born infants are prone to nutritional vitamin D deficiency rickets as a result of increased vitamin D requirements due to rapid growth and development, which is complemented by insufficient vitamin D stored in the body.

Vitamin K, also known as clotting vitamins, is vital to human health. Vitamin K can be obtained from food and can also be synthesized and synthesized by intestinal bacteria. However, newborns are at risk of vitamin K deficiency because their immature livers do not use vitamin K effectively. In addition, due to the low content of vitamin K in breast milk, and vitamin K is difficult to transfer through the placental barrier, intestinal sepsis, their vitamin K reserves tend to be low (1,2). Vitamin K has been shown to be associated with bone metabolism in addition to coagulation and neonatal bleeding disorders. It affects the bone health of infants and children to a great extent (3,4).

Bone R-hydroxy glutamic acid protein (GLa), short for osteocalcin, falls into the category of vitamin K-dependent calcium-binding proteins. It is a sensitive and specific indicator reflecting osteoblast activity and bone metabolism status, and serves as a new biochemical marker with a broader application prospect.

Vitamin K is necessary for the activation of coagulation factors VII (proconvertin), IX (antihemophilic B), X (stuart factor) and prothrombin. By differentiating osteogenic, osteoclastogenic and stimulating cells in bone tissue, it upregulates the expression of bone marker genes by promoting bone mineralization in the extracellular matrix and inhibits the functional expression of osteoclasts. In other words, it exerts beneficial effects on both osteoclastogenesis and bone quality enhancement. Furthermore, vitamin K increases the rate of bone mineralization and inhibits bone matrix dissolution and bone calcium loss by promoting GLa protein γ -glutamate carboxylation and calcium salt deposition to achieve net bone calcium accumulation (5). In this sense, vitamin K can be inferred to be related to bone mineral density (BMD). A study in The Netherlands showed that infants and children have six times higher concentrations of uncarboxylated osteocalcin (ucOCN) compared to adults; this, combined with their low vitamin K status, increases the potential risk of osteoporosis (5). Data from a domestic study related to the nutritional status of pediatric skeletal vitamin K revealed a correlation between pediatric skeletal vitamin K deficiency and age; the more severe degree of skeletal vitamin K deficiency was predominantly in the age group of more than 3 months to 1 year, which is also the stage where the supply of vitamin K to the skeleton is also the most deficient. This is consistent with the finding that children in this age group are clinically prone to abnormal bone metabolism and susceptible to rickets (6,7).

Therefore, vitamin K is crucial in preventing fractures in children, apart from the relevance of vitamin D for children's bone health (8). Late vitamin K deficiency usually coexists with vitamin D deficiency rickets (9). A favorable vitamin K status has a close bearing on a significant increase in bone mass in children during puberty. It has been found that concomitant vitamin K and vitamin D supplementation in children with osteoporosis caused by long-term glucocorticoid use is significantly more effective in improving lumbar spine bone mineral density and blood osteocalcin concentration in children (10). Vitamin D levels are broadly accepted as one of the biochemical indexes for evaluating healthy bone growth. A favorable vitamin K status has a close bearing on a significant increase in bone mass in children during puberty. As for the possibility of vitamin K level as one of the biochemically sensitive indexes for the evaluation of bone metabolism and as one of the diagnostic indexes of vitamin D deficiency rickets, more in-depth investigations need to be carried out. In this study, children with vitamin D deficiency rickets were recruited to analyze the serum vitamin K levels in children with vitamin D deficiency rickets and to investigate the clinical diagnostic and therapeutic value of vitamin K in vitamin D deficiency rickets. By doing so, we aimed to provide some clinical guidance for the diagnosis and treatment of vitamin D deficiency rickets.

STUDY SUBJECTS AND METHODS

STUDY SUBJECTS

Fifty children with vitamin D deficiency rickets admitted to our hospital from March 2021 to March 2022 were recruited as the case group using convenience sampling; and an additional 50 children without bone health diseases during the same period of health checkup were selected as the control group.

The inclusion criteria were as follows:

1. Children diagnosed with vitamin D deficiency rickets according to the Guidelines for the Diagnosis and Treatment of Osteochondrosis and Rickets (9) developed by the Osteoporosis and Bone Mineral Salt Diseases Branch of Chinese Medical Association;
2. Inclusion criteria of abnormal bone metabolism: normal BMD ($Z > -1.0$), mild BMD deficiency ($-1.5 < Z \leq -1.0$), moderate BMD deficiency ($-2.0 < Z \leq -1.5$), severe BMD deficiency ($Z \leq -2.0$); this index was formulated and implemented with reference to the Z-value scoring criterion of Ultrasonic velocity in *Study on the Correlation Between Vitamin K Deficiency and Abnormal Bone Metabolism in Children* (11) by Wanyan Zewei; for the convenience of the study, those with mild, moderate, and severe BMD deficiencies were included in the abnormal BMD group;
3. Those aged 3 months-2 years of either gender;
4. Those with normal weight by reference to the *Reference Values for Body Weight, Body Length and Head Circumference for Chinese Infants aged 0 to 13 Weeks* (12);
5. Those with complete and valid medical records; and

6. Those in the control group who did not suffer from vitamin K deficiency, vitamin D deficiency rickets, bone pain, low bone density, bone morphology and other abnormal changes in bone diseases.

The exclusion criteria were as follows:

1. Children < 1 or > 2 years old;
2. Those with normal bone metabolism;
3. Those with combination of other underlying diseases, such as cold, cough, and runny nose;
4. Those with combination of severe respiratory, cardiovascular, cerebrovascular, urinary, immune, hepatic, biliary, endocrine system and other critical diseases;
5. Those with allergic diseases (e.g., skin needling, drug allergy) and history of taking vitamin D, K, etc. and history of taking drugs for other diseases within 3 months prior to enrollment;
6. Children with genetic diseases;
7. Those with an overweight;
8. Those with an incomplete grade of information; and
9. Those whose guardians did not sign the informed consent form or who were unwilling to participate in the experiment, whose clinical data were missing, whose compliance was poor and who did not follow the prescribed treatment, or who withdrew from the experiment in the middle of the study, resulting in the inability to obtain the real medical records, or whose data were mutilated, damaged, or had unclear handwriting.

The study was approved by the Ethics Committee of the hospital. The guardians of the subjects signed an informed consent form.

STUDY METHODS

Measurement of vitamin D

Sample collection

In the early morning fasting state, 2 mL of blood from the external elbow vein was collected and stored in a biochemical tube (labeled) (normal room temperature: 23 °C, storage time: 1 h), and centrifuged (centrifugation rate: 4000 rev/min, centrifugation time: 10 min); then the supernatant ($\geq 200 \mu\text{L}$) was placed in clean EP tubes and stored in a light-proof environment (light-proof environment: 4 °C) for subsequent testing.

Testing method

HPLC – MS / MS: 10 μL of internal standard working solution was placed in a centrifuge tube (1.5 mL), followed by the addition of 100 μL of blood sample to be tested, and then ethyl acetate (1.2 mL) was pipetted into the above centrifuge tube with a pipette gun, and mixed well (time: 5 min), then centrifuged again (centrifugation rate: 15,000 rev/min, centrifugation time: 10 min), and 1 mL of the supernatant was taken and blown dry;

next, 100 μL of methanol was added for mixing (time: 1 min), and 100 μL of the supernatant was fed in five injections of 20 μL /dose; finally, the final results were obtained.

Measurement of vitamin K

Sample collection

The same procedure as that for vitamin D.

Testing method

HPLC – MS / MS: 10 μL of internal standard working solution was placed in a centrifuge tube (1.5 mL), followed by the addition of 200 μL of blood sample to be tested, and then ethyl acetate (1000 μL) was pipetted into the above centrifuge tube with a pipette gun, and mixed well (time: 5 min), then centrifuged again (centrifugation rate: 15000 rev/min, centrifugation time: 10 min), and 900 μL of the supernatant was taken and blown dry; next, 150 μL of methanol was added for mixing (time: 1 min), and 100 μL of the supernatant was fed in ten injections of 10 μL /dose; finally, the final results were obtained.

Measurement of BMD, bone alkaline phosphatase (BALP) and trace elements: BMD was measured by ultrasonic bone strength and electronic spondrometer, BALP was measured by automated enzyme marker, and trace elements (calcium, phosphorus, etc.) were measured by atomic absorption spectrophotometry.

Diagnostic criteria for decreased BMD and osteoporosis

Normal bone mass ($Z > -1$), decreased BMD ($-2.5 \leq Z < -1$), osteoporosis ($Z < -2.5$), and abnormal BMD defined as $Z \leq -1$, which was formulated according to the *Guidelines for the Diagnosis and Treatment of Primary Osteoporosis (2017 Edition)* (13).

Classification criteria of vitamin D

Deficiency ($< 10 \text{ ng/mL}$), insufficiency (10-20 ng/mL), normal (20-100 ng/mL) and overdose ($> 100 \text{ ng/mL}$) in four dimensions according to the *Recommendations for the Prevention and Control of Micronutrient Deficiencies in Children (2010 Edition)* (14).

Classification criteria of vitamin K

Vitamin K1 and K2 are divided into three dimensions: deficiency ($K1 < 0.1 \text{ ng/mL}$, $K2 < 0.1 \text{ ng/mL}$), normal ($0.1 \leq K1 \leq 2.2 \text{ ng/mL}$, $0.1 \leq K2 \leq 0.86 \text{ ng/mL}$), and overdose ($K1 > 2.2 \text{ ng/mL}$, $K2 > 0.86 \text{ ng/mL}$) according to relevant standards issued by the Mayo Clinic of the U.S. and the MDI Biological Laboratory and in Germany (15).

DATA COLLECTION

Routine clinical data such as age, gender, height, weight, blood calcium, blood phosphorus, bone alkaline phosphatase (BALP), and 25 hydroxyvitamin D3 [25-(OH)D3] were collected from both groups.

STATISTICAL ANALYSIS

All data in this study were statistically processed using SPSS 26.0 statistical software. The K-S method was used for normality test; normally distributed measurement data were expressed as ($x \pm s$), and the t test was used for comparison of means between groups. Count data were expressed as frequency (n) or rate (%), and were tested by the χ^2 test. Pearson's correlation coefficient was used to calculate the correlation coefficient r . Furthermore, the risk factors for the development of vitamin D deficiency rickets were explored using logistic regression analysis; the predictive value of each index for the development of vitamin D deficiency rickets was investigated using the receiver operating characteristic curve (ROC). All tests were two-sided, with the test level set at $\alpha = 0.05$.

RESULTS

GENERAL DATA

In the case group, there were 50 cases, 29 males and 21 females, with a mean age of 1.29 ± 0.56 years; in the con-

trol group, there were 50 cases, 31 males and 19 females, with a mean age of 1.23 ± 0.34 years. No statistically significant difference was observed between the two groups in terms of gender, age, height, weight, blood calcium, blood phosphorus, and BALP ($p > 0.05$). However, there were statistically significant differences between the two groups in the level of 25-(OH)D3, the proportion of breastfeeding, and the proportion of preterm birth, as shown in table I.

Comparison of vitamin K levels and deficiency between the two groups

There were statistically significant differences in the levels of vitamin K1, the proportion of those with vitamin K1 deficiency, the levels of vitamin K2, and the proportion of those with vitamin K2 deficiency between the two groups; the levels of vitamin K1 and K2 in the case group were lower than those in the control group, and the proportion of those with deficiency was higher than that in the control group, as shown in table II.

Pearson correlation analysis of vitamin K and vitamin D deficiency rickets

Positive correlations were found between vitamin K1 and 25-(OH)D3, blood calcium, and blood phosphorus; likewise, positive correlations were also found between vitamin K2 and 25-(OH)D3, blood calcium, and blood phosphorus, as shown in table III.

Table I. Comparison of general data

Index	Control group (n = 50)	Case group (n = 50)	t/ χ^2 value	p-value
Age (yrs, $x \pm s$)	1.23 ± 0.34	1.29 ± 0.56	0.156	0.870
Gender (male/female)	31/19	29/21	0.167	0.683
Height (cm, $x \pm s$)	73.65 ± 5.87	73.45 ± 5.69	0.805	0.423
Weight (kg, $x \pm s$)	9.43 ± 1.56	8.88 ± 1.72	1.563	0.087
Blood calcium (mmol/L, $x \pm s$)	2.30 ± 0.13	2.28 ± 0.14	0.452	0.653
Blood phosphorus (mmol/L, $x \pm s$)	1.43 ± 0.31	1.41 ± 0.26	0.599	0.551
BALP (U/L, $x \pm s$)	181.11 ± 25.57	180.45 ± 26.54	0.144	0.886
25(OH)D3 (ng/L, $x \pm s$)	57.06 ± 13.57	13.88 ± 2.09	17.398	< 0.001
Feeding mode (cases)			43.717	< 0.001
Breastfeeding	40	7		
Artificial feeding	10	43		
Preterm birth (cases)	7	23	12.190	< 0.001

BALP: bone alkaline phosphatase; 25(OH)D3: 25-hydroxyvitamin D3.

MULTIFACTORIAL ANALYSIS OF VITAMIN D DEFICIENCY RICKETS

A logistic regression model was constructed with the occurrence of vitamin D deficiency rickets as the dependent variable (occurrence = 1, no occurrence = 0) and the statistically significant factors in the univariate analysis as the independent variables (25-(OH) D3 is an indicator of the body's vitamin D reserve. Low levels of 25-(OH) D3 indicate vitamin D deficiency, and the causal association between 25-(OH) D3 and vitamin D deficiency rickets has been established, so it was not included in the analysis). The grouping and coding of the variables are shown in table IV. Regression analysis showed that artificial feeding, preterm birth, vitamin K1 deficiency, and vitamin K2 deficiency were risk factors for the development of vitamin D deficiency rickets, as shown in table V.

PREDICTIVE VALUE OF INDEXES ON THE OCCURRENCE OF VITAMIN D DEFICIENCY RICKETS

Artificial feeding, preterm birth, vitamin K1, and vitamin K2 were all of predictive value for the development of vitamin D deficiency rickets. The area under the curve (AUC) of artificial feeding for predicting vitamin D deficiency rickets was 0.843 (95 % CI: 0.771-0.916); the AUC of preterm birth for predicting vitamin D deficiency rickets was 0.856 (95 % CI: 0.745-0.924); the AUC of vitamin K1 deficiency in predicting vitamin D deficiency rickets was 0.867 (95 % CI: 0.784-0.948); and the AUC of vitamin K2 deficiency in predicting vitamin D deficiency rickets was 0.912 (95 % CI: 0.897-0.988). Among them, the highest AUC of the combination of each index in predicting the occurrence of vitamin D deficiency rickets was 0.951 (95 % CI: 0.910-0.991), as shown in table VI.

Table II. Comparison of vitamin K levels and deficiency between the two groups

Index		Control group (n = 50)	Case group (n = 50)	t/ χ^2 value	p-value
Vitamin K1	Level (ng/L, $\bar{x} \pm s$)	1.432 \pm 0.654	0.076 \pm 0.021	9.393	< 0.001
	Number of deficiencies	2	15	11.977	< 0.001
Vitamin K2	Level (ng/L, $\bar{x} \pm s$)	0.719 \pm 0.213	0.078 \pm 0.021	8.593	< 0.001
	Number of deficiencies	5	38	44.431	< 0.001

Table III. Pearson's correlation analysis of vitamin K and vitamin D deficiency rickets

Item		Correlation coefficient <i>r</i>	p-value
Vitamin K1	25-(OH)D3	0.359	0.011
	Blood calcium	0.322	0.021
	Blood phosphorus	0.326	0.018
Vitamin K2	25(OH)D3	0.512	< 0.001
	Blood calcium	0.489	< 0.001
	Blood phosphorus	0.368	0.011

Table IV. Variable grouping and coding

Variable	Grouping	Coding
Artificial feeding	No	1
	Yes	2
Preterm birth	No	1
	Yes	2
Vitamin K1 level	Input at original value	
Vitamin K2 level	Input at original value	

Table V. Logistic regression analysis of risk factors for vitamin D deficiency rickets

Influencing factors	S.E.	Wald χ^2	p-value	OR	OR (95 % CI)
Artificial feeding	0.345	8.234	0.001	2.796	1.575-7.123
Preterm birth	2.256	6.208	0.001	3.456	2.757-5.112
Vitamin K1 deficiency	0.978	6.763	0.001	6.371	5.731-21.633
Vitamin K2 deficiency	1.123	7.423	0.001	9.563	7.931-32.263

Table VI. Predictive value of indexes on the occurrence of vitamin D deficiency rickets

Item	AUC	95 % CI	Cut-off value	Sensitivity (%)	Specificity (%)
Artificial feeding	0.843	0.771-0.916	-	81.31	84.54
Preterm birth	0.856	0.745-0.924	-	83.61	81.70
Vitamin K1 deficiency	0.867	0.784-0.948	0.216 ng/mL	90.44	89.48
Vitamin K2 deficiency	0.912	0.897-0.988	0.184 ng/mL	93.01	95.82
Combined prediction	0.951	0.910-0.991	-	95.24	97.73

DISCUSSION

Vitamin D deficiency rickets is associated with a deficiency of vitamin D during bone growth. It was previously believed that adequate vitamin D supplementation was sufficient for patients with vitamin D deficiency rickets. As modern medicine develops and advances, vitamin K intake is also found to be of necessity. Vitamin K is involved in human bone metabolism (16). Osteocalcin, also known as vitamin K-dependent bone γ -hydroxyglutamic acid protein, is abundant to the extent that its concentration and degree of carboxylation reflect the status of BGP in the femur, which accounts for 1-2 % of bone protein. BGP levels in children with vitamin D deficiency rickets were significantly higher than in normal children before treatment, which decreased significantly after treatment (17). Under the action of vitamin K-dependent carboxylase, all three glutamate residues at the BGP site (amino acids 17, 21, and 24) are evolved into carboxylated osteocalcin (cOC) by carboxylation. Once Ca^{2+} and carboxyapatite are deposited in combination with cOC, they participate in the bone mineralization process. Uncarboxylated osteocalcin (ucOC), as a specific expression in the structure of BGP (< 3 carboxylated residues), can be used as a sensitive indicator of the body's vitamin K status due to its extreme ease of release into the bloodstream (18). The BALP levels in the vitamin K2 group (< 0.1 ng/mL) were lower than those in the vitamin K2 group (\geq 0.1 ng/mL), suggesting a correlation between vitamin D deficiency and BALP. In the case of vitamin D deficiency, the absorption of calcium and phosphorus in the intestines is reduced, resulting in impaired bone formation and compensatory osteoblastic activity. BALP is a direct response to osteoblast activity. The degree of increased BALP activity has a significant grade correlation with children, susceptibility to fright, sleep disturbance, hyperhidrosis, cranial softening and pregnancy factors (such as dietary monotony, no vitamin D preparations).

The possible mechanisms linking vitamin K2 and vitamin D deficiency rickets can be categorized as follows: First, vitamin K2 is involved in the transcription of bone-specific genes. Vitamin K2 has been shown to induce the production of osteoblast markers, indirectly activating steroids and human steroid xenobiotics. It is not only beneficial for increasing ALP and insulin-like growth factor expression, but also broadens

bone formation capacity and growth space (supported by osteocalcin, collagen, etc.), thereby contributing to the structure of calcium salt deposition. Secondly, vitamin K2 is a coenzyme of γ -glutamyl-carboxylase, which not only maintains a special affinity and activity for carboxylation into osteocalcin (OC) and Ca^{2+} structure, but also facilitates calcium salt deposition and bone mineralization rate enhancement. Adequate vitamin K2, a source of bone deposition and mineralization, is beneficial in improving Ca^{2+} expression in the blood of children with vitamin D deficiency rickets (19). Third, vitamin K2 inhibits calcium loss and the expression of osteoclast differentiation factors such as IL-1 and IL-6 in the blood of children with vitamin D deficiency rickets. All these confirm the correlation of bone metabolism between vitamin K2 deficiency and children with vitamin D deficiency rickets.

It was also shown in the present study that there is an association between vitamin K and vitamin D deficiency rickets and that vitamin K deficiency is a risk factor for the development of vitamin D deficiency rickets in children, which is consistent with the above findings. This suggests that vitamin K2 deficiency may lead to reduced bone mass and undermineralization in children with vitamin D deficiency rickets, thereby participating in the onset, progression, and prognosis of the disease (20,21). Regarding the improvement of BMD and BGP, the clinical effects of vitamin K2 supplementation are superior to those of vitamin D supplementation as evidenced by numerous previous studies (22,23).

We also found that preterm delivery and artificial feeding are risk factors for the development of vitamin D deficiency rickets. Seventy-five percent of fetal calcium and phosphorus are stored during the last three months of gestation. Therefore, the calcium and phosphorus levels in infants and children born prematurely are significantly lower than those in normal term infants, depending on the date of preterm birth and individual circumstances. It has been reported in the relevant literature (24) that preterm infants may have relatively weak calcium retention capacity due to early separation from their mothers, and they are at high risk of rickets because of their fast growth rate, presence of growth catch-up growth period, and high requirement of vitamin D and calcium compared with normal term infants.

Recent years have witnessed the rapid development of modern society, with scientists and nutritionists sparing no effort

to improve dairy products. This has led to the widespread use of artificial feeding, which is gradually replacing breastfeeding. Chinese infant formula food industry standard “Food Safety National Standard Infant Formula Food” (GB10765-2010) (25) and “Food Safety National Standard Infant and early Childhood Formula Food” (GB10767-2010) (26) clearly specify the nutritional requirements of infant artificial milk, including the content of vitamins, protein, fatty acids, etc., in order to ensure that the nutritional needs of infants are met. However, despite being as close as possible to breast milk in terms of nutritional value, artificial milk products have never been able to replace breast milk. This is because the nutritional composition of breast milk is very complex and perfect, with hundreds of ingredients, many of which are bioactive and contain many unique growth factors, which are very important for the development and growth of neonatal brain nerve tissue. Although formula can imitate and add certain nutrients, formula lacks many ingredients in breast milk, including many kinds of living cells, cholesterol, polyamines, free amino acids, enzymes and many other bioactive ingredients. Moreover, the disinfection process used to produce formula slightly changes the structure of milk protein, thus missing the anti-infective protection of cross-species (27). There is a significant correlation between the feeding mode and the prevalence of rickets in infants within 6 months of age, and the prevalence of rickets is higher in artificially fed infants. Breast milk contains all the nutrients needed by infants. While preventing diarrhea and respiratory infections, it reduces nutrient loss and consumption, and plays a vital preventive role in the prevention and treatment of rickets (28). In this regard, breastfeeding should be strongly advocated, and complementary foods should be added in a timely manner, so as to develop good eating habits, avoid partiality and picky eating, and rationalize the diet to ensure balanced nutrition.

Nevertheless, there are some limitations in this study. First, the relatively small sample included in this study may lead to a bias between the results of the study and the actual clinical situation. Second, the inclusion of only those admitted to our hospital may have biased the extrapolation of the findings. Finally, time constraints in the study process may have resulted in some shortcomings in the observation time.

CONCLUSION

In conclusion, children suffering from vitamin D deficiency rickets present significant vitamin K deficiency, being more pronounced in the case of vitamin K2 deficiency. Vitamins K1 and K2 are known to influence bone metabolism in children with vitamin D deficiency rickets; they show a positive correlation with vitamin D deficiency rickets. Preterm birth, artificial feeding, and vitamin K1 and K2 deficiency are independent risk factors for the development of bone metabolism in children with vitamin D-deficiency rickets. Preterm birth, artificial feeding, and vitamins K1 and K2 are of predictive and diagnostic value in the diagnosis and management of vitamin D deficiency rickets.

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Trabajo Original

Decision tree model development and *in silico* validation for avoidable hospital readmissions at 30 days in a pediatric population

Desarrollo de un modelo de árbol de decisión y validación in silico de reingresos hospitalarios evitables a 30 días en una población pediátrica

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Abstract

Background and objective: identifying patients at high risk of avoidable readmission remains a challenge for healthcare professionals. Despite the recent interest in Machine Learning in this topic, studies are scarce and commonly using only black box algorithms. The aim of our study was to develop and validate *in silico* an interpretable predictive model using a decision tree inference to identify pediatric patients at risk of 30-day potentially avoidable readmissions.

Methods: a retrospective cohort study was conducted with all patients under 18 years admitted to a tertiary university hospital. Demographic, clinical and nutritional data were collected from electronic databases. The outcome was the potentially avoidable 30-day readmissions. The J48 algorithm was used to develop the best-fit trees capable of classifying the outcome efficiently. Leave-one-out cross-validation was applied and we computed the area under the receiver operating curve (AUC).

Results: the most important attributes of the model were C-reactive protein, hemoglobin and sodium levels, besides nutritional monitoring. We obtained an AUC of 0.65 and accuracy of 63.3 % for the full training and leave-one-out cross-validation.

Conclusion: our model allows the identification of 30-day potentially avoidable readmissions through practical indicators facilitating timely interventions by the medical team, and might contribute to reduce this outcome.

Keywords:

Hospital readmission.
Pediatrics. Decision tree.
Algorithms. Supervised machine learning.

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Artificial intelligence: the authors declare not to have used artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

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Resumen

Antecedentes y objetivo: identificar a los pacientes con alto riesgo de readmisión sigue siendo un desafío para los profesionales de la salud. A pesar del interés reciente en el uso del aprendizaje automático en este tema, los estudios son escasos y comúnmente utilizan solo algoritmos de caja negra. El objetivo de nuestro estudio fue desarrollar y validar *in silico* un modelo predictivo interpretable utilizando una inferencia de árbol de decisión para identificar a los pacientes pediátricos en riesgo de readmisiones potencialmente evitables a los 30 días.

Métodos: estudio de cohortes retrospectivo realizado con todos los pacientes menores de 18 años ingresados en un hospital universitario terciario. Se recopilaron datos demográficos, clínicos y nutricionales de bases de datos electrónicas. El resultado fue la readmisión potencialmente evitable a los 30 días. Se utilizó el algoritmo J48 para desarrollar los árboles de mejor ajuste capaces de clasificar el resultado de manera eficiente. Se aplicó la validación cruzada *leave-one-out* y se calculó el área bajo la curva operativa del receptor (AUC).

Resultados: los atributos más importantes del modelo fueron la proteína C-reactiva, los niveles de hemoglobina y sodio, además del monitoreo nutricional. Obtuvimos una AUC de 0,65 y una precisión del 63,3 % en el entrenamiento completo y la validación cruzada *leave-one-out*.

Conclusión: nuestro modelo permite la identificación de readmisiones potencialmente evitables a los 30 días mediante indicadores prácticos, facilitando intervenciones oportunas por parte del equipo médico y podría contribuir a reducir este resultado.

Palabras clave:

Readmisión hospitalaria.
Pediatria. Árbol de decisión.
Algoritmos. Aprendizaje
automático supervisado.

INTRODUCTION

Pediatric hospital readmissions have received attention in recent decades. The 30-day readmission rate for hospitalized children is still high, ranging from 4.40 to 29.50 % (1,2). Studies show that hospital readmission can negatively influence patients' quality of life (3) with short and long-term consequences (3-7). Besides, they can contribute substantially to the increase in healthcare costs (8-10). A study of pediatric patients revealed that the hospital cost for all admissions and readmissions is US\$17.3 billion, of which 21.5 % (US\$3.71 billion) was spent during a readmission hospital stay (10). Another study found that of the US\$11.6 billion spent annually for all hospitalizations, being US\$2.0 billion (16.9 % of total hospitalization costs) related to all-cause readmissions within 30 days (9).

Despite that, identifying patients at high risk of readmission and implementing timely interventions remains a challenge for healthcare professionals. Recently, predictive modeling has been pointed out as an efficient method to stratify the risk of readmission, allowing the targeting of preventive interventions to patients at risk, thus optimizing the allocation of clinical resources (11). Tools capable of early identification of patients at risk of readmission have been proposed in order to helping to minimize the incidence of hospital readmissions (2,12-15). However, there is still a lack of practical and easily understood predictive models to support clinical decisions. The reported models are often poorly designed, being mainly based on black-box algorithms (2,12-15), which makes it impossible to know how clinical factors led to forecasts.

For healthcare applications, the model's interpretability is as important as its performance. So, when it is possible to observe the attributes and the decision paths rationally, the predictive clinical model became easier for their application by the health team. Given this, decision trees, based on a supervised machine learning approach, can be an excellent option. Since this method relates the nodes to each other hierarchically (16), resulting in an easy model to interpret. Despite the known nutritional problems with negative outcomes, are scarce the studies investigating these aspects. So, some studies with artificial intelligent have highlighted that nutrition should be considered in several areas of health that keep a biological relationship with nutrition (17).

Therefore, the aim of our study is to build an interpretable predictive model using a decision tree algorithm to identify patients at the risk of 30-day potentially avoidable readmissions.

METHODS

STUDY DESIGN AND SETTINGS

A retrospective cohort study was conducted at a tertiary university hospital from January 1st, 2014 to December 31st, 2018. We included 528 children and adolescents between 0 and 18 years old, who had all data retrieved from electronic databases (biochemical exams and nutritional monitoring). We excluded hospitalizations that resulted in hospital death (not at risk for readmission outcome), discharges against medical advice (not at the opportunity to implement care plan and discharge instruction) and patients with incomplete data in the electronic databases.

In order to avoid algorithmic bias when we perform machine learning techniques, we try to minimize the class imbalance since that can produce classifiers whose predicted class probabilities are geared toward the majority class ignoring the significance of minority classes. To address class imbalance problems, a 1:1 nested case-control design was performed, we included patients who readmitted and had complete data (cases) and randomly selected patients with complete data who did not readmit (controls) (Fig. 1). The university's Ethics Committee approved this study (CAAE 51706221.3.0000.5152, protocol number: 5.003.236). This manuscript followed the guide "Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis" (TRIPOD) statement for the reporting of the prediction model.

PREDICTORS SELECTION

Demographic data (age and sex) and clinical data (wards, admission type, diagnoses and length of hospital stay — number of days), biochemical exams (blood count, leukogram, sodium and C-reactive protein — CRP) and presence or absence of any nutritional monitoring during hospitalization and were obtained from electronic databases.

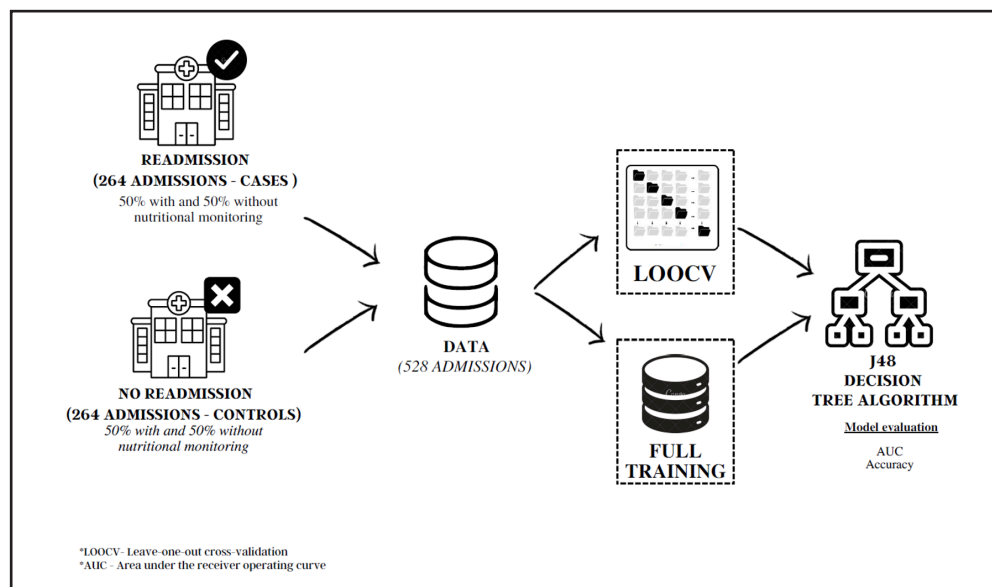


Figure 1.

Study flow diagram.

We classified the age of patients in six groups, according to childhood and adolescence periods of growth and development: < 1 years, ≥ 1 to < 5 years, ≥ 5 to < 9 years, ≥ 9 to < 13 years, ≥ 13 to < 16 years and ≥ 16 years. Length of hospital stay (LOS) was categorized into quartiles: < 8, ≥ 8 to < 17, ≥ 17 and < 38 and ≥ 38 days. All blood tests were performed at a single laboratory. CRP was measured by methods immunoturbidimetry using a Cobas® 6000 analyzer, sodium measured by potentiometric methods and hematological parameters were analyzed using an automated Sysmex XN-3000™ hematology analyzer. We categorized biochemical exams as altered and normal, considering age and sex. Nutritional data were not filled in a standardized way in the electronic databases, so it was not possible to classify the nutritional status of patients. Therefore, we could only observe whether the child had any nutritional monitoring during hospitalization. Therefore, we created a variable showing patients who had nutritional monitoring during hospital stay (with or without nutritional monitoring during hospitalization).

OUTCOME

The outcome was the 30-day potentially avoidable readmissions, considered as a new admission within this short period after the immediately previous hospital discharge. Thus, all unavoidable readmissions, all patients admitted to wards with planned hospitalizations (obstetrics, gynecology and transplant) or with predictable admissions, such as labour/delivery, and chemotherapy or radiotherapy treatments (ambulatory care) were excluded.

STATISTICAL ANALYSIS

Descriptive data were summarized using proportions or means (\pm standard deviation, SD). For the statistical analysis, we use the

R Project (version 4.0.3), the RStudio (version 4.0.2), and considered the 95 % confidence intervals (95 % CI). The machine learning-based decision tree algorithm J48, present in the Weka suite, was used to develop best-fit trees in order to select the minimum set of characteristics capable of classify patients at risk of 30-day potentially avoidable readmissions efficiently. The J48 algorithm produces decision trees based on the concept of information gain ratio, thereby reducing entropy and improving the tree's predictive accuracy. Based on this concept, the J48 algorithm searches for the best attribute and threshold and divides the data into two subsets: those with attribute values above the threshold and those below or equal. This process is repeated for each subset created until a stop criterion is found, which ensures that the most informative attributes are used to construct a decision tree that effectively models the underlying patterns in the data.

The leave-one-out cross-validation (LOOCV) applied to estimate the classification accuracy and test the generalizability of the model. We computed the area under the receiver operating curve (AUC). We also estimate others measures of diagnostic performance model such as the specificity, sensitivity, post-positive predictive value and negative predictive values. We performed the analyses using WEKA software (*Waikato Environment for Knowledge Analysis*, version 3.6.1).

RESULTS

Of the 528 patients aged between 0 and 18 years, 60.2 % (318) were male, 33.5 % (177) had under one year of age. The frequency of 30-day potentially avoidable readmissions was 50.0 % (264). Of these, 31.10 % (82) had a length of hospital stay less than 8 days, 70.8 % (187) and 85.6 % (226) had hemoglobin and CRP levels altered, respectively (Table I).

Considering all available predictors, a decision tree inferred by from the J48 method was constructed to classify

patients with a risk of 30-day potentially avoidable readmissions (Fig. 2). Regarding the model, the health team should look the C-reactive protein firstly. If the C-reactive protein is greater than 0.5mg/d, the hemoglobin should be observed. If it's showed a normal level, the nutrition monitoring should be considered because if the patient has not a monitoring the readmission risk is greater. The decision tree algorithm

to classify readmission vs non-readmission proposed the use of CRP, hemoglobin, sodium levels and nutritional data, obtaining an AUC of 0.65 and accuracy of 63.3 % the full training (FULL) and leave-one-out cross-validation (LOOCV) with specificity (68.37 %) and sensitivity (60.4 %). Besides that, their positive and negative predictive values were 76.52 % and 50.76 %, respectively (Fig. 2).

Table I. Demographic, clinical and biochemical variables for potentially avoidable 30-day readmission

Predictors	All % (n)	30-day readmissions % (n)	
		No 50 (264)	Yes 50 (264)
Sex, male % (n)	60.2 (318)	53.8 (142)	66.7 (176)
<i>Age group, years</i>			
< 1	33.5 (177)	43.9 (116)	23.1 (61)
≥ 1 and < 5	26.9 (142)	25.8 (68)	28.0 (74)
≥ 5 and < 9	13.8 (73)	12.9 (34)	14.8 (39)
≥ 9 and < 13	11.7 (62)	5.3 (14)	18.2 (48)
≥ 13 and < 16	7.8 (41)	6.8 (18)	8.7 (23)
≥ 16	6.3 (33)	5.3 (14)	7.2 (19)
<i>Wards</i>			
Clinical	76.1 (402)	70.1 (185)	82.2 (217)
Urgent/Emergency/Surgical	10.6 (56)	9.1 (24)	12.1 (32)
Newborns	13.3 (70)	20.8 (55)	5.7 (15)
<i>Admission type</i>			
Elective	9.1 (48)	11.0 (29)	7.2 (19)
Urgent or Emergency	90.9 (480)	89.0 (235)	92.8 (245)
<i>Length of hospitalization, days</i>			
< 8	23.5 (124)	15.9 (42)	31.1 (82)
≥ 8 and < 17	25.2 (133)	31.4 (83)	18.9 (50)
≥ 17 and < 38	26.1 (138)	23.9 (63)	28.4 (75)
≥ 38	25.2 (133)	28.8 (76)	21.6 (57)
<i>Hemoglobin, g/dL</i>			
Normal	38.3 (202)	47.3 (125)	29.2 (77)
Altered	61.7 (326)	52.7 (139)	70.8 (187)
<i>Red cell distribution width, %</i>			
Normal	2.3 (12)	2.7 (7)	1.9 (5)
Altered	97.7 (516)	97.3 (257)	50.2 (259)
<i>C-reactive protein, mg/dL</i>			
Normal (< 0.5)	22.0 (116)	29.5 (78)	14.4 (38)
Altered (≥ 0.5)	78.0 (412)	70.5 (186)	85.6 (226)
<i>Sodium, mEq/L</i>			
Normal (≥ 134)	94.7 (500)	92.8 (245)	96.6 (255)
Altered (< 134)	5.3 (28)	7.2 (19)	3.4 (9)
<i>Nutritional monitoring</i>			
Yes	50.0 (264)	50.0 (132)	50.0 (132)
No	50.0 (264)	50.0 (132)	50.0 (132)

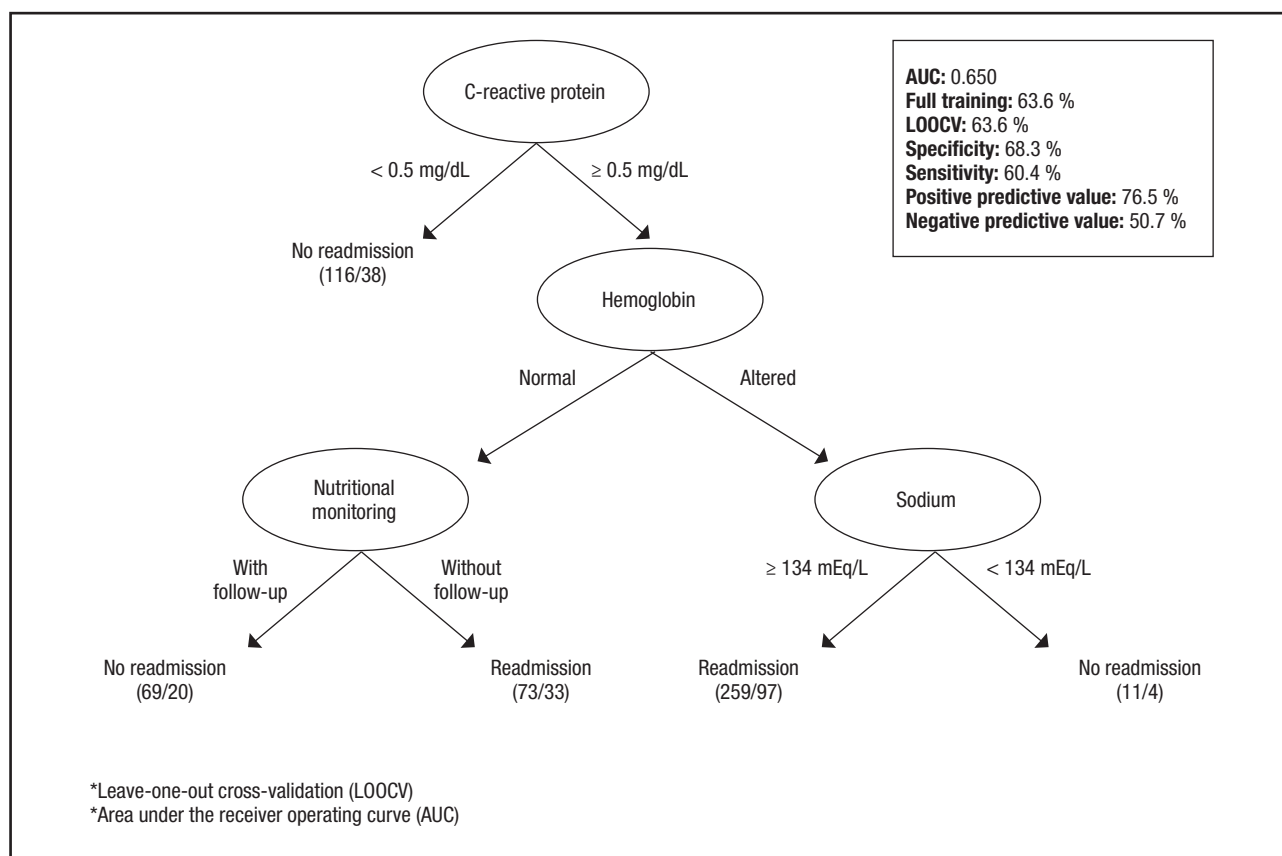


Figure 2.

Decision tree algorithm proposed to differentiate patients with 30-day potentially avoidable readmissions. The total number of classified admissions (correct and incorrect) for each class is shown in parentheses for each terminal node. Incorrectly classified admissions appear after a slash "/". The area under the receiver operating curve (AUC), full training (FULL) and leave-one-out cross-validation (LOOCV) accuracies are shown in the figure.

DISCUSSION

In this study, we used the J48 algorithm to build a classification model for 30-day potentially avoidable readmissions. The most important attributes for the model were CRP, hemoglobin and sodium levels, besides nutritional monitoring. Our findings were confirmed using the leave-one-out cross-validation. To the best of our knowledge, our study is the first to build a prediction model based on a decision tree with only three levels and confirmation by leave-one-out cross-validation. Being a model of easy understanding and application in clinical practice, making clear the contribution and direction of each association, as well as using attributes routinely found in hospital services. Furthermore, the rule found by our model applies to 63.6 % of new cases.

Previous studies had reported many risk factors involved with increased risk of hospital readmission: age (18-20), multimorbidity (11,13,19,21), prolonged duration of the last hospital stay (18,21,22), polypharmacy (15,23) and presence of diagnostics/conditions like anemia, malnutrition, cancer and global developmental delay (1,20). However, hospital readmission is still a

recurring problem and difficult clinical management, involved with short and long-term deleterious effects (3-7), besides contributing substantially to hospital costs (8-10). A study investigating Intensive Care Unit (ICU) readmissions observed that early markers can be used to anticipate patients at high risk of clinical deterioration after ICU discharge (24). The early identification of patients at greater risk of readmission provides opportunities for targeting interventions and allocating clinical and financial resources. In this sense, predictive models have been proposed in the literature, with variable performances such as AUC of 0.65 using Naive Bayes for all-cause 30-day readmission (12), AUC of 0.65 with Gradient Boosted for 30-day unplanned hospital readmissions (13), AUC of 0.73 using Support Vector Machines with Polynomial Kernel for at-discharge models (14), and even AUC of 0.81 with XGBoost for unplanned readmissions within 30 days (2) all for 30-day hospital readmission. However, there are few practical and interpretable models that are easy to understand and apply, capable of supporting clinical decisions.

In this sense, we use a machine learning decision tree-based algorithm in order to build an interpretable model capable of

identifying patients at risk of hospital readmission. Despite presenting a modest performance, $AUC = 0.65$, our results are relevant and capable of identifying new patients with a risk of readmission in 63.6 % of cases ($LOOCV = 63.6\%$). This validation *in silico* performed by leave-one-out cross-validation simulates the model performance as if it were another population (Wong, 2015). Besides that, we found good specificity (68.37 %) and sensitivity (60.4 %) besides a lower probability of negative predictive values, reinforcing a good model performance.

Therefore, with these measures of diagnostic performance, our model can effectively contribute to clinical practice, since it is a model that is easy to understand and apply in hospital routine, besides employing only relevant and easily got attributes in medical services.

In the model built, using the J48 algorithm, we identified that the most relevant attribute was the CRP levels, with more information in each iteration, being placed as the root of our decision tree, in which their high levels contribute to a risk of readmission. CRP is an acute phase protein, considered a sensitive and rapid response marker of inflammation. Studies have suggested that high CRP concentrations are correlated with the presence of ongoing organ dysfunction (25,26). So, the elevated CRP may serve as an indirect marker of disease severity, and could be linked to a higher risk of hospital readmission (25,26). A study found that high CRP levels were associated with a higher risk of readmission at 7 days (25), and also with a higher risk of adverse outcome after discharge from the intensive care unit (26).

Our decision tree also used hemoglobin levels in order to identify patients at risk of readmission. For patients with normal hemoglobin levels, it is necessary to assess the presence or absence of nutritional monitoring during hospitalization. Patients without nutritional support during hospitalization have a risk of being readmitted when compared to those followed up by a nutritionist.

Nutritional data have already been explored in previous observational studies, however, in most cases, they only assess the association of malnutrition with hospital readmission (1,20). However, they cannot address the relevance of nutritional monitoring during hospitalization. At least 80 % of patients admitted to a hospital must undergo nutritional screening within the first 24 hours of admission (27). Nutritional screening is the initial step allowing the identification of patients at nutritional risk and early intervention when necessary, minimizing deleterious effects related to nutritional status (28). However, regarding the nutritional approach in pediatric patients at the hospital level, there is still no consensus and the tools are scarce and little used (29). A study carried out in Brazil revealed that 43.3 % of medical records did not contain any records of the children's nutritional status (30). According to the authors, this reiterates the under-reporting of this important data by the entire health team that assists hospitalized children (30). Because of this deficiency, many hospitalized patients may not receive any type of nutritional monitoring, which would make it difficult to identify nutritional losses with negative effects on their health. Therefore, it is relevant, besides malnutrition, to assess the effectiveness of nutritional monitoring and its contribution to hospital readmission.

On the other hand, if the hemoglobin levels are altered, it is necessary to assess the sodium levels. One study found that the hemoglobin level is inversely correlated with 30-day hospital readmission rates (31). Low hemoglobin levels may be related to anemia, a condition often diagnosed in hospitalized children (32-34) that can be both a symptom and a complication of many diseases. Studies suggest that anemia is a negative prognostic factor and may contribute to the worsening of clinical outcomes, besides negatively affecting the child's health, with long-term deleterious effects (32,35). Moreover, sodium levels may contribute to identifying patients at risk of hospital readmission. Abnormal sodium levels are one of the most common electrolyte disturbances in hospitalized patients and have been associated with worse clinical outcomes. Studies have revealed that hyponatremia is associated with hospital readmission (36-38). However, in our study, we found no association for sodium levels below 134 mEq/L. One hypothesis, for the absence of association, may be because of the low frequency of hyponatremia (5.3 %) in the evaluated patients. Nevertheless, sodium levels above 134 mEq/L were associated with hospital readmission, and this rule applies to almost 50 % of the patients evaluated. Studies suggest that sodium levels may be a marker of the severity of the underlying disease, being related to an increase in negative health outcomes such as mortality (36,39,40), increased length of stay (36,37,40), or yet hospital readmission (36-38).

Hospital readmission is a challenging outcome, it contributes substantially to increased costs and is often associated with adverse health outcomes. Therefore, models capable of predicting the risk of readmission are of interest, these tools can help identify and reduce readmission, improve overall patient care and reduce healthcare costs. In our study we built a classification model for 30-day potentially avoidable readmissions using the J48 algorithm. We showed that one of the relevant predictors was nutritional monitoring, often neglected by predictive models. Future studies should be carried out exploring nutritional data, aiming to deepen knowledge and make health professionals aware of the importance of nutritional screening.

Some limitations for this study need to be pointed out. First of all, the extrapolation of the data must be careful, since this study was carried out with pediatric patients from a tertiary university hospital. Secondly, the small sample size, since the absence of complete data made it impossible to have a larger database. Algorithms are more effective when used in large databases. However, the present study has strengths; we evaluated all available data during the study period, applied LOOCV cross-validation, used predictors relevant to the pediatric population and were easily accessible, and finally, we sought to build a model that was easy to interpret and apply in practice.

CONCLUSION

The decision tree model found making showed that the CRP, hemoglobin, sodium levels and nutrition monitoring are the most important to classify 30-day potentially avoidable readmissions.

Our model allows the identification of individuals at risk of readmission, in an easy and practical way, facilitating the targeting of interventions by the medical team, and contributing to minimize this outcome.

STATEMENT OF AUTHORSHIP

Dr. Silva conceptualized and investigate the study, designed the methodology, performed the formal analyses and data curation of the study, drafted the initial manuscript and reviewed the manuscript. Drs. Laurence Amaral, Matheus Gomes and Pedro Bertarini designed the methodology, performed the formal analyses and data curation of the study, critically reviewed and revised the manuscript. Drs. Marcelo Albertini, André Backes conceptualized and investigated the study, critically reviewed and revised the manuscript. Dr. Pena conceptualized and investigated the study, performed data curation, critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

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Trabajo Original

Obesidad y síndrome metabólico

Prevalence of the genetic variant rs61330082 and serum levels of the visfatin gene in Mexican individuals with metabolic syndrome: a clinical and bioinformatics approach

Prevalencia de la variante genética rs61330082 y niveles séricos del gen de la visfatina en individuos mexicanos con síndrome metabólico: una aproximación clínica y bioinformática

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Abstract

Background: metabolic syndrome (MetS) is a group of clinical anomalies that share an inflammatory component of multifactorial etiology.

Objectives: the present study aims to relate the genetic variant (rs61330082 C/T) with dietary patterns in the presence of MetS and the application of molecular docking according to the genotype and associated transcription factors.

Methods: 197 individuals aged 18 to 65 were included, from whom anthropometric measurements were taken, and a blood sample from the forearm. DNA extraction and enzymatic digestion were performed to determine the genotype of each participant by PCR-RFLP. Dietary patterns were analyzed using a nutritional questionnaire validated for the Mexican population. Serum levels of the protein visfatin were assessed by ELISA. Finally, bioinformatics tools were used for molecular docking to infer the binding of transcriptional factors in the polymorphic region.

Results: the TT genotype was present in only 10 % of the population. Women carrying the CT+TT genotype, according to the dominant genetic model, had higher serum levels of triglycerides and VLDL-C. Statistical analysis did not show a significant association between the presence of MetS and the dominant CT+TT model (OR = 1.41, 95 % CI = 0.61-3.44, $p = 0.53$). We identified PAX5 as a transcription factor binding to the polymorphic site of this genetic variant.

Conclusions: this study demonstrated a significant association between the genetic variant (rs61330082 C/T) and lipid parameters. Women carrying the T allele have a higher risk of high triglyceride levels, a criterion for metabolic syndrome.

Keywords:

Metabolic syndrome.
Genetic variant. *Visfatin*.
Dietary patterns.
Bioinformatics.

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Abstract

Objetivos: el presente estudio pretende relacionar la variante genética (rs61330082 C/T) con los patrones dietéticos en presencia de SM y la aplicación del acoplamiento molecular según el genotipo y los factores de transcripción asociados.

Métodos: se incluyeron 197 individuos de entre 18 y 65 años, a los que se tomaron medidas antropométricas y una muestra de sangre del antebrazo. Se realizó una extracción de ADN y una digestión enzimática para determinar el genotipo de cada participante mediante PCR-RFLP. Los patrones dietéticos se analizaron mediante un cuestionario nutricional validado para la población mexicana. Los niveles séricos de la proteína visfatina se evaluaron mediante ELISA. Finalmente, se utilizaron herramientas bioinformáticas de acoplamiento molecular para inferir la unión de factores transcripcionales en la región polimórfica.

Resultados: el genotipo TT solo estaba presente en el 10 % de la población. Las mujeres portadoras del genotipo CT+TT, según el modelo genético dominante, presentaban niveles séricos más elevados de triglicéridos y VLDL-C. El análisis estadístico no mostró una asociación significativa entre la presencia de MetS. y el modelo dominante CT+TT (OR = 1,41; IC 95 % = 0,61-3,44; $p = 0,53$). Identificamos PAX5 como un factor de transcripción que se une al sitio polimórfico de esta variante genética.

Conclusiones: este estudio demostró una asociación significativa entre la variante genética (rs61330082 C/T) y los parámetros lipídicos. Las mujeres portadoras del alelo T presentan un mayor riesgo de niveles elevados de triglicéridos, un criterio de síndrome metabólico.

Palabras clave:

Síndrome metabólico.
Variante genética. Visfatina.
Patrones dietéticos.
Bioinformática.

INTRODUCTION

Metabolic syndrome (MetS) is a severe health problem worldwide, with a global prevalence of 37.4 % (1). In 2020, Mexico reported a 41.7 % prevalence of MetS in a population of subjects aged 35-70 years (2). The diagnosis of MetS is defined by the presence of three or more metabolic alterations, such as high concentrations of cholesterol, triglycerides, decreased HDL cholesterol, glucose intolerance, and the presence of visceral obesity (3-5), the latter being an essential factor, since it predisposes to arterial disease, diabetes-related complications and various types of cancer (3,4).

The pathophysiology of MetS is not fully described, but it is known to be influenced by environmental (such as dietary habits) and genetic variables. However, how these factors interact is not fully understood since MetS is significantly affected by chronic low-grade inflammation (5). Adipose tissue is an organ with important endocrine functions, including the stimulation of anti-inflammatory cytokines such as IL-10 and IL-5 and proinflammatory cytokines such as IL-32 and visfatin secreted by monocytes, and therefore actively participates during MetS progression (6,7).

Nicotinamide phosphoribosyltransferase, also known as visfatin/NAMPT/PBEF, has been recognized as an adipokine, cytokine, and NAD⁺ precursor enzyme and plays an important role in metabolism (8,9). This adipokine is mainly expressed in adipose tissue but is also secreted in other tissues such as skeletal muscle, spleen, testes, and bone marrow (10,11). Visfatin can increase cytokine synthesis in monocytes, so elevated levels of these proinflammatory markers can trigger different systemic signaling cascades in organs and tissues (12).

The *visfatin* gene, located on chromosome 7q22.2.2, consists of 11 exons and ten introns, has a length of 36,908 bp, which translates into a protein of 491 amino acids that varies in weight from 52 to 57 kDa, and has a promoter region, in which some genetic variants have been described, including -1535C/T (rs61330082), which has been related to alterations in the transcriptional rate of visfatin (13,14). This genetic variant has been associated with effects on tumorigenesis and chronic inflammation, which increases the risk of different types of cancer and diabetes *mellitus* (15).

As visfatin is secreted in various target tissues and affects rather complex biological pathways, it isn't easy to understand its role in the development of MetS (16). Bioinformatics is fundamental to researching and understanding metabolic syndrome. These analysis offers tools and methods to analyze large amounts of biological data due to its ability to interact between biology and informatics, considering sciences such as genomics, transcriptomics, and metabolomics, which is essential for deciphering the mechanisms underlying the pathogenesis of MetS. Bioinformatics can identify potential biomarkers, understand molecular interactions, and design more precise therapeutic strategies through data integration and biological network analysis (17).

Due to the epidemiological burden of MS in Mexico, intervention through prevention and control studies is crucial (18); therefore, the present study evaluates for the first time in a grouped manner the genetic, biochemical and pathophysiological parameters of MS and visfatin in a Mexican population of young adults.

The study aimed to examine the impact of the NAMPT rs61330082 genetic variant and serum levels of this adipokine on risk factors for metabolic syndrome, as well as the interaction of molecular docking according to genotype and associated transcription factors.

SUBJECTS AND METHODS

STUDY POPULATION

This was a cross-sectional study with subject selection centered on non-probabilistic sampling; 197 individuals participated, who met the inclusion criteria (147 women and 50 men), aged between 18 and 65 years, who were previously informed about the implications of their participation before signing the informed consent. The study was conducted at the Centro de Atención Médica Integral, under the Centro Universitario de Los Altos, with the full approval of the institutional ethics committee under number (CEI-04/2022-08), complying with the guidelines established by the general health law on research and the declaration of Helsinki. Participants with autoimmune diseases, consumption of anti-inflammatory drugs, and pregnant women were excluded.

METABOLIC SYNDROME PARAMETERS

Anthropometric analysis was performed by determining weight and height with the Tanita BC-533. Each subject presented at least three of the five established risk criteria: fasting triglycerides ≥ 150 mg/dL, HDL cholesterol (HDL-c) $< 40/50$ mg/dL in men/women, increased waist circumference $\geq 102/88$ cm, men/women, blood pressure $\geq 130/85$ mmHg, systolic and diastolic, respectively or antihypertensive treatment, as well as elevated fasting glucose ≥ 110 mg/dL predetermined from the MetS. Patients without MetS did not present the characteristics described by ATP III (19).

GENOTYPING

According to the provider's guidelines, DNA was extracted from peripheral blood leukocytes using the PureLink™ Genomic DNA Mini Kit (K182002). Genotyping of the rs61330082 genetic variant was performed by polymerase chain reaction-restriction fragment length (PCR-RFLP), with the conditions described in a previous study (20). A 283-bp fragment was amplified using primers specific for the rs61330082 fragment of the *visfatin* gene, which had the following sequence 5'TGTTTCAAACCTC-GTTGTTGCTGA-3' and 5'AGTGATGGTGGTGGTGGTGA-3'. The PCR cycling conditions using Applied Biosystems™, Simpli-Amp™ Thermocycler (A24811) were as follows: initial denaturation at 95 °C for 5 min, followed by 32 cycles of denaturation at 95 °C for 30 s; subsequently, alignment was carried out at a temperature of 60 °C for 45 s, culminating in an extension at 72 °C for 1 min and an extension at 72 °C for 10 min. Once the fragment of interest was amplified, enzymatic digestion was performed using the *Bst*NI enzyme, and the products were visualized in 6.0 % polyacrylamide gel stained with silver nitrate. Three genotypes could be characterized: homozygous polymorphic TT (218 and 65 bp), heterozygous CT (283, 218, and 65 bp), and homozygous wild-type CC (283 bp).

SERUM VISFATIN MEASUREMENTS AND BIOCHEMICAL PARAMETERS

Visfatin levels were measured by enzyme-linked immunosorbent assay (ELISA) using the commercial Human Visfatin/PBEF ELISA kit, R&D Systems, catalog number DY4335-05. A microplate reader determined the absorbance at 450 and 570 nm (Multiskan GO, Thermo Scientific). All participants had a peripheral blood sample taken after fasting for 8 hours. For serum collection, tubes were centrifuged for 20 minutes at 3500 rpm. Laboratory analyses included the following biochemical parameters: serum glucose, triglycerides (TG), total cholesterol (CHOL), and high-density lipoprotein cholesterol (HDL-C) levels, which were performed with an Abbott Aeroset automatic analyzer. The Friedewald equation determined low-density lipoprotein cholesterol (LDL-C) levels. Finally, to obtain the very low-density lipoprotein cholesterol (VLDL-C) values, total TG (mg/dL) was divided among five.

EVALUATION AND APPLICATION OF MINI-ECCA

The dietary pattern survey of the study population was applied at the same time as the anthropometric measurements; these data were evaluated using the Mini-ECCA questionnaire, which was previously developed and validated by Bernal et al. (21). The Mini-ECCA includes 12 items based on Mexican and international guidelines on food and non-alcoholic beverage consumption, using images to estimate portions. Each item receives a score of 0 (unhealthy) or 1 (healthy), and according to the total score, each participant is classified into a group according to dietary quality. The Mini-ECCA presented significant reproducibility ($\rho = 0.713$, $p < 0.001$) and high precision concordance (ICC = 0.841, 95 % CI: 0.779-0.885). These results indicate that this survey is a highly reliable tool, appropriate for dietary assessment and orientation in the university population as well as in young adults (22,23).

BIOINFORMATICS ANALYSIS

We searched for possible transcription factors that bind to the region of the genetic variant using the HaploReg v4.2 websites (24). The 3D DNA structure was then generated using BIOVIA Discovery Studio V21.1.0.20298 software. The sequences used were 5'AAAGATCATGGAAGTGAAGGTATCACCACGCACTCACCAATGTAGTAAATACTAGTAC3' and 5'AAAGATCATGGAAGTGAAGGTATCACCATGCACTCACCAATGTAGTAAATACTAGTAC3'. The protein structures of the transcription factors were obtained from the AlphaFold website (25). DNA-protein docking was performed with pyDockDNA server software (26), with standard parameters, and the results obtained were visualized in BIOVIA Discovery Studio V21.1.0.20298 software.

STATISTICAL ANALYSIS

The patients' characteristics were reported in frequency, percentages, mean, and standard deviation. The SPSS v.22 statistical program was used, taking into account a significance level of 0.05. The inheritance model of the allelic and genotypic frequencies of the variant rs61330082 was analyzed by chi-square test, previously confirming the Hardy-Weinberg equilibrium. Disease risk was estimated using the odds ratio, with a 95 % confidence interval. After the corresponding normality tests, the association between quantitative study variables was analyzed using the Mann-Whitney U test or student's t-test. The sample size was determined by considering the global allele frequencies according to the National Center for Biotechnology Information (NCBI) database of the rs61330082 variant of the NAMPT gene.

To calculate the sample size, the estimation formula for a proportion was used considering the following parameters: a confidence level of 95 %, precision of 5 %, and an expected proportion of the variant of 15 %, resulting in a sample size of 196 individuals.

RESULTS

One hundred ninety-seven patients were recruited for the present research, classified as patients with metabolic syndrome ($n = 31$) and controls ($n = 166$). These current data represent a prevalence of 15 % in the population studied, as shown in table I. As expected, the five diagnostic criteria considered for the presence of MetS were significantly different from the control group. The control group had slightly higher visfatin levels but did not represent a significant difference between groups. After analyzing the dietary pattern data acquired from the Mini-ECA, no significant variations in food consumption were found between the control group and the people with MetS (Table I).

Table II shows the distribution of the rs61330082 genetic variant in the study, according to the presence or absence of Mets. The genotypic frequencies in the total population studied were as follows: the CC genotype 72 (36 %), CT 107 (54 %), and TT 19 (10 %), the frequency for the C allele was 62 %, and for the T allele it was 38 %. Likewise, we used the dominant pattern genetic model (CC vs CT+TT) as well as the recessive model (TT vs CC+CT) to determine the risk of presenting metabolic syndrome according to the five criteria evaluated by the ATP III, which showed no statistically significant association between the control and MetS groups.

Likewise, we found that within the diagnostic criteria for MetS, the female carriers of the CT+TT genotype (dominant genetic pattern) had higher levels of TG and VLDL-C ($p = 0.006$ and $p = 0.026$, respectively), as shown in table III. This same result was also observed in the whole sample analyzed but not in the group of men. We also evaluated the association between inheritance patterns and serum visfatin levels, which did not show a statistically significant difference between the study groups. In addition, according to mini-ECCA, dietary habits showed no association when analyzed by any of the three inheritance models (data not shown).

Finally, we decided to explore the effect of this genetic variant on the binding of some transcription factors using a bioinformatics approach. We infer three transcription factors that probably bind to the site of this genetic variant: NRSF, NRSF, and SIX5. We then verified these results by DNA-protein docking, the results of which are shown in figure 1. The polymorphic variant does not appear to affect the binding energetics of the NRSF and SIX5 transcription factors. However, it does affect the binding of PAX5, as a significant change in pyDockDNA scoring is observed. pyDockDNA scoring represents the total binding energy between transcription factors and DNA from electrostatic, solvation, and Van der Waals energies between protein and DNA.

Table I. Anthropometrics, criteria MetS, nutritional and biochemical parameters of the study population

Criteria MetS*	MetS (n = 166)	Controls (n = 31)	p
Age (years)	37.60 ± 14.03	25.77 ± 9.44	< 0.001
SBP (mmHg)	129.13 ± 20.52	111.77 ± 12.47	< 0.001
DBP (mmHg)	86.47 ± 13.25	75.89 ± 8.50	< 0.001
Fasting glucose (mg/dl)	114.26 ± 31.23	92.58 ± 23.71	< 0.001
Total cholesterol (mg/dl)	193.83 ± 70.74	169.41 ± 76.73	0.106
Triglycerides (mg/dl)	196.62 ± 89.92	114.78 ± 55.22	< 0.001
HDL-cholesterol (mg/dl)	40.89 ± 19.30	46.54 ± 20.16	0.156
Waist circumference (cm)	95.55 ± 14.38	78.20 ± 12.28	< 0.001
Visfatin (ng/mL)	16.32 ± 19.72	31.61 ± 50.14	0.102
Sex			
Male n (%)	12 (40.0)	38 (22.8)	0.066
Female n (%)	19 (60.0)	128 (77.2)	
Dietary patterns Mini-ECCA			
Unhealthy food intake n (%)	18 (58.1)	88 (48.9)	0.543
Habits in need of improvement n (%)	2 (6.5)	29 (16.1)	
Unhealthy eating habits n (%)	8 (25.8)	47 (26.1)	
Healthy food intake n (%)	3 (9.7)	16 (8.9)	

*Quantitative variables are presented as mean ± SD.

Table II. Genotype visfatin rs61330082 C > T and allele distributions in MetS patients and control subjects

Models and alleles	MetS, n (%)	Control, n (%)	p	OR, 95 % CI
<i>Codominant</i>				
CC	9 (30.0)	63 (37.5)	Reference	
CT	19 (63.3)	88 (52.4)	0.344	0.66 (0.28-1.55)
TT	2 (6.7)	17 (10.1)	0.814	1.21 (0.24-6.15)
<i>Dominant</i>				
CC	9 (30)	63 (37.8)	Reference	
CT + TT	21 (70)	104 (62.3)	0.530	1.41 (0.61-3.44)
<i>Recessive</i>				
CC + CT	28 (89.82)	150 (93.33)	Reference	
TT	2 (10.18)	17 (6.67)	0.740	0.63 (0.13-2.51)
<i>Alleles</i>				
C	37 (61.7)	214 (64)	Reference	
T	23 (38.3)	122 (36)	0.720	0.90 (0.51-1.61)

Categorical variables were compared using the χ^2 test. Odds ratios (OR) and 95 % confidence intervals (CI) were used for the assessment of risk factors. Significance level: $p < 0.05$.

Table III. Analysis of biochemical parameters according to the dominant model of inheritance in women

Variable	CC, n = 52	CT + TT, n = 95	p
SBP (mmHg)	110.04 ± 14.28	113.48 ± 14.64	0.142
DBP (mmHg)	77.38 ± 10.66	77.22 ± 10.09	0.781
Fasting glucose (mg/dL)	92.33 ± 16.20	91.81 ± 12.02	0.415
Total cholesterol (mg/dL)	173.50 ± 88.19	176.39 ± 79.58	0.417
Triglycerides (mg/dL)	103.90 ± 52.00	131.20 ± 63.18	0.006
HDL-cholesterol (mg/dL)	42.78 ± 19.74	46.96 ± 19.65	0.200
VLDL-cholesterol (mg/dL)	19.53 ± 10.85	24.38 ± 13.17	0.026
Waist circumference (cm)	76.90 ± 10.69	77.37 ± 12.76	0.697
Visfatin (ng/mL)	20.10 ± 23.40	25.78 ± 37.35	0.759

*Quantitative variables are presented as mean ± SD.

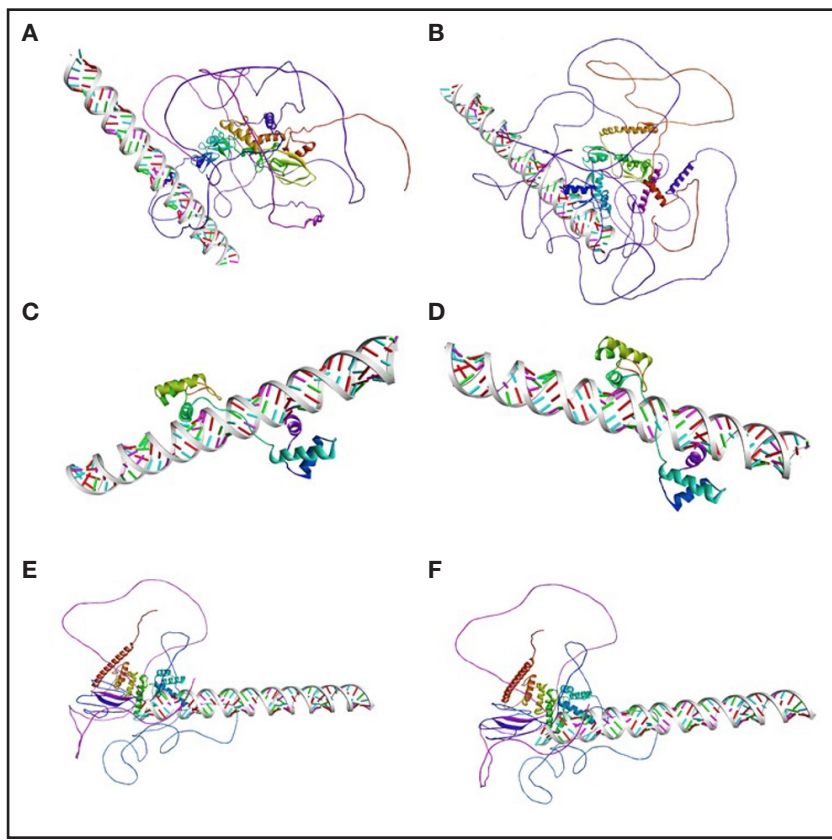


Figure 1.

Docking protein-DNA analysis between the gene region where the gene variant is located and the inferred transcription factors. A. Docking wild variant-NRSF, pyDockDNA scoring -115.02. B. Docking polymorphic variant-NRSF, pyDockDNA scoring -159.26. C. Docking wild variant-PAX5, pyDockDNA scoring -192.66. D. Docking polymorphic variant-PAX5, pyDockDNA scoring -192.47. E. Docking wild variant-SIX5, pyDockDNA scoring -58.21. F. Docking polymorphic variant-SIX5, pyDockDNA scoring -58.20.

DISCUSSION

One of the most significant results in the present study is the association between the presence of the genotypes CT+TT of the rs61330082 genetic variant and the increase in triglyceride levels, as well as VLDL in women from western Mexico diagnosed with metabolic syndrome.

It is important to consider each component of MetS, as TG levels in the Mexican population have been associated with an increased risk of coronary artery disease (2). Studies in different populations worldwide have evaluated a series of genetic variants in the promoter region of the *visfatin* gene. The results show an association with metabolic abnormalities associated with the diagnostic criteria for MetS (27–29). Ooi et al. reported for the first time that the genetic variant -3187 G>A is in linkage disequilibrium with the variant rs61330082, which indicates that the alleles -3187 A/-1535 T behave the same, so therefore our results coincide with this author regarding the increase of triglycerides in women carriers of the dominant model CT+TT (30).

The rs61330082 variant found in the promoter region can transcriptionally influence variations promoted by the genotype (27). Pleiotropic capacities of visfatin have been observed, so alterations in the transcriptional rate of visfatin promote changes in NAD⁺ cosubstrate levels, including at the intracellular level (iNAMPT). It has been described that iNAMPT catalyzes the rate-limiting step in the NAD⁺ biosynthesis pathway from nicotinamide. Therefore, NAD⁺

insufficiency contributes to various diseases, such as metabolic disorders, cancer, aging, and inflammation, by producing TNF- α and IL-6. When NAD⁺ concentrations are decreased, there is an energy imbalance between NADH/NADPH, leading to a more significant amount of oxidative stress due to the activation of the HIF1- α pathway under hypoxic conditions, which plays a crucial role in positively regulating NAMPT, influencing lipid processing, glucose homeostasis and dietary intake (31). It has also been shown that an adequate amount of NAD⁺ activates SIRT3, which promotes an improvement in oxidative metabolism and, in turn, a decrease in lipid abnormalities, such as elevated triglyceride levels (32).

In our study population, no difference was found between subjects with and without MetS concerning serum visfatin levels. However, Masood et al. investigated the association of other visfatin genotypes with MetS in the Pakistani population, finding significant differences in serum visfatin levels in subjects who presented MetS vs controls (33). In a study conducted on Mexican women with COPD, a decrease in serum visfatin levels was observed in the control group (34). These data are relevant since our population was predominantly female and without MetS. eNAMPT has not been associated with sustained viral response (15). Still, as an adipocytokine generated mainly through visceral adipose tissue, it impacts glucose and lipid metabolism while attenuating chronic inflammation associated with obesity. The connection between visfatin and metabolic abnormalities in patients with obesity or insulin resistance is still debated.

In our study, we evaluated the rs61330082 genotype and the dietary patterns associated with the development of MS in the population of western Mexico for the first time. However, no associations were found between the dietary component, the genetic variant of *visfatin*, and the risk of developing MetS. Some authors have been able to show that there is a positive association, which has an essential influence on the increase in susceptibility in the biochemical alterations of the components of MetS, among which is the change in eating habits, lifestyle, and the genetic factor of the Mexican population (35,36). Therefore, the associations not found in our study could be due to the characteristics of the study population, which has a mean age of 27 years. Higgins et al. showed that subjects in the university stage are less likely to develop metabolic alterations related to MetS criteria (37).

The evaluation of dietary patterns, assessed using the Mini-EC-CA, suitable for the Mexican population, showed a greater orientation towards an intake of unhealthy foods. Still, no significant differences were obtained between MetS and dietary patterns. On the other hand, considering the genetic variant (rs61330082) and dietary patterns, it has been shown that other factors, considering the microbiota, circadian cycles, regular exercise, and mental health in the Latino population, could delay the development of MetS (37-39).

The presumed promoter region before the *visfatin* gene has been confirmed with multiple binding sites for transcription factors. Therefore, in this study, we performed a molecular docking test with a computational approach based on structures that predict the interactions between ligands and targets, generate the binding mode, and estimate the corresponding affinity. Another important finding of this study highlights the impact on transcriptional regulation. Our bioinformatics analyses show the strong coupling effect of the transcription factor PAX 5 with the polymorphic genetic variant, so we suggest that there is an influence on transcriptional regulation. When a protein-ligand complex's binding free energy (ΔG) is lower, the complex is more stable (40). In previous studies of biological process analysis, the role of PAX5 in transcriptional processes and the regulation of proinflammatory genes has been identified (41).

Finally, we are aware that our work has some limitations. This study is cross-sectional. Therefore, it is impossible to infer cause and effect in the development of MetS from personal genetic variations with nutritional interactions. Consequently, further studies on MetS are needed to understand the complexity of the factors involved in its pathogenesis. Therefore, the application of a longitudinal study that considers nutritional and genetic variables of *visfatin* and its involvement in systemic inflammation could explain the development of MetS and thus promote personalized nutrition and precision treatment with the aim of preventing comorbidities such as cardiometabolic risks.

An important limitation of the study was the lack of an instrument to assess caloric intake and the food groups from which daily calories were obtained, which prevented an adequate analysis of the caloric intake of the study subjects. In addition, the absence of an instrument to assess physical activity limited the ability to assess sedentary lifestyle and energy expenditure. An-

other limitation of this study is the low prevalence of MetS in the study subjects since we cannot deduce the incidence in the general population. However, more participants covering a broader age spectrum are required. Lastly, it is necessary to support the results of the *in silico* analysis with laboratory tests of an experimental nature.

CONCLUSION

This study found an association of the rs61330082 genetic variant in women carrying the CT+TT genotype with higher levels of TG and VLDL-C. However, no significant association was found between genotype and MetS development or serum *visfatin* levels. It should be noted that our bioinformatics study showed the interaction of the genotype with the transcription factor PAX5. Through the results obtained from this work, it is important to encourage translational studies with a dietary, genetic, inflammatory, and bioinformatics approach so that prevalent pathologies in the world population can be addressed in a preventive manner due to the tremendous epidemiological burden in health that it is currently facing.

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Trabajo Original

Obesidad y síndrome metabólico

Differences in the cluster of depressive symptomatology among bariatric surgery candidates, long-term bariatric surgery patients, and subjects with a major depressive disorder without obesity

Diferencias en el perfil de síntomas depresivos entre pacientes candidatos a cirugía bariátrica, pacientes intervenidos de cirugía bariátrica a largo plazo y personas con trastorno depresivo sin obesidad

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Abstract

Introduction: depression is more frequent among people with obesity (PwO) compared to the general population. Depression seems to improve after bariatric surgery (BS) at short term, but data are inconclusive at long term. Besides, it is not known whether depressive symptoms among PwO are similar to those people with a major depression without obesity.

Objectives: we aimed to study whether there are differences regarding depressive symptomatology among subjects seeking BS or patients after BS in the long-term compared with subjects with MDD.

Methods: the Beck Depression Inventory (BDI) was administered to three groups: 52 patients seeking BS (OB), 135 patients with a BS with a minimum follow-up of 18 months (BS) and 45 subjects with a MDD (MDD).

Results: the MDD obtained the higher score with the BDI whether compared to the OB (18.9 ± 12.7 vs 14.2 ± 6.9 ; $p = 0.01$) or the BS (18.9 ± 12.7 vs 8.1 ± 8 ; $p < 0.0001$). Also, BS presented a lower BDI than the OB (8.1 ± 8 vs 14.2 ± 6.9 ; $p < 0.0001$). The MDD scored higher in the psychological domain than patients in the OB (9.9 ± 7.5 vs 5.7 ± 5.1 ; $p < 0.0001$) as well as in the BS (9.9 ± 7.5 vs 3.1 ± 3 ; $p < 0.0001$). There was a negative correlation between a greater score in the somatic domain and %EPP ($p = 0.04$).

Conclusions: at long term, depressive symptomatology among subjects with a BS remained lower compared to PwO seeking BS. PwO presented a different cluster of depression compared to individuals with a MDD. BS reduces the somatic depressive cluster at long term, although its presence is associated to a lesser weight loss.

Keywords:

Obesity. Bariatric surgery. Depression. Long-term.

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Resumen

Introducción: la depresión es más frecuente entre las personas con obesidad (PwO) en comparación con la población general. La depresión parece mejorar después de la cirugía bariátrica (CB) a corto plazo, aunque los datos no son concluyentes a largo plazo. Además, no se sabe si los síntomas depresivos entre las PwO son similares a los de las personas con depresión mayor (TDM) sin obesidad.

Objetivos: nuestro objetivo fue estudiar si existen diferencias con respecto a la sintomatología depresiva entre sujetos en protocolo de CB o pacientes sometidos a CB a largo plazo en comparación con pacientes con TDM.

Métodos: se administró el Inventario de Depresión de Beck (BDI) a tres grupos: 52 pacientes en lista de CB (OB), 135 pacientes intervenidos de CB con un seguimiento mínimo de 18 meses (CB) y 45 sujetos con TDM.

Resultados: el TDM obtuvo mayor puntuación en el BDI sea comparado con OB ($18,9 \pm 12,7$ vs. $14,2 \pm 6,9$; $p = 0,01$) o CB ($18,9 \pm 12,7$ vs. $8,1 \pm 8$; $p < 0,0001$). Además, CB presentó un BDI menor que OB ($8,1 \pm 8$ vs. $14,2 \pm 6,9$; $p < 0,0001$). TDM obtuvo puntuaciones más altas en el dominio psicológico que los pacientes del OB ($9,9 \pm 7,5$ vs. $5,7 \pm 5,1$; $p < 0,0001$) y del CB ($9,9 \pm 7,5$ vs. $3,1 \pm 3$; $p < 0,0001$). Hubo una correlación negativa entre un mayor puntaje en el dominio somático y %EPP ($p = 0,04$).

Conclusiones: a largo plazo, la sintomatología depresiva entre los pacientes sometidos a CB permaneció más baja en comparación con PwO que buscaban CB. Las personas con CB presentaron sintomatología depresiva diferente en comparación con las personas con TDM. La CB reduce el cuadro depresivo somático a largo plazo, aunque su presencia se asocia a una menor pérdida de peso.

Palabras clave:

Obesidad. Cirugía bariátrica. Depresión. Largo plazo.

INTRODUCTION

Obesity has become one of the leading health problems over the last century (1). This disease is not only associated with metabolic comorbidities but also psychological conditions. In fact, it is well known that obesity and depressive disorder share common pathopsychological pathways, and that there is a bidirectional association between these two diseases. It has been shown that obesity increases the risk of presenting a major depressive disorder (MDD) (RR = 1.55) as well as a MDD is a predisposing factor for obesity (RR = 1.58). Moreover, the lifetime prevalence of a MDD among the general population is about 10 % and increases up to 20 % among subjects with obesity seeking bariatric surgery (2).

Bariatric surgery (BS) is nowadays the most effective procedure for weight loss among subjects with severe obesity and it accounts for significant amelioration and/or resolution of medical comorbidities related to obesity. However, the effects of this surgical procedure on psychological conditions and, specifically on depression or depressive symptomatology, are controversial. At short-term, most studies published so far have found that there is a significant amelioration or even a remission regarding depressive symptomatology. It is possible that depression may not influence weight loss in the short-term because initial weight loss is more driven by metabolic factors due to anatomical changes in the gastrointestinal tract than psychological or behavioral factors. However, the effects of BS at long-term, when weight loss has reached a plateau, are more controversial and, some of the studies performed at this time suggest that there could be a relapse in depressive symptoms among these patients. This could be of particular interest because up to 20-30 % of patients regain weight after BS in the long-term, and psychological factors have been proposed as one of the precipitating factors of this relapse in weight (3,4).

On the other hand, MDD comprises a wide and heterogeneous spectrum of depressive symptomatology. Particularly among subjects with type 2 diabetes, it has been shown that, despite

the prevalence of this psychiatric disorder is greater compared to general population, the type of depressive symptoms is different than the typical melancholic depression, showing more physical symptomatology (5). What is more, when considering people with obesity, few studies have suggested that these subjects could present more frequently with an atypical depression rather than a melancholic one (6-8). Therefore, failure to examine depressive subtypes may explain some of the inconsistencies in the literature and suggest these subtypes may be important to determine their impact on weight outcomes.

We aimed to study whether there are significant differences regarding depressive symptomatology among subjects seeking bariatric surgery or patients after BS in the long-term compared with subjects with a MDD without obesity.

MATERIAL AND METHODS

SUBJECTS

For this cross-sectional study, participants were recruited consecutively from the outpatient's clinic of an Endocrine and a Psychiatry Department from a Tertiary Center. The sample comprised three groups: patients attending an obesity unit seeking bariatric surgery (OB), patients who had undergone a bariatric surgery procedure with a minimum follow-up of 18 months (BS) and subjects with a diagnosis of a MDD who attended the outpatient's Psychiatry Department (MDD). For all groups, the inclusion criterion was being 18 years of age or older. Other additional inclusion criteria for the OB group were having a BMI equal or greater than 35 kg/m² and not having undergone a bariatric surgery procedure before. Exclusion criteria for the MDD group were having another psychiatric condition other than depression, such as schizophrenia, bipolar disorder or suicide attempt. Written informed consent was obtained for both groups prior to study participation. The study was approved by the Ethics Committee of the hospital.

ASSESSMENT OF DEPRESSIVE DISORDER

To rule out the presence and the severity of depressive disorder, the Spanish version of the Beck Depression Inventory (BDI) was administered to all participants. The BDI is a 21-item questionnaire that assesses mood over the previous month. Total scores range from 0 to 63 with greater scores indicating more symptoms of depression. The BDI has been widely used as a screening tool for depression in the general population. In this setting, a cutoff equal or higher than 13 is suggestive of significant depressive symptoms. The BDI has a high coefficient alpha (0.80), its construct validity has been well established, and it is a valuable tool which differentiates between depressed from non-depressed people. Also, among subjects with a known MDD, BDI has been proved to be useful to assess the severity of depressive symptoms as well as the response to the antidepressant therapy prescribed. In people with a MDD, a total score of 0-13 is considered a minimal range, 14-19 is mild, 20-28 is moderate and 29-63 is severe. However, among people living with obesity, a cutoff equal or greater than 16 for the entire 21-item measure exhibited the best balance between sensitivity and positive predictive value. This greater cutoff would be able to detect more than 70 % of the patients with a MDD yet provide more than 70 % of certainty that a person screening positive has this condition. Furthermore, as scores in every question of the BDI range between 0 and 3, we considered as a significant result equal to or greater than 2. Also, apart from the total scored obtained after administering the BDI, we divided all items of the BDI into three categories: psychological/cognitive sub score (score ranging from 0 to 33), negative emotions sub score (score ranging from 0 to 6) and somatic sub score (score ranging from 0 to 24) (9,10).

SOCIODEMOGRAPHIC AND CLINICAL PARAMETERS

In all groups, gender, age, height, weight, BMI, educational level, partnership status and employment situation were recorded

from electronic medical records. Height and weight were measured while each participant was wearing indoor clothing, without shoes. BMI was calculated as weight divided by height squared.

STATISTICAL ANALYSIS

Statistical analyses were performed using the IBM® SPSS® Statistics Version 21.0. Initial analyses were descriptive and included calculation of mean, median and standard deviation for continuous variables and frequencies for categorical variables. The distribution of the sample was analyzed by the Kolmogorov-Smirnov test. The three groups were compared regarding sociodemographic variables, BMI and BDI by using χ^2 tests for categorical variables and t tests and univariate analysis of variance (ANOVA) for continuous variables. The statistical significance level for all tests was set at an α of $p < 0.05$.

RESULTS

DESCRIPTIVE CHARACTERISTICS

A total of 135 patients were included in the BS group (72.6 % ♀, 50.1 ± 12.8 years, initial BMI = 46.9 ± 6.7 kg/m², time since surgery 86.9 ± 45.8 months, current BMI = 35.3 ± 6.9 kg/m²), 52 subjects in the OB group (65.4 % ♀, 49.2 ± 12.2 years, BMI = 46.9 ± 6.9 kg/m²), and a total of 45 subjects were included in the MDD group (53.3 % ♀, 38 ± 13.9 years, BMI = 25.9 ± 3.2 kg/m²).

Group comparisons on BMI and sociodemographic characteristics are represented in table I. As expected, BMI was significantly greater in the two groups that included people with obesity compared to the MDD group (46.9 ± 6.7 kg/m² vs 35.3 ± 6.9 kg/m² vs 25.9 ± 3.2 kg/m²; $p < 0.0001$). Also, current BMI was higher among OB group subjects compared to the BS sample (46.9 ± 6.9 kg/m² vs 35.3 ± 6.9 kg/m²; $p < 0.0001$).

Table I. Demographic and clinical parameters of patients with obesity (OB), subjects who underwent bariatric surgery (BS) and individuals with a major depressive disorder (MDD)

	OB group (n = 52)	BS group (n = 135)	MDD group (n = 45)	p
Sex (female) (%)	65.4	72.6*	53.3*	0.02
Age (years)	49.2 ± 12.2	50.1 ± 12.8	38 ± 13.9	< 0.001
Educational level (superior) (%)	31	30	32	NS
Employment situation (active)	33	32	34	NS
Marital status (single) (%)	37	41	35	NS
Time since BS (months)	NA	86.9 ± 45.8	NA	-
Current BMI (kg/m ²)	46.9 ± 6.9	35.3 ± 6.9	25.9 ± 3.2	< 0.0001
Presurgical BMI (kg/m ²)	NA	46.9 ± 6.7	NA	-

Data are mean \pm SD or %. BS: bariatric surgery; BMI: body mass index.

Furthermore, patients with a MDD were younger compared with both OB (38 ± 13.9 vs 49.2 ± 12.2 years; $p < 0.001$) and BS groups (38 ± 13.9 vs 50.1 ± 12.8 years; $p < 0.0001$). Besides, there were more women included in the BS group than in the MDD sample (72.6% vs 53.3% ; $p = 0.02$). However, no differences were seen among the three groups regarding sociodemographic characteristics.

ASSESSMENT OF DEPRESSIVE SYMPTOMATOLOGY

Table II and figure 1 present the results of the different groups comparisons regarding both the total score obtained with the BDI, and the three sub scores (psychological/cognitive, negative emotions and somatic depressive symptoms). There were significant differences among the three groups regarding the scores obtained in both total and different compounds of the BDI. The MDD group obtained the higher score for significant depressive symptoms by using the BDI, whether compared to the OB group (18.9 ± 12.7 vs 14.2 ± 6.9 ; $p = 0.01$) or the BS group (18.9 ± 12.7 vs 8.1 ± 8 ; $p < 0.0001$). Also, patients on the BS presented a significantly lower BDI score than subjects on the OB (8.1 ± 8 vs 14.2 ± 6.9 ; $p < 0.0001$).

When we considered the psychological domain of the BDI, subjects included in the MDD group scored higher than patients in the OB group (9.9 ± 7.5 vs 5.7 ± 5.1 ; $p < 0.0001$) as well as in the BS sample (9.9 ± 7.5 vs 3.1 ± 3 ; $p < 0.0001$). Moreover, the OB group had also a greater punctuation in this psychological sub score compared to subjects who had undergone BS (5.7 ± 5.1 vs 3.1 ± 3 ; $p = 0.006$).

Negative emotions and suicidal thoughts are included in the negative emotions sub-score. The MDD group showed the greater score in this sub-scale, whether compared with the OB group (1.5 ± 1 vs 0.4 ± 0.3 ; $p < 0.0001$) or the BS sample (1.5 ± 1 vs 0.4 ± 0.2 ; $p < 0.0001$). No differences were seen in terms of negative emotions between the OB and the BS group (0.4 ± 0.3 vs 0.4 ± 0.3 ; $p = 0.9$).

Somatic sub-score did not differ between the MDD group, and the subjects included in the OB group (7.4 ± 4.5 vs 8 ± 2.9 ; $p = 0.4$). However, in BS patients, the score obtained in this somatic sub-scale was significantly lower, either comparing with the MDD group (4.6 ± 3.8 vs 7.4 ± 4.5 ; $p < 0.0001$) or the OB group (4.6 ± 3.8 vs 8 ± 2.9 ; $p < 0.0001$).

When we only considered subjects included in the OB group, we found that there was a negative correlation between a greater score in the somatic domain of depressive symptomatology and the percentage of excess weight loss (%EPP) ($p = 0.04$).

Table II. Comparison of the global score, and psychological, negative emotions and somatic subscores among patients with obesity (OB), subjects who underwent bariatric surgery (BS) and individuals with a major depressive disorder (MDD)

	OB group (n = 52)	BS group (n = 135)	MDD group (n = 45)	p
BDI global score	$14.2 \pm 6.9^*$	$8.1 \pm 8^\#$	$18.9 \pm 12.7^{**}$	$0.01^* < 0.0001^\#$
Psychological subscore	$5.7 \pm 5.1^*$	$3.1 \pm 3^\#$	$9.9 \pm 7.5^{**}$	$< 0.0001^{**}$
Negative emotions subscore	$0.4 \pm 0.3^*$	$0.4 \pm 0.2^\#$	$1.5 \pm 1^{**}$	$< 0.0001^{**}$
Somatic subscore	$8 \pm 2.9^\#$	$4.6 \pm 3.8^{**}$	$7.4 \pm 4.5^*$	$< 0.0001^{**}$

Data are mean \pm SD. BDI: Beck Depression Inventory.

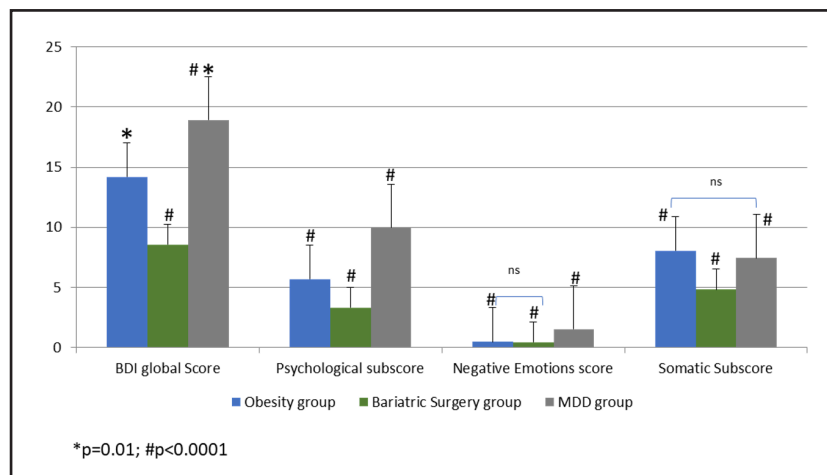


Figure 1.

Comparison of the global score, and psychological, negative emotions and somatic subscores among patients with obesity (OB), subjects who underwent bariatric surgery (BS) and individuals with a major depressive disorder (MDD).

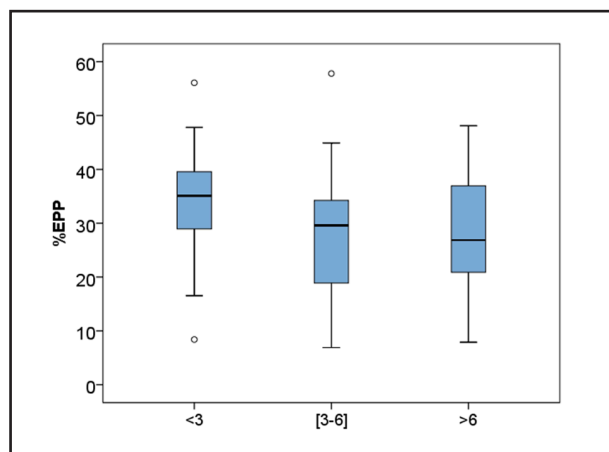


Figure 2.

Negative correlation between a greater score in the somatic domain of depressive symptomatology and the percentage of excess weight loss (%EPP) ($p = 0.04$).

We could not find any association between the %EPP and the presence of psychological or negative depressive symptoms. Data are represented in figure 2.

DISCUSSION

Our study found that, depressive symptomatology among patients long term after BS, was lower than subjects with obesity without having undergone this surgical procedure. However, and despite being on a pharmacological and psychological tailored treatment, patients with a major depression without obesity showed higher levels of depressive symptoms compared with patients living with obesity, either having or not a bariatric procedure. Also, depressive symptomatology was significantly different among those subjects with obesity, with a predominance of somatic symptoms (atypical depression) compared to subjects with a diagnosis of a MDD without this metabolic condition, where the greater scores were obtained by both psychological/cognitive sub-scales and the negative items in the BDI (melancholic or classical depression). Moreover, although depressive symptomatology among BS patients remained lower even on the long term, we found a negative association between atypical depressive symptoms and %EPP.

In a former study, we found similar results when we compared patients with type 2 diabetes and significant depressive symptoms with subjects with a MDD without a glycemic disorder. We concluded that the predominance of this somatic-biological cluster among subjects with type 2 diabetes could reflect symptoms related to a poor metabolic control as well as a difficulty to adapt to a chronic metabolic condition rather than a classical depression *per se*. Therefore, this heterogeneity in the symptomatology of depression might reflect a potential different response to antidepressant therapy among these patients (5).

In this sense, Osterhues et al. investigated depression in 192 bariatric surgery candidates and 96 in-patients with mental disorders from a psychosomatic medicine department. They also included 96 non-clinical volunteers with overweight or class 1 obesity as well as 103 postoperative bariatric surgery patients. They found lower physical health related quality of life (HRLQ) among patients seeking for BS compared to inpatients who were currently receiving psychotherapeutic hospital treatment. However, subjects waiting for BS perceived better subjective mental well-being and poorer physical HRQL, despite similar depression scores, than psychotherapy inpatients (6). Also, and in line with other studies published previously, depressive symptomatology, both somatic and mental, decreased significantly after BS, at short term (8,11-14). However, the psychotherapeutic inpatient group included, not only patients with a MDD, but also many other different psychiatric conditions, such as eating disorders, anxiety disorders, post-traumatic stress disorder, borderline personality disorder or any impulse control disorder. Therefore, comparisons with patients with depression and obesity, regardless of the BS situation, as well as with our results, should be interpreted with caution. In addition, the bariatric surgery sample included patients who underwent this procedure on the short term after this evaluation (6).

Moreover, evidence suggests that weight loss after BS is related to short and medium term decrease in depressive symptomatology (11,14-17). The LABS study included more than 2000 BS patients who completed the BDI at baseline and at different time points over a period of 3 years after surgery. Despite the amelioration of depressive symptoms after BS on the short term, after the first year the scores obtained with the BDI increased, suggesting a small worsening of depressive symptomatology (11,18). However, depressive symptoms were reduced significantly at 2-3 years after BS (12,14,19). There was a positive association between the decrease in BMI and the amelioration of depressive symptoms. The link between the decrease in BMI and the improvement in depressive symptoms post-BS could be explained by different biological pathways, such as a reduction both in the low-grade inflammatory state and the insulin resistance or the normalization of the HPA-axis dysregulation (20). Psychosocial factors could also exert a positive influence, such as more activities in daily life, satisfaction with the body image, among others (21-26). However, the nature and evolution of long-term post-BS changes in depressive symptomatology, as well as the influence of these changes exerts on weight loss remains unclear. The German multi-center Essen Bochum Obesity Treatment Study (EBOTS) showed that despite a significant improvement in depressive symptoms on the short and medium term after BS in 152 patients, there was a deterioration between 4 and 9 year follow-up, showing HADS depression scores comparable to presurgical levels (27). Conversely, we found that depressive symptomatology remained lower than the presurgical period.

Furthermore, it should be considered whether the deterioration in depressive symptoms on the long-term could increase the risk of suicide among this population. A meta-analysis that included 61 studies and more than 142,000 patients showed that pooled

postoperative suicide prevalence of 0.3 % was below the global suicide rate (1.4 %) (28). However, 3 longitudinal studies, including 43,406 patients, showed that the risk for suicide or attempt was increased following BS compared to baseline rates within the same population (29). A very low score in the negative emotions questions in the BDI among these patients might explain this lower suicide rate. A history of suicidal ideation seems to be the strongest predictor of suicidal ideation 1-year post-surgery, followed by a younger age (30). This increased suicidality could be the result of a combination of unfavorable medical, biological, genetic, and psychosocial factors. The main contributor could be a new onset of depression or the worsening of depressive symptomatology, given that the presence of a depression is one of the most consistently reported risk factors for suicide attempts or complete suicide (31,32). However, changes in the absorption of antidepressant medications after BS (33), changes to excessive eating to alcohol dependence after BS (34), disappointment from unrealistic expectations about surgical treatment, body image dissatisfaction due to hanging skin, etc., may also play an important role (26). Therefore, it is extremely important a continuous psychological evaluation after BS, also on the long term, to identify increases in depressive symptomatology, as well as classify the predominant depressive symptomatology.

A point to consider is whether some types of depressive symptomatology could have a negative impact on weight loss after a BS procedure. In this sense, we found a negative correlation between the presence of somatic symptoms and the %EPP among subjects who underwent BS, on the long term. This finding could reflect the negative influence of physical symptoms on the acquisition of healthy lifestyle habits, such as regular physical activity. In a previous study, we found that the presence of chronic pain among subjects who underwent BS, at long term, was related to a greater presence of depressive symptomatology and a lesser degree of regular physical activity (35). Smith et al included 345 patients waiting for BS and with a psychological presurgical evaluation. They found that patients who reported atypical depressive symptoms prior to BS were more likely to meet criteria for BED but did not have poorer weight loss within 18 months post-surgery (8). However, data regarding the effects of the different symptoms of depression on weight are scarce and inconclusive.

However, as most of the studies published so far, we conducted a cross-sectional study and, therefore, causal relationships between depressive symptomatology and obesity cannot be made. In this sense, it is noteworthy to point out that atypical depression could be a risk factor for obesity. In fact, the population-based prospective Zurich Cohort Study found a trend for a positive association between atypical depression and the average rate of weight gain over 20 years (36). Also, Lasserre et al. investigated, in a population-based cohort study including more than 3000 subjects, whether the different subtypes of depression (melancholic, atypical, combined, or unspecified) were predictive of adiposity in terms of incidence of obesity and changes in BMI, waist circumference and fat mass. They found that only participants with an atypical depression at baseline revealed a higher increase in adiposity (BMI, waist circumference and fat

mass) during the 5.5 years of follow-up compared with participants without depression (37).

As mentioned before, one of the main limitations of the present study was its cross-sectional design and, therefore, a causal relationship between changes in depressive symptomatology before and after BS cannot be made. We used self-report assessments instead of a structured interview. However, BDI is a validated tool among subjects with obesity and previous research has produced valid results using a similar methodology. Also, we could not generalize our results to non-Caucasian populations. As far as we know, this is the first study that compares the types of depressive symptomatology among subjects with a MDD, patients with obesity seeking BS and subjects who underwent a BS procedure on the long term.

CONCLUSION

In conclusion, over the long term, subjects who underwent bariatric surgery displayed lower levels of depressive symptoms compared to those patients with obesity seeking this surgical procedure. Notably, the cluster of depression differed between individuals with obesity and subjects with a major depressive disorder without obesity, with a predominance of negative emotions in the last ones. Furthermore, despite bariatric surgery reduces somatic symptoms of depression over the long term, its presence is associated to a lesser weight loss.

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Trabajo Original

Obesidad y síndrome metabólico

Cambios metabólicos, clínicos y de composición corporal en adultos mexicanos sometidos a cirugía bariátrica

Metabolic, clinical and body composition changes in Mexican adults undergoing bariatric surgery

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Resumen

Introducción: la obesidad mórbida es un importante problema de salud pública que va en aumento. En la actualidad existen un número limitado de estudios hechos en población mexicana que describan los efectos de la cirugía bariátrica.

Objetivo: establecer en personas sometidas a cirugía para perder peso las diferencias metabólicas y de composición corporal antes y después de la cirugía bariátrica.

Material y métodos: se realizó un estudio observacional, analítico, prospectivo y longitudinal en 50 pacientes con obesidad mórbida sometidos a gastrectomía en manga por laparoscopia (LSG) y *bypass* gástrico en Y de Roux por laparoscopia (LRYGB). Se midieron la composición corporal y los marcadores metabólicos en sangre. Se analizaron las diferencias en el perfil metabólico antes y después de la cirugía en todo el grupo de estudio, y se realizó un subanálisis por técnica quirúrgica bariátrica. Asimismo se determinó el porcentaje de remisión de las comorbilidades.

Resultados: después de la intervención, existe una disminución significativa de todos los marcadores metabólicos y de composición corporal excepto el colesterol HDL, que mostró tendencia al incremento sin ser significativa. Las mujeres con LRYGB tienen mayor disminución de masa libre de grasa. El LRYGB disminuyó más la prevalencia de hígado graso, reflujo gastroesofágico, resistencia a la insulina e hipercolesterolemia; en cambio, la LSG disminuyó más la prevalencia de hipertensión, osteoartritis, hipotiroidismo e hipertrigliceridemia.

Conclusiones: la cirugía bariátrica induce cambios metabólicos que podrían contribuir a mejorar las comorbilidades asociadas a la obesidad. En general, la mejoría metabólica es mayor con el LRYGB comparado con la LSG.

Palabras clave:

Cirugía bariátrica.
Composición corporal.
Comorbilidades asociadas a la obesidad.

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Abstract

Background: morbid obesity is a major public health problem that is increasing. Currently, there are a limited number of studies carried out in the Mexican population that describe the effects of bariatric surgery.

Objective: to establish in obese people who undergoing weight loss surgery, the metabolic and body composition difference before and after bariatric surgery.

Material and methods: an observational, analytical, and longitudinal study was carried out in 50 patients with morbid obesity who underwent laparoscopic sleeve gastrectomy (LSG) and laparoscopic Roux-en-Y gastric bypass (LRYGB). Body composition and metabolic markers in blood were measured. Differences in the metabolic profile before and after surgery were analyzed in the entire study group and a subanalysis was performed by bariatric surgical technique. It was also determined the percentage of remission of comorbidities.

Results: after the intervention, there is a significant decrease in all metabolic and body composition markers, except HDL cholesterol, which showed a tendency to increase without being significant. Women with LRYGB have a greater decrease in fat-free mass. LRYGB decreased the prevalence of fatty liver, gastroesophageal reflux, insulin resistance, and hypercholesterolemia more, while LSG decreased the prevalence of hypertension, osteoarthritis, hypothyroidism, and hypertriglyceridemia more.

Conclusion: bariatric surgery induces metabolic changes that could contribute to improving comorbidities associated with obesity. In general, metabolic improvement is greater in LRYGB compared to LSG.

Keywords:

Bariatric surgery. Body composition. Chronic degenerative diseases.

INTRODUCCIÓN

La obesidad mórbida se define como el estado en el cual un individuo tiene con un peso actual que es 100 % superior al peso ideal o con un índice de masa corporal (IMC) $\geq 35 \text{ kg/m}^2$ asociado a comorbilidad, generalmente cardiometabólica (1,2). La obesidad es un problema importante de salud pública. México ocupa el segundo lugar a nivel mundial, con los índices más altos de obesidad en adultos (3,4); la prevalencia es del 35,3 %, de la cual el 34 % padecen obesidad mórbida (4). Los costos en salud para el tratamiento de la obesidad y sus comorbilidades se estimaron en 200 millones de dólares en el año 2019, sin contar las pérdidas económicas en el mercado laboral por ausentismo, desempleo y jubilación anticipada. Además la obesidad mórbida aumenta la morbimortalidad y disminuyen la esperanza y la calidad de vida de quien la padece (5).

El tratamiento de la obesidad mórbida implica modificar el estilo de vida mediante un plan de alimentación, ejercicio y manejo conductual. En algunos casos, el tratamiento con medicamentos para perder peso puede ser efectivo; sin embargo, la cirugía bariátrica ofrece una opción adicional de tratamiento cuando las anteriores han fracasado (6). El *bypass* gástrico en Y de Roux, LRYGB por sus siglas en inglés (*Laparoscopic Roux-en-Y Gastric Bypass*), y la gastrectomía en manga, LSG por sus siglas en inglés (*Laparoscopic Sleeve Gastrectomy*), son procedimientos quirúrgicos bariátricos que modifican la anatomía, fisiología y endocrinología del tracto gastrointestinal, reduciendo la ingestión y/o absorción de nutrientes, lo que induce una pérdida dramática y sostenida de masa corporal, facilitando la disminución del 50 al 70 % del exceso de peso corporal y la masa grasa. La evidencia actual reporta que el LRYGB promueve más pérdida de peso y mejoría metabólica que la LSG (7,8).

La cirugía bariátrica proporciona mejoras metabólicas no solo debido a la pérdida de peso, sino también a factores como la modificación de la secreción de hormonas intestinales, de ácidos biliares y de moléculas del sistema nervioso, así como mejoras de la función inmunitaria y modificación de la microbiota intestinal (9,10). Estudios hechos en humanos con obesidad sometidos a cirugía bariátrica observaron que después de los 3, 6 meses y 1 año hay una disminución significativa de la composición corporal, metabólica e inmunológica: del peso corporal, de la glucosa, los triglicéridos, la insulina y la hemoglobina glicosilada (HbA1c), de la resistencia a la insulina (RI), y de las moléculas proinflamatorias (7,11,12).

Por lo anterior, la hipótesis planteada en el presente estudio es que los pacientes sometidos a cirugía bariátrica presentan cambios positivos y significativos en sus variables metabólicas, clínicas y de composición corporal. El objetivo de la investigación es describir los cambios metabólicos y de composición corporal en personas que viven con obesidad mórbida después de ser sometidos a LRYGB o LSG.

MATERIALES Y MÉTODOS

Se realizó un estudio observacional, analítico, prospectivo y longitudinal en adultos de ambos sexos con obesidad mórbida sometidos a LRYGB y LSG del año 2020 al año 2023 en la Clínica de Obesidad del Hospital General Dr. Manuel Gea González de la Ciudad de México. Los criterios de inclusión fueron: adultos viviendo con obesidad grave en protocolo de cirugía bariátrica, con comorbilidades asociadas a la obesidad, que firmaron la carta de consentimiento informado. Los criterios de exclusión fueron: personas que viven con obesidad con diagnóstico de infección, embarazo, enfermedad renal con diálisis y/o cáncer, o consumo de antiinflamatorios o inmunosupresores. Los criterios de eliminación fueron: retiro voluntario del estudio, desarrollo de alguna complicación posquirúrgica durante los primeros 6 meses del postoperatorio e individuos con datos faltantes. Se midió la población de estudio un mes antes y seis meses después de la cirugía bariátrica, recabando medidas antropométricas, composición corporal, presión arterial y química sanguínea (Fig. 1).

El peso y la estatura se midieron con una balanza Seca 704s TM con estadímetro (Seca, México). La circunferencia de la cintura (CC) se midió con una cinta métrica de acero inoxidable Executive 6FT W606P (Lufkin, Englewood, EUA). Estas mediciones se realizaron siguiendo el protocolo estandarizado de la Sociedad Internacional para el Avance de la Cineantropometría (ISAK). El IMC, la grasa corporal total (GCT), la masa libre de grasa (MLG) y la grasa visceral (GV) se obtuvieron de un analizador de composición corporal Tanita BC-568 (Tanita, México). Se solicitó a cada paciente que no realizara ejercicio físico intenso durante las 24 horas previas al estudio y que acudiera a su cita en ayunas de al menos 4 horas, no haber ingerido líquidos, no haber consumido bebidas alcohólicas y no estar menstruando. De lo contrario, la distribución de líquidos en el cuerpo cambia y se subestima o sobrees-

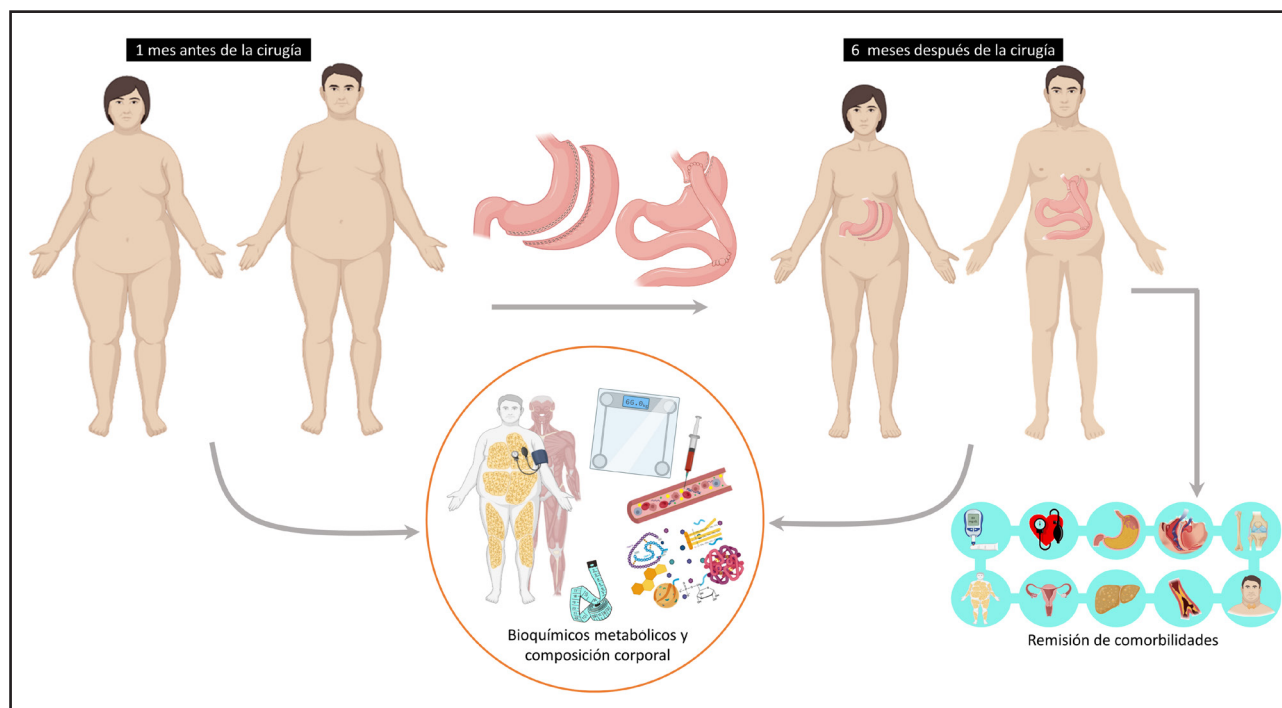


Figura 1.

Diseño del estudio de pacientes antes y después de la cirugía bariátrica. Los individuos se organizaron en dos cortes (un mes antes y seis meses después de la cirugía bariátrica) y después en dos subgrupos según la técnica quirúrgica bariátrica recibida. De cada individuo se obtuvieron medidas antropométricas y de composición corporal, así como otros marcadores metabólicos, bioquímicos y clínicos con el fin de comparar las diferencias antes y después de la cirugía (fuente: se construyó utilizando imágenes libres del software Biorender).

tima la masa libre de grasa. Para diagnosticar el grado de obesidad se utilizó el porcentaje de GCT según los criterios de la Organización Mundial de la Salud (OMS).

Las muestras de sangre periférica se recogieron en tubos Vacutainer™ de 5 ml Becton Dickinson, USA de los participantes después de haber ayunado durante al menos 8 horas. Se midieron las siguientes moléculas en sangre periférica: glucosa, triglicéridos, colesterol total, lipoproteínas de alta densidad (HDL), lipoproteínas de baja densidad (LDL), hemoglobina glucosilada (HbA1c), insulina y proteína C-reactiva (PCR), y se calculó el modelo homeostático de evaluación de la resistencia a la insulina (HOMA-IR por sus siglas en inglés: *Homeostatic Model Assessment for Insulin Resistance*) según la siguiente fórmula: $\text{insulina en ayunas } (\mu\text{U/L}) \times (\text{glucosa en ayunas } (\text{nmol/L}) \times 0,0551) / 22,5$. Los valores superiores a 3,0 indicaron resistencia a la insulina (13). Se midió por duplicado la presión arterial con base en los lineamientos de la Norma Oficial Mexicana para la Prevención, Detección, Diagnóstico, Tratamiento y Control de la Hipertensión Arterial Sistémica (PROY-NOM-030-SSA2-2017).

ANÁLISIS ESTADÍSTICO

Las comparaciones de datos se determinaron con base en el tiempo del tratamiento (1 mes antes y 6 meses después de la cirugía) y según la técnica quirúrgica realizada (Fig. 1). Se utilizó el método ajustado de Kolmogorov-Smirnov (prueba de Lilliefors)

para determinar la normalidad de los datos. Las variables que no pasaron la prueba de normalidad se transformaron por pares. Se obtuvieron la media y la desviación estándar de las variables no transformadas, así como la mediana y el rango intercuartílico de las variables transformadas. Se aplicó la prueba "t" para muestras relacionadas en cada variable con el objetivo de encontrar diferencias estadísticas. Para determinar las diferencias de cambio se obtuvieron las deltas (Δ), que son las diferencias de las variables antes de la cirugía menos las mismas variables después de la cirugía por cada individuo. Para obtener el porcentaje de cambio después de la cirugía, este se calculó multiplicando la delta media ($\bar{X}-\Delta$) por 100 entre la media antes de la cirugía por cada individuo. La diferencia estadísticamente significativa se determinó con un valor de p menor de 0,05 y un intervalo de confianza del 95 %. El análisis se realizó utilizando los paquetes estadísticos implementados en v3.6.7 (CreateSpace 2009; Scotts Valley, CA, USA) e IBM SPSS Statistics versión 25.0.

RESPONSABILIDADES ÉTICAS

Todos los procedimientos que involucraron participantes humanos se realizaron con base en el reglamento de la Ley General de Salud en Materia de Investigación para la Salud en México, fue sometido a evaluación y cumplió con los estándares éticos del Comité de Ética institucional del hospital anfitrión

Dr. Manuel GEA González (número de referencia de aprobación: 46-119-2019) y con los principios de la Declaración de Helsinki.

RESULTADOS

Se estudiaron 50 individuos un mes antes y seis meses después de la cirugía bariátrica, con una edad media de $36,8 \pm 9,4$ años. La mayoría fueron mujeres (70 %, $n = 35$). El grupo de pacientes operados con LRYGB representó el 60 % ($n = 30$) y el grupo de la LSG representó el 40 % ($n = 20$).

CAMBIOS METABÓLICOS, CLÍNICOS Y DE COMPOSICIÓN CORPORAL

Después de la cirugía bariátrica se observó una disminución, con diferencia significativa, de todos los parámetros metabólicos, clínicos y de composición corporal excepto las HDL, que tuvieron un ligero aumento pero sin ser estadísticamente significativo (Tabla I).

DIFERENCIAS METABÓLICAS Y DE COMPOSICIÓN CORPORAL ENTRE EL BYPASS GÁSTRICO Y LA GASTRECTOMÍA EN MANGA

El 88,6 % de los pacientes de ambos sexos sometidos a LRYGB pasaron de obesidad clase 4 a obesidad clase 1 y 2; y el 80 % de los pacientes sometidos a LSG pasaron de obesidad clase 4 a obesidad clase 3. Los pacientes sometidos a LRYGB tuvieron mejorías significativas en todos los marcadores metabólicos y de composición corporal excepto el HDL. Los pacientes sometidos a LSG también presentaron mejorías metabólicas significativas excepto en colesterol total, HDL y LDL. El LRYGB en comparación con la LSG promovió en mayor medida la mejoría metabólica en los pacientes con obesidad (Tabla II), ya que disminuyó en mayor proporción el peso [LRYGB: 26,2 % vs. LSG: 21,8 %], el IMC [LRYGB: 26,2 % vs. LSG: 8,2 %], la GCT [LRYGB: 24,7 % vs. LSG: 9,2 %], el porcentaje de peso excedido (PE) [LRYGB: 64,2 % vs. LSG: 54,1 %], el PE en kilogramos [LRYGB: 64,2 % vs. LSG: 53,6 %], la HbA1c [LRYGB: 22,1 % vs. LSG: 5,0 %] y el c-LDL [LRYGB: 20,5 % vs. LSG: 3,1 %].

Tabla I. Diferencias metabólicas, clínicas y de composición corporal antes y después de la cirugía

Variable	Antes de la cirugía	Después de la cirugía	Porcentaje de cambio después la cirugía*	p
Glucosa (mg/dL)	104,0 (95,4-118,6)	87,0 (80,0-93,5)	↓ 22,8 %	< 0,001
Insulina (μUI/mL)	22,5 (15,0-31,6)	7,9 (5,7-12,0)	↓ 56,2 %	< 0,001
HbA1c (%)	5,7 (5,5-6,0)	5,3 (5,0-5,4)	↓ 15,6 %	< 0,001
HOMA-IR	5,9 (3,8-9,3)	1,5 (1,1-2,5)	↓ 66,0 %	< 0,001
Colesterol total (mg/dL)	177,6 ± 31,4	153,1 ± 23,0	↓ 12,9 %	< 0,001
HDL (mg/dL)	40,4 (35,0-47,2)	43,0 (36,0-49,5)	↑ 2,4 %	0,075
LDL (mg/dL)	102,5 ± 27,2	88,2 ± 18,9	↓ 13,1 %	0,001
Triglicéridos (mg/dL)	150,0 (106,7-195,0)	110,0 (86,5-136,0)	↓ 30,5 %	< 0,001
PAS (mmHg)	121,3 ± 11,7	110,9 ± 10,8	↓ 9,1 %	< 0,001
PAD (mmHg)	80 (70-84)	70 (69-77,5)	↓ 7,9 %	< 0,001
Peso (kg)	115,0 ± 26,1	87,5 ± 19,8	↓ 24,1 %	< 0,001
IMC (kg/m ²)	42,6 ± 7,0	32,3 ± 5,2	↓ 24,1 %	< 0,001
GCT (%)	46,6 ± 6,9	35,9 ± 8,6	↓ 22,3 %	< 0,001
MLG (%)	53,3 ± 6,9	64,0 ± 8,6	↑ 19,1 %	< 0,001
MLG (kg)	54,3 (50,0-75,7)	49,5 (45,6-66,7)	↓ 9,7 %	< 0,001
CC (cm)	127,6 ± 17,8	107,9 ± 15,9	↓ 16,1 %	< 0,001
PE (%)	66,5 ± 25,5	26,6 ± 19,5	↓ 63,2 %	< 0,001
PE (kg)	46,3 ± 20,29	18,72 ± 14,3	↓ 60,7 %	< 0,001
GV (U)	18,5 (13-20)	8 (7-12)	↓ 43,4 %	< 0,001

HbA1c: hemoglobina glucosilada; HOMA-IR: modelo homeostático de evaluación de la resistencia a la insulina; HDL: lipoproteínas de alta densidad; LDL: lipoproteínas de baja densidad; PAS: presión arterial sistólica; PAD: presión arterial diastólica; IMC: índice de masa corporal; CC: circunferencia de la cintura; GCT: grasa corporal total; MLG: masa libre de grasa; PE: peso excedido; GV: grasa visceral; p: significancia estadística a través de la prueba T para muestras relacionadas. *Se calculó para cada variable multiplicando $\bar{x}\Delta$ por 100 entre la media antes de la cirugía. El valor en porcentaje se muestra con una flecha arriba (↑) para representar el aumento o con una flecha abajo (↓) para representar la disminución.

Tabla II. Diferencias metabólicas, clínicas y de composición corporal antes y después de la cirugía por técnica quirúrgica

Variable (n = 50)	LRYGB			LSG			LRYGB vs. LSG	
	n = 30		p	n = 20		p	pΔ	pΔ@
	Antes	Después		Antes	Después			
Glucosa (mg/dL)	111 (98-126)	90 (83-95)	< 0,001	101 (93-106)	86 (78-91)	< 0,001	0,414	0,347
Insulina (μU/mL)	23 (16-34)	8 (6-12)	< 0,001	21 (13-31)	9 (6-14)	0,001	0,155	0,361
HbA1c (%)	5,9 (5,6-6,9)	5,1 (4,9-5,5)	< 0,001	5,6 (5,5-5,8)	5,3 (5,1-5,4)	< 0,001	0,031	0,082
HOMA-IR	6,3 (4,3-10,4)	1,5 (1,2-2,5)	< 0,001	5,6 (2,9-8,5)	1,6 (1,1-2,8)	< 0,001	0,251	0,211
Cholesterol total (mg/dL)	180 ± 33	145 ± 25	< 0,001	175 ± 30	169 ± 16	0,451	0,974	0,976
HDL (mg/dL)	40 (34-44)	43 (36-48)	0,108	41 (37-52)	45 (38-56)	0,397	0,991	1,000
LDL (mg/dL)	103 ± 27	81 ± 19	< 0,001	104 ± 22	101 ± 13	0,655	0,022	0,047
Triglicéridos (mg/dL)	164 (98-208)	119 (111-136)	0,001	112 (89-116)	115 (83-136)	0,001	0,985	0,015
PCR (mg/dL)	0,825 (0,235-1,160)	0,237 (0,153-0,818)	< 0,001	0,570 (0,238-1,035)	0,210 (0,104-0,547)	0,024	0,752	0,939
PAS (mmHg)	124 ± 12	112 ± 10	< 0,001	120 ± 14	109 ± 11	0,015	0,810	0,784
PAD (mmHg)	80 (70-84)	71 (70-80)	0,001	78 (69-80)	70 (66-76)	0,010	0,331	0,461
Peso (kg)	120 ± 24	89 ± 18	< 0,001	108 ± 28	85 ± 22	< 0,001	0,002	< 0,001
IMC (kg/m ²)	44 ± 6,8	33 ± 5	< 0,001	41 ± 7	32 ± 6	< 0,001	0,002	0,003
GCT (%)	46 ± 6,7	35 ± 10	< 0,001	48 ± 7	39 ± 6	< 0,001	0,002	0,467
MLG (%) (kg)	54 ± 6,7	65 ± 10	< 0,001	53 ± 7	61 ± 6	< 0,001	0,197	0,438
	58 (52-78)	50 (46-70)		52 (47-60)	48 (46-53)	0,020	0,190	0,043
CC (cm)	132 ± 17	111 ± 17	< 0,001	122 ± 17	101 ± 13	< 0,001	0,965	0,482
PE (%) (kg)	70 ± 26	26 ± 20	< 0,001	63 ± 25	28 ± 19	< 0,001	0,005	0,008
	50 ± 20	18 ± 14		42 ± 21	19 ± 15		0,002	< 0,001
GV (U)	19 (13-21)	9 (7-13)	< 0,001	18,0 (11-20)	8 (7-10)	< 0,001	0,037	0,024

LRYGB: bypass gástrico en Y de Roux; LSG: gastrectomía en manga; HbA1c: hemoglobina glucosilada; HOMA-IR: modelo homeostático de evaluación de la resistencia a la insulina; HDL: lipoproteína de alta densidad; LDL: lipoproteína de baja densidad; PCR: proteína C-reactiva; PAS: presión arterial sistólica; PAD: presión arterial diastólica; IMC: índice de masa corporal; CC: circunferencia de la cintura; GCT: grasa corporal total; MLG: masa libre de grasa; PE: peso excedido; GV: grasa visceral; n: número de individuos; p: significancia estadística antes versus después de la cirugía bariátrica; pΔ: significancia estadística entre LRYGB y LSG; pΔ@: significancia estadística entre LRYGB y LSG ajustada por sexo. p < 0,05 es estadísticamente significativo. Los datos se presentan como media ± desviación estándar o mediana (rango intercuartílico).

Las mujeres con LRYGB tuvieron mayor pérdida de MLG en kilogramos [LRYGB: 10,5 % vs. LSG: 5,8 %] y de triglicéridos [LRYGB: 32,9 % vs. LSG: 26,1 %]. Los hombres con LRYGB tuvieron mayor disminución de peso, IMC, PE y LDL.

REMISIÓN DE COMORBILIDADES ASOCIADAS A LA OBESIDAD

Al comparar las dos técnicas quirúrgicas en función de la remisión de comorbilidades asociadas a la obesidad, se encontró que la prevalencia de comorbilidades fue más alta antes de la cirugía en los individuos con LRYGB comparado con los de LSG. El SHO/SAOS (síndrome de hipoventilación asociado a la obesidad/síndrome de apnea obstructiva del sueño) remitió al 100 % y el SOP (síndrome del ovario poliquístico) remitió al 50 % con ambas técnicas quirúrgicas. En los individuos sometidos a LRYGB disminuyó más la prevalencia de síndrome metabólico (SM), enfermedad por reflujo gastroesofágico (ERGE) y resistencia a la insulina y/o diabetes *mellitus* de tipo 2 (RI/DM2), hipercolesterolemia, hiperlipemia por LDL e hipoalfalipoproteinemia por HDL. Por otro lado, en los individuos sometidos a LSG disminuyó más la prevalencia de HAS (hipertensión arterial sistémica), osteoartritis, hipotiroidismo e hipertrigliceridemia. Sin embargo, en general, el LRYGB promovió mayores porcentajes de mejoría de las comorbilidades en comparación con la LSG (Fig. 2).

DISCUSIÓN

Los pacientes con obesidad mórbida después de ser sometidos a cirugía bariátrica presentaron mejorías metabólicas

estadísticamente significativas excepto en HDL, logrando llegar a parámetros de normalidad en glucosa, insulina, HbA1c, HOMA-RI, colesterol total, triglicéridos y presión arterial diastólica (PAD). Además, de remitir al 100 % el SHO/SAOS y la enfermedad venosa periférica (EVP) al 100%, también lo hicieron: al 87,5 % la HAS, al 82,4 % la enfermedad de hígado graso asociado a disfunción metabólica, al 75 % el SM, al 70,5 % la RI/DM2, al 50 % el síndrome de ovario poliquístico (SOP), la osteoartritis y el hipotiroidismo, y al 12,8 % la dislipidemia en tan solo 6 meses tras el tratamiento, lo que coincide con otros estudios (14-17). Ello comprueba los beneficios metabólicos que provocan los procedimientos quirúrgicos bariátricos para el tratamiento de la obesidad, que contribuyen de forma significativa a disminuir la morbimortalidad por enfermedades metabólicas (18) y que estos efectos pueden durar más allá de los 2 años, siempre que haya también un cambio profundo y trascendente en el estilo de vida. (14). Del mismo modo, la disminución del SM se suman a la mejoría de la inflamación asociada a la obesidad, lo que coincide con otros estudios (7,8,11,18-22).

Es interesante añadir que en los individuos sometidos a LRYGB se espera, como resultado excelente, una disminución del exceso de peso mayor del 65 % después de un año tras la cirugía, (23,24) y en los pacientes del presente estudio, tanto con el LRYGB como con la LSG, se observó una disminución del peso excedido del 64,2 % y el 54,1 %, respectivamente, en tan solo 6 meses (Tabla II).

Es curioso observar que, después de las cirugías, no hubo una mejora significativa del HDL (Tablas I y II, y Fig. 2) y que la remisión de las dislipidemias fue solo del 12,18 %. Se sabe que el colesterol-HDL se considera un marcador bioquímico

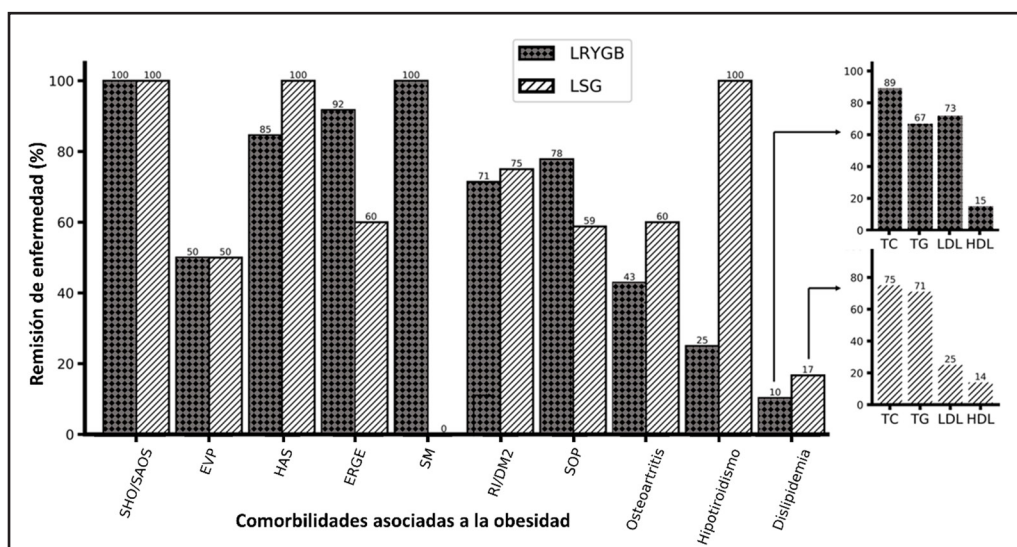


Figura 2.

Porcentaje de remisión de las comorbilidades asociadas a la obesidad entre el *bypass* gástrico y la gastrectomía en manga (abreviaturas: LRYGB: *bypass* gástrico en Y de Roux por laparoscopia; LSG: gastrectomía en manga por laparoscopia; SHO: síndrome de hipoventilación asociado a la obesidad; SAOS: síndrome de apnea obstructiva del sueño; EVP: enfermedad venosa periférica; HAS: hipertensión arterial sistémica; ERGE: enfermedad por reflujo gastroesofágico; SM: síndrome metabólico; RI/DM2: resistencia a la insulina y/o diabetes *mellitus* de tipo 2; SOP: síndrome de ovario poliquístico; TC: hipercolesterolemia; TG: hipertrigliceridemia; LDL: hiperlipemia por LDL; HDL: hipoalfalipoproteinemia por HDL).

inflamatorio y se mantiene disminuido en presencia de inflamación (25). Asimismo, en la población latina, los niveles de HDL son menores por razones genéticas, socioculturales y ambientales, comparados con los de otras poblaciones (26). Además, los niveles de HDL en sangre se ven disminuidos por la falta de actividad física (27) y los pacientes del presente estudio, después de la cirugía, no realizan ejercicio al menos durante el primer mes del postoperatorio, por lo que la inflamación propia de la obesidad, la raza latina y la poca actividad física pueden ser la causa por la que a pesar de la cirugía bariátrica, siga existiendo una alta prevalencia (85 %) de dislipidemia principalmente por hipoalfalipoproteinemia.

Por otro lado, en el presente estudio se observó que, después de la cirugía bariátrica, los kilogramos de MLG disminuyeron significativamente en un 9,7 %. Y al comparar las dos técnicas quirúrgicas se halló que el LRYGB indujo más la pérdida de kilogramos de MLG en las mujeres (10,5 %), comparado con la LSG (5,8 %) (Tabla II). Esto coincide con los estudios de Nuijten y cols., (2020 y 2022) donde observaron que en los primeros 6 meses después de la cirugía se da la mayor pérdida de kilogramos de MLG (28). Del mismo modo, en el estudio de Davidson y cols., (2018) observaron que el LRYGB promovió la pérdida de MLG en las mujeres (29). Es importante añadir que los cambios de MLG generalmente reflejan los cambios en el músculo esquelético, y en los pacientes con LRYGB la pérdida de MLG representa casi toda la pérdida de músculo esquelético. Por ello, la disminución en kg de la MLG se puede explicar en parte por la disminución del peso corporal total, y es de esperar que después de la pérdida de peso haya también una pérdida de MLG. Sin embargo, esta pérdida puede variar según el procedimiento quirúrgico, el grado de pérdida de peso, la frecuencia e intensidad de la actividad física, el consumo de proteínas en la dieta y posiblemente el método de evaluación que se utilizó para medirla (29).

Por último, es sensato admitir que en el presente estudio hubo limitaciones principalmente en los grupos donde se compararon las dos técnicas quirúrgicas, ya que no fueron homogéneos, además al hacer la subdivisión por técnica quirúrgica, en un grupo habían menos de 30 participantes estudiados. Asimismo, tampoco se logró la homogeneidad en relación con el sexo porque existe un número diferente de hombres y mujeres: la mayoría de los participantes fueron mujeres. El sexo es un factor que influye en la obesidad, así como en la participación en los estudios y programas de salud. Por todo ello, se considera en un futuro, hacer un muestreo más completo para tener una población más equilibrada.

A pesar de las limitaciones mencionadas se considera que el presente trabajo ha contribuido con la generación de datos útiles por mejorar la comprensión de los cambios metabólicos, clínicos, de composición corporal y mejoría en la prevalencia de comorbilidades asociadas a la obesidad de los seres humanos con obesidad sometidos a cirugía para perder peso, comparados por sexo y entre las dos técnicas quirúrgicas bariátricas más utilizadas en México, lo que puede contribuir en un futuro a la decisión terapéutica de los pacientes con obesidad.

CONCLUSIÓN

El tratamiento de la obesidad con cirugía bariátrica produce mejoras metabólicas significativas en tan solo 6 meses aun cuando persista la obesidad definida por IMC o porcentaje de masa grasa. Con ambas técnicas se observa una pérdida significativa de peso: el LRYGB induce mayor pérdida de peso, de masa grasa y de grasa visceral, reportándose mayores porcentajes de mejoría metabólica. Es importante continuar realizando estudios en este tipo de población y durante periodos de tiempo mayores para observar a largo plazo si la mejoría metabólica y la remisión de la comorbilidad es más favorable, explorando la existencia de la enfermedad recidivante.

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Trabajo Original

Obesidad y síndrome metabólico

Weight-adjusted waist index predicts metabolic syndrome in Caucasian patients with obesity

El índice de cintura ajustado al peso predice el síndrome metabólico en pacientes caucásicos con obesidad

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Abstract

Background and aims: the usefulness of the weight-adjusted waist index (WWI) among persons with metabolic syndrome (MS) has not been previously evaluated. The objective of this study was to evaluate the ability of WWI to predict MS in a Caucasian population with obesity.

Methods: we conducted a cross sectional study in 2162 Caucasian patients with obesity. Anthropometric data (weight, height, body mass index [BMI], waist circumference, [WWI]), bioimpedancimeter parameters (total fat mass [FM], skeletal muscle mass [SMM] and skeletal muscle mass index [SMMI]), blood pressure, presence of MS and biochemical parameters were recorded and compared by tertiles of WWI.

Results: a total of 1,176 subjects had MS (54.4 %) and 986 did not show MS (45.6 %). Compared with the lowest WWI category Q1 (< 11.24 cm/√kg), the prevalence of MS increased in the logistic regression model adjusted by sex and age in the Q3 group (OR = 2.53, 95 % CI = 1.71-3.23; $p = 0.001$). In addition, the prevalence of MS was higher in the Q3 group than in Q2 (OR = 1.65, 95 % CI = 1.25-2.17; $p = 0.005$). Finally, the prevalence of MS in Q2 was higher than in the Q1 group (OR = 1.21, 95 % CI = 1.06-3.11; $p = 0.01$). The area under the curve (AUC) to assess the ability of WWI to identify MS showed values of 0.811 (0.687-0.871; $p = 0.001$). The cut-off point according to the Youden index was 11.59, with sensitivity and specificity of 70 % and 93.4 %, respectively.

Conclusion: we described a good accuracy of WWI to identify MS an independent association between WWI in Caucasian patients with obesity.

Keywords:

Metabolic syndrome.
Obesity. Weight-adjusted
waist index.

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Statement of ethics: this study protocol was reviewed and approved by the HCVUA Committee, approval number No. 6/2021. Written Informed consent was obtained from all individual participants included in the study.

Consent to participate statement: a signed informed consent was obtained from all participants. This research complies with the guidelines for human studies in accordance with the World Medical Association Declaration of Helsinki.

Authors' contributions: Daniel Antonio de Luis designed the study and wrote the article. Juan José López Gómez, Daniel Rico and Olatz Izaola performed the nutritional evaluations. D Primo and D de Luis performed the biochemical evaluations.

Data availability statement: all data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Conflicts of interest statement: the authors have no conflicts of interest to declare.

Artificial intelligence: the authors declare not to have used artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

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Resumen

Antecedentes y objetivos: la utilidad del índice de cintura ajustado al peso (ICAP) entre personas con síndrome metabólico (SM) no se ha evaluado previamente. El objetivo de este estudio fue evaluar la capacidad de ICAP para predecir la SM en una población caucásica con obesidad.

Métodos: realizamos un estudio transversal en 2,162 pacientes caucásicos con obesidad. Los datos antropométricos (peso, altura, índice de masa corporal (IMC), circunferencia de la cintura, ICAP), parámetros del bioimpedanciómetro (masa grasa total [MG], la masa de músculo esquelético [MME] y el índice de masa de músculo esquelético [iMME]), la presión arterial, la presencia de SM y los parámetros bioquímicos se registraron y compararon por terciles del ICAP.

Resultados: un total de 1176 sujetos tenían SM (54,4 %) y 986 no presentaban SM (45,6 %). En comparación con la categoría más baja del ICAP, Q1 (< 11,24 cm/√kg), la prevalencia de SM aumentó en el modelo de regresión logística ajustado por sexo y edad en el grupo Q3 (OR = 2,53, IC 95 % = 1,71-3,23; $p = 0,001$). Además, la prevalencia del SM fue mayor en el grupo Q3 que en el Q2 (OR = 1,65, IC 95 % = 1,25-2,17; $p = 0,005$). Finalmente, la prevalencia de SM en el grupo Q2 fue mayor que en el grupo Q1 (OR = 1,21, IC 95 % = 1,06-3,11; $p = 0,01$). El área bajo la curva (AUC) para evaluar la capacidad del ICAP para identificar la SM mostró valores de 0,811 (0,687-0,871; $p = 0,001$). El punto de corte según el índice de Youden fue 11,59, con sensibilidad y especificidad del 70 % y el 93,4 %, respectivamente.

Conclusión: describimos una buena precisión del ICAP para identificar el SM, y una asociación independiente entre ICAP en pacientes caucásicos con obesidad.

Palabras clave:

Síndrome metabólico.
Obesidad. Índice de cintura ajustado al peso.

INTRODUCTION

Obesity is defined as excess of body fat; this fact is a well-known risk factor for various entities including dyslipidaemia, diabetes *mellitus* type 2, hypertension, non-alcoholic fatty liver disease, metabolic syndrome and cardiovascular diseases (1). In this context, body mass index (BMI) is the most widely used measure of obesity (2). Many studies showed a linear association between BMI and risk of diabetes *mellitus*, hypertension and cardiovascular diseases (3,4). Despite, inverse or inconsistent associations between BMI and mortality have resulted in the “obesity paradox” (5,6). Some physiopathological explanations for this paradox have been implied (7,8). Moreover, some authors have implied the limitation of BMI as a real measure of obesity, as this marker does not differentiate between fat mass and lean mass (9).

On the other hand, waist circumference (WC) has been indicated as a more accurate body adiposity index for the prediction of metabolic disorders than BMI, it has a good correlation with abdominal fat imaging and excellent association with mortality and cardiovascular risk factors (10,11). Moreover, WC is correlated with BMI, and it is limited as an independent measure of BMI. Moreover, the ‘Obesity Paradox’ has also been described when waist circumference (WC) is used as an obesity index (12). A novel adiposity index called the weight-adjusted waist index (WWI) was described in 2018 as a new obesity anthropometric index (13). BMI cannot distinguish between muscle and fat mass, but WWI can better distinguish both components and mainly shows the problem of central obesity independent of total body weight (14). A lot of evidence confirmed that the value of WWI is a useful risk factor for heart failure, hyperuricemia, abdominal aortic calcification, diabetes *mellitus* type 2 and urinary albumin excretion (15-18). However, the relationship of WWI with metabolic syndrome (MS) has not been investigated. Metabolic Syndrome (MS) is a constellation of risk entities related with obesity; including glucose intolerance or diabetes *mellitus*, abdominal obesity, hyperlipidemia and high blood pressure levels (19). MS therefore marks patients with high cardiovascular risk and it is necessary to identify them with a simple methodology in routine clinical practice.

Thus, the objective of this study was to evaluate the ability of WWI to predict MS in a Caucasian population with obesity.

PATIENTS AND METHODS

SUBJECTS

Caucasian patients with obesity living in our Health Area in western Castile and Leon, Spain, were included in the study from January 2020 to December 2022. The participants were selected through convenience sampling. Patients were recruited consecutively upon arrival at our Nutrition Unit for assessment of their obesity. In all 2,162 adults of both genders, aged 18 year and older with obesity were recruited. Recruited patients signed a consent form. The protocol complies with the Declaration of Helsinki as well as with local institutional guidelines. The Ethics Committee (code of registration 03/2020) approved it.

The inclusion criteria for this study were the following; obesity assessed as body mass index (BMI) ≥ 30 kg/m² and age above 18 years. Exclusion criteria were the next; presence of any associated condition (e.g., chronic kidney disease (glomerular filtration ≤ 45 ml/min), chronic liver disease (Child stage B or C), heart failure (ventricular excretion fraction ≤ 50 %), malignant tumours, history of alcoholism, use of medications that potentially influenced weight or metabolic parameters (statins, fibrates and drugs to treat diabetes *mellitus*), inability to walk or being bedridden.

The evaluated parameters of the present study included; anthropometric data (weight, height, body mass index [BMI], waist circumference, weight-adjusted waist index [WWI]), bioimpedanciometer parameters (total fat mass [FM], skeletal muscle mass [SMM] and skeletal muscle mass index [SMMi]), blood pressure and biochemical assessment. During the basal visit, 15 ml of venous blood after an 8 hour overnight fast were obtained and aliquoted in ethylenediaminetetraacetic acid EDTA-coated tubes. All patients recorded their daily dietary intake and physical activity. Finally, patients with three or more of the criteria listed in the text were considered as having metabolic syndrome, as defined using the Adult Treatment Panel III (ATPIII) criteria (19): elevated fasting glucose or treatment for diabetes *mellitus*, elevated tri-

glycerides (> 150 mg/dl) or treatment for hyperlipidemia, low HDL-cholesterol < 40 mg/dl (males) or < 50 mg/dl (females), elevated systolic or diastolic blood pressure ($> 130/85$ mmHg or antihypertensive treatment) and increased waist circumference (> 88 cm, females or > 102 cm, males).

ANTHROPOMETRIC PARAMETERS, BLOOD PRESSURE AND LIFESTYLE PARAMETERS

Height, weight and waist circumference were measured using standardized techniques, while the patients were wearing only light clothing. Weight was measured to the nearest 0.1 kg using a digital scale (Omrom, LA, CA, USA). Stature was measured bare footed to the nearest 0.5 cm using a stationary stadiometer (Omrom, LA, CA, USA). Waist circumference was measured at the nearest 0.1 cm just above the ilium with a flexible tape (Omrom, LA, CA). Weight and stature were used to calculate BMI; weight in kilograms divided by height in squared meters. Weight-adjusted waist index (WWI) was calculated with the following formula; waist circumference in centimeters divided by square root of weight. Subjects were divided into three groups based on WWI tertiles. WWI tertiles were defined as follows: < 11.24 cm/ $\sqrt{\text{kg}}$ (Q1), ≥ 11.24 and < 11.92 cm/ $\sqrt{\text{kg}}$ (Q2), ≥ 11.92 cm/ $\sqrt{\text{kg}}$ (Q3).

Total fat mass (FM) and skeletal muscle mass (SMM) were obtained by bioelectrical impedance analysis with an accuracy of 50 g (20) (EFG BIA 101 Anniversary, Akern, It). SMMi (skeletal muscle mass index) was obtained by dividing SMM by squared height. Blood pressure was measured using a standard sphygmomanometer (Omrom, LA, CA, USA). Systolic and diastolic blood pressures were measured two consecutive times on the right arm after 10 minutes rest, and average of the two measures was calculated.

BIOCHEMICAL PROCEDURES AND ADIPONECTIN

All samples were measured in our central laboratory. Glucose, insulin, C-reactive protein (CRP), total cholesterol, HDL-cholesterol and triglyceride were measured according to the manufacturer using the COBAS INTEGRA 400 analyser (Roche Diagnostic, Basel, Switzerland). LDL-cholesterol was calculated using Friedewald equation (LDL cholesterol = total cholesterol - HDL cholesterol-triglycerides / 5) (21). Based on glucose and insulin levels, homeostasis model assessment for insulin resistance (HOMA-IR) was obtained using these values (glucose (mmol/L) x insulin (UI/L) / 22.5) (22). Adiponectin, interleukin-6 and leptin were measured by enzyme immunoassay (ELISA) (R&D systems, Inc., Minnesota, USA) (23).

STATISTICAL ANALYSIS

Data analysis was performed using IBM SPSS Statistical Package for Social Sciences, version 24.0 (SPSS Statistics, IBM, Ar-

monk, NY, USA). Sample size was calculated to detect significant statistical correlation between WWI and MS criteria with 90 % power and 5 % significance ($n = 2000$). Continuous data were expressed as mean \pm standard deviation. An independent t test was used to compare factors with continuous variables between two groups for parametric variables and Mann-Whitney test for non-parametric variables. ANOVA for continuous variables among tertiles of WWI was used. Chi-squared test or Fischer exact test, as appropriated, was used to compare categorical variables. Spearman's or Pearson's correlation analysis were used to explore the relationship among WWI with other parameters. Multiple logistic regression models were used to estimate odds ratios (ORs) and 95 % confidence intervals (CIs) in order to examine the relationship between MS and WWI. The receiver operating characteristic (ROC) curve and the area under the ROC curve (AUC) were used to assess the ability of WWI to identify MS. And the cutoff points were elucidated by two methods: the area under the curve (AUC) that had the best specificity and sensitivity values for the test in question, and the Youden Index as (sensitivity + specificity) - 1). p -values below 0.05 were considered statistically significant.

RESULTS

A total of 2,162 subjects with obesity were recruited, 927 males (42.9 %) and 1,235 females (57.1 %) with an average age of 50. 2 ± 10.3 years. A total of 1,176 subjects had MS (54.4 %) and 986 did not show MS (45.6 %).

Table I summarizes the clinical and anthropometric details of the study population according to WWI categories. Compared with the subjects in the lower WWI tertile (< 11.24 cm/ $\sqrt{\text{kg}}$) Q1, those in the higher WWI categories (Q2) (≥ 11.24 and < 11.92 cm/ $\sqrt{\text{kg}}$) and (Q3) (≥ 11.92 cm/ $\sqrt{\text{kg}}$) had higher values of BMI, weight, fat mass and systolic blood pressure. And vice versa, the subjects in Q2 and Q3 groups compared with subjects in Q1 group had lower muscle mass and muscle mass index.

Table II shows the biochemical parameters of the study population. Compared with the subjects in the lower WWI category (< 11.24 cm/ $\sqrt{\text{kg}}$) Q1, those in the higher WWI tertiles (Q2) (≥ 11.24 and < 11.92 cm/ $\sqrt{\text{kg}}$) and (Q3) (≥ 11.92 cm/ $\sqrt{\text{kg}}$) had higher values of fasting glucose, triglycerides, insulin, HOMA-IR, leptin, interleukin-6 and CRP levels. And vice versa, the subjects in Q2 and Q3 groups compared with subjects in Q1 group had higher adiponectin levels.

Table III displays the correlation analysis of WWI with biochemical and anthropometric parameters. WWI values were positive correlated with BMI, weight, WC, FM, glucose, insulin, HOMA-IR, triglycerides, interleukin-6, CRP and leptin levels. Moreover, WWI values were negative correlated with SMM, SMMi, phase angle and leptin levels.

Table IV summarizes the percentage of each MS criteria and the total MS percentage in each tertile groups of WWI. Percentage of MS, central obesity, hypertriglyceridemia, hypertension and hyperglycaemia were higher in groups (Q2) (≥ 11.24

and < 11.92 cm/ $\sqrt{\text{kg}}$) and (Q3) (11.92 cm/ $\sqrt{\text{kg}}$) than group (Q1) (< 11.24 cm/ $\sqrt{\text{kg}}$). Percentage of low HDL-cholesterol levels were similar among tertile groups. Patients with 0 or 1 criteria's of MS were 53.1 % in Q1 group, 30.7 % in Q2 group and 19.9 % in Q3 group ($p = 0.003$). Finally, compared with the lowest WWI category Q1 (< 11.24 cm/ $\sqrt{\text{kg}}$), the prevalence of MS increased in the logistic regression model adjusted by sex and age in Q3 group (OR = 2.53, 95 % CI = 1.71-3.23; $p = 0.001$). In addition, the prevalence of MS was higher in Q3 group than Q2

(OR = 1.65, 95 % CI = 1.25-2.17; $p = 0.005$). Finally, prevalence of MS in Q2 was higher than Q1 group (OR = 1.21, 95 % CI = 1.06-3.11; $p = 0.01$), too.

The ROC curve of the WWI index for MS is shown in figure 1. The area under the curve (AUC) according ATPIII criteria showed values of 0.811 (0.687-0.87; $p = 0.001$). The cut-off point according to the Youden index was 11.59, with sensitivity and specificity of 70 % and 93.4 %, respectively, and a positive likelihood ratio of 10.4 and negative likelihood ratio of 0.34.

Table I. Clinical and anthropometric parameters of the study participants by weight-adjusted waist index in tertiles (mean \pm SD)

Parameters	< 11.24 cm/ $\sqrt{\text{kg}}$ (Q1)	≥ 11.24 and < 11.92 cm/ $\sqrt{\text{kg}}$ (Q2)	≥ 11.92 cm/ $\sqrt{\text{kg}}$ (Q3)	p -value
Gender (female/male) (n)	412/309	413/308	410/311	0.45
Age (years)	41.5 \pm 5.3	50.1 \pm 5.2	58.1 \pm 5.1	0.01
BMI (kg/m ²)	34.8 \pm 1.5	37.3 \pm 1.7	40.1 \pm 2.4	0.01
Weight (kg)	95.1 \pm 2.0	98.4 \pm 3.0	99.8 \pm 1.7	0.02
Fat mass (kg)	44.4 \pm 9.0	43.3 \pm 9.1	45.3 \pm 8.4	0.03
Skeletal muscle mass (kg)	39.2 \pm 1.1	38.4 \pm 1.2	37.4 \pm 1.4	0.02
Skeletal muscle mass index (kg/m ²)	14.8 \pm 0.3	14.0 \pm 0.1	13.1 \pm 0.9	0.02
WC (cm)	103.6 \pm 11.1	114.3 \pm 10.7	124.3 \pm 9.3	0.01
SBP (mmHg)	125.7 \pm 12.0	130.5 \pm 8.0	134.5 \pm 8.1	0.04
DBP (mmHg)	80.3 \pm 4.1	82.2 \pm 3.1	82.6 \pm 4.0	0.41

BMI: body mass index; DBP: diastolic blood pressure; SBP: systolic blood pressure; WC: waist circumference.

Table II. Biochemical parameters of the study participants by weight-adjusted waist index in tertiles (mean \pm SD)

Parameters	< 11.24 cm/ $\sqrt{\text{kg}}$ (Q1)	≥ 11.24 and < 11.92 cm/ $\sqrt{\text{kg}}$ (Q2)	≥ 11.92 cm/ $\sqrt{\text{kg}}$ (Q3)	p -value
Fasting glucose (mg/dl)	97.9 \pm 3.1	102.1 \pm 2.1	111.1 \pm 2.3	0.01
Total cholesterol (mg/dl)	196.2 \pm 21.8	202.9 \pm 19.8	202.3 \pm 12.8	0.24
LDL-cholesterol (mg/dl)	119.7 \pm 18.9	121.7 \pm 12.9	120.7 \pm 13.1	0.29
HDL-cholesterol (mg/dl)	52.6 \pm 3.1	53.4 \pm 4.0	52.5 \pm 3.2	0.28
Triglycerides (mg/dl)	120.7 \pm 11.0	129.9 \pm 12.0	135.4 \pm 9.0	0.03
Insulin (UI/l)	14.6 \pm 1.2	15.9 \pm 1.1	17.7 \pm 2.1	0.02
HOMA-IR	3.4 \pm 0.8	4.0 \pm 0.4	4.8 \pm 0.2	0.03
Leptin (ng/ml)	56.9 \pm 9.8	69.8 \pm 8.7	91.9 \pm 7.9	0.01
Adiponectin (ng/ml)	22.9 \pm 0.9	17.4 \pm 0.7	13.9 \pm 0.9	0.01
Interleukin-6 (pg/ml)	1.4 \pm 0.8	2.1 \pm 0.7	4.4 \pm 1.1	0.01
CRP (mg/dl)	3.3 \pm 1.3	4.2 \pm 0.8	6.3 \pm 0.9	0.03

HOMA-IR: homeostasis model assessment.

Table III. Correlation analysis between weight-adjusted waist index, bioelectric impedance and biochemical parameters

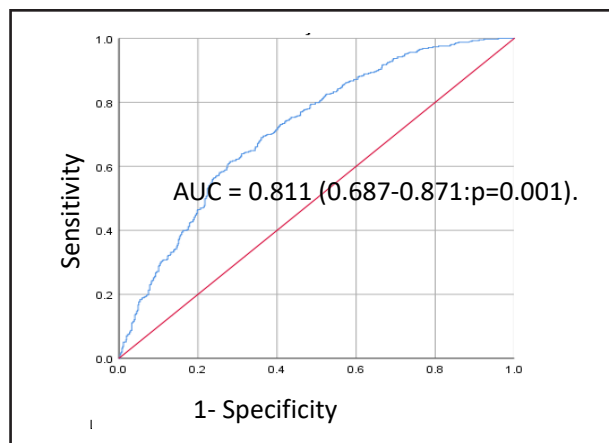
Anthropometric parameters and blood pressure	Weight-adjusted waist index	Biochemical parameters	HOMA-IR
BMI (kg/m ²)	$r = 0.277, p = 0.01$	Glucose (mg/dl)	$r = 0.337, p = 0.59$
Weight (kg)	$r = 0.361, p = 0.002$	Insulin (MU/L)	$r = 0.299, p = 0.001$
Waist circumference (cm)	$r = 0.676, p = 0.001$	HOMA-IR	$r = 0.329, p = 0.003$
Fat mass (kg)	$r = 0.191, p = 0.02$	Triglycerides (mg/dl)	$r = 0.174, p = 0.012$
Skeletal muscle mass (kg)	$r = -0.24, p = 0.005$	Adiponectine (ng/ml)	$r = -0.210, p = 0.005$
Skeletal muscle mass index (kg/m ²)	$r = -0.27, p = 0.003$	Leptin (ng/ml)	$r = 0.182, p = 0.02$
Systolic blood pressure	$r = 0.19, p = 0.001$	CRP (ng/m)	$r = 0.230, p = 0.01$
Phase angle	$r = -0.14, p = 0.001$	Interleukin-6	$r = 0.218, p = 0.02$

BMI: body mass index; CRP: C-reactive protein; HOMA-IR: homeostasis model assessment.

Table IV. Metabolic syndrome and components of metabolic syndrome percentages by weight-adjusted waist index in tertiles

Parameters	< 11.24 cm/√kg (Q1),	≥ 11.24 and < 11.92 cm/√kg (Q2)	≥ 11.92 cm/√kg (Q3)	p-value
Percentage of MS	29.8 %	48.7 %	64.4 %	0.001
Percentage of central obesity	60.6 %	90.0 %	99.5 %	0.001
Percentage of hypertriglyceridemia	6.5 %	10.2 %	12.8 %	0.02
Low HDL cholesterol	32.3 %	34.3 %	33.2 %	0.53
Percentage of hypertension	32.3 %	46.3 %	59.4 %	0.001
Percentage of hyperglycaemia	10.8 %	19.0 %	35.5 %	0.001

MS: metabolic syndrome. The criteria cutoff points included: central obesity (waist circumference > 88 cm in females and > 102 cm in males), hypertension (systolic BP > 130 mmHg or diastolic BP > 85 mmHg or specific treatment), hypertriglyceridemia (triglycerides > 150 mg/dl or specific treatment) or hyperglycaemia (fasting plasma glucose > 110 mg/dl or drug treatment for elevated blood glucose). Statistical differences between groups established when $p < 0.05$.

**Figure 1.** ROC curve.

DISCUSSION

In this cross-sectional study among Caucasian patients with obesity older than 18 years, we confirmed that the prevalence of metabolic syndrome (MS) increased with the weight-adjusted waist index (WWI) tertiles and that there was a significant correlation between WWI and some anthropometric and biochemical parameters in these patients.

A lot of evidence confirms that obesity increases the risk of hypertension, diabetes *mellitus* type 2, hyperlipemia, cardiovascular disease and metabolic syndrome (24). Several studies reported the predictive value of BMI as an important indicator of obesity is limited in that it is unable to distinguish between fat mass and muscle mass (25). For all this, it is necessary to identify an adiposity index with the accuracy to predict the risk of metabolic disorders associated to obesity to decrease future cardiometabolic mortality in these subjects. As a novel adiposity index, WWI, which is easier to estimate, is an important predictor of morbidity which has been joined to cardiometabolic disease (13). To our knowledge, this is the first investigation examining the association between WWI and prevalence of MS. WWI has been previously evaluated in a huge range of diseases, such as hyperuricemia, albuminuria, hypertension, heart hypertrophy and abdominal aortic calcification (14-18).

Our present results reinforce the effectiveness of WWI as a novel marker of central obesity to predict MS in Caucasian patients with obesity. Some hypotheses have been implied to explain the positive association between BMI and Metabolic syndrome. Firstly, the increment of WWI may reflect the alteration of adipose tissue; this fact causes an increase in immune cell infiltration, proinflammatory cytokines, and producing insulin resistance and lipid disorders (26). Secondly, obesity is related with increased inflammatory markers as our study shows with CRP and IL-6, this inflammatory status is directly associated with insulin resistance. Other pathways, such as NK-kB, JNK and alteration in adipokine levels (high leptin and low adiponectin) have been implied in these pathogenic processes (27-30). In our design, we reported a direct correlation of IL-6, CRP, leptin with WWI, and secondarily WWI with insulin resistance (HOMA-IR). These results are in agreement with the hypotheses presented previously. Perhaps, this new anthropometric index reflects the visceral adipose tissue of the body, based on waist standardized with body weight in the equation. Until now, there have been no studies on the recognition capability for MS in Caucasian subjects with obesity. Our study found a cut-off point (WWI = 11.59) to determine the presence of MS with a high specificity and a medium sensitivity. This high specificity characterizes the WWI's ability to detect the absence of MS in subjects with obesity and the medium sensitivity value characterizes the WWI's ability to detect MS in subjects with obesity, too.

Besides, WWI could be an indicator of muscle and fat composition. Measurement of muscle mass has become increasingly important as a measure of body composition and health status in patients with obesity (31). However, determination of muscle mass without a special device (bioelectrical impedance, com-

puterized axial tomography, Dual X-ray Absorptiometry, nuclear magnetic resonance and so on) is difficult. Similar to previous studies on WWI in non-Caucasian populations, our results presented indicate that WWI is a good tool to differentiate muscle and fat mass in obesity populations (32).

In addition, previous studies have confirmed that WWI had correlation with some biochemical parameters such as albuminuria (17) and uric acid (18). In one of these studies (17), the inflection point of WWI was 10.93, with a high correlation of albuminuria with WWI in this point. This cut-off point is close to our point (11.59) to detect MS. On the other hand, in our study we have detected a positive correlation with CRP, leptin and IL-6, and a negative one with adiponectin, these being the first data in the literature demonstrating this correlation with WWI. These data are consistent with the WWI relationship with visceral fat mass and insulin resistance.

The limitations of our study are as follows: firstly, the design has been realized only in Caucasian subjects with obesity and metabolic syndrome, so the data are not generalizable to other ethnicities, overweight subjects, or other patients with obesity and without MS. Secondly, the investigation as a cross-sectional design does not allow any inference causality. Thirdly, the subjects came from a single center. Some strengths of our study are the large sample size and that the representation of both genders was similar.

In conclusion, we described a good accuracy of WWI to identify MS in Caucasian patients with obesity. WWI is positive related with inflammatory markers such as CRP, IL-6 and leptin. Furthermore, WWI can be a useful intervention tool to decrease MS incidence. We can consider the changes in WWI values to determine the effectiveness of body weight control and intervention programs. WWI is an easy tool to monitor risk of MS without the need for a blood draw for glucose or lipid determination as is necessary to determine MS, or the need to measure blood pressure. For all of this, WWI may serve as an effective and simple anthropometric index in clinical practice.

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Trabajo Original

Obesidad y síndrome metabólico

El combate de los análogos de GLP-1: efectos de semaglutida 0,5 mg semanales versus liraglutida 3 mg diarios sobre los parámetros antropométricos durante 3 meses en la vida real

The GLP-1 analogue battle: effects of semaglutide 0,5 mg/weekly versus liraglutide 3 mg/daily on anthropometric parameters after 3 months in a real world-scenario

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Resumen

Introducción: casi dos tercios de los pacientes en tratamiento con 3 mg de liraglutida no lograron los objetivos de pérdida de peso, lo que lleva a la búsqueda de otras opciones farmacológicas. El STEP 8 demostró la superioridad de la semaglutida, 2,4 mg/semana, en comparación con la liraglutida, 3 mg/día. Evaluamos los efectos de 0,5 mg de semaglutida sc semanal en comparación con 3 mg de liraglutida/día en personas con obesidad (PwO) sobre los parámetros antropométricos en la vida real durante 3 meses.

Métodos: 179 PwO (91,9 % mujeres, 45,7 ± 10 años e IMC de 33,3 ± 7 kg/m²) recibieron tratamiento con aGLP-1 e intervenciones en el estilo de vida y fueron evaluadas retrospectivamente al inicio y después de 3 meses. A 99 pacientes se les prescribió semaglutida sc, 0,5 mg semanales, con indicación fuera de la ficha técnica para reducción del peso, y se les comparó con 80 pacientes tratados con 3 mg día de liraglutida sc. Se estudió la evolución de los parámetros antropométricos y de composición corporal en ambos grupos.

Resultados: las PwO experimentaron una reducción significativa del peso con la semaglutida sc en dosis de 0,5 mg semanales (96,67 ± 20,83 vs. 91,44 ± 19,6 kg; $p < 0,01$) y la liraglutida en dosis de 3 mg al día (90,73 ± 21,88 vs. 80,13 ± 18,38 kg; $p < 0,01$). No se observaron diferencias significativas entre los grupos en la cantidad de peso perdida ni en términos de la masa grasa ni de la masa libre de grasa.

Conclusión: tanto la semaglutida en dosis de 0,5 mg y como la liraglutida en dosis de 3 mg son tratamientos eficaces y seguros para reducir el peso en las PwO sin impacto negativo sobre la masa magra. Además, en la vida real, las dosis bajas de semaglutida fueron similares a las de 3 mg de liraglutida para reducir el peso corporal a corto plazo.

Palabras clave:

Obesidad. Liraglutida.
Semaglutida. Sobre peso.
Nutrición.

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Abstract

Background: the prevalence of obesity is reaching a pandemic status. The SCALE trials showed that liraglutide 3 mg among people with obesity (PwO) was effective to reduce bodyweight and related complications. The fact that almost two-thirds of patients did not achieve the desired weight loss with the maximum dose of liraglutide made almost mandatory the development of other pharmacological options. The STEP 1-5 trials showed the effectiveness of semaglutide in reducing bodyweight in a dose-dependent manner. Moreover, the STEP 8 trial proved the superiority of semaglutide 2,4 mg/week versus liraglutide 3 mg/daily. We aimed to assess the effects of subcutaneous (s.c.) semaglutide 0.5 mg/weekly compared with s.c. liraglutide 3 mg/daily in PwO on anthropometric parameters in a real world-scenario for 3 months.

Methods: we retrospectively evaluated 179 PwO (91.9 % ♀, 45.7 ± 10 years, and 33.3 ± 7 kg/m²) who received treatment with aGLP-1 as add-on therapy to lifestyle interventions. Patients were evaluated at baseline and after 3 months. Ninety-nine patients were prescribed s.c. semaglutide 0.5 mg/weekly with an off-label indication for weight reduction. These patients were compared with 80 patients treated with s.c. liraglutide 3 mg/daily. The main reason for prescribing of s.c. semaglutide was economic. Body composition was evaluated using a bioimpedance device (Tanita MC 580M[®]).

Results: baseline weight was significantly greater with semaglutide compared to liraglutide (97.19 ± 21.09 vs. 90.73 ± 21.88 kg; $p < 0.01$) as was fat mass (42.43 ± 15.04 vs. 34.84 ± 16.07 kg; $p < 0.01$), whereas baseline lean mass was lesser among subjects treated with semaglutide (31.62 ± 7.56 vs 45.69 ± 15.51 kg; $p < 0.01$). PwO experienced a significant reduction in weight using s.c. semaglutide 0.5 mg/weekly (96.67 ± 20.83 vs. 91.44 ± 19.6 kg; $p < 0.01$) or s.c. liraglutide 3 mg/daily (90.73 ± 21.88 vs. 80.13 ± 18.38 kg; $p < 0.01$)

No significant differences were seen between the amount of weight lost (5.28 ± 4.22 vs 5.72 ± 1.62 kg; $p = 0.5$) in the two groups. Furthermore, both groups were comparable in fat mass (2.69 ± 5.34 vs 0.96 ± 4.22 kg; $p = 0.3$) and fat-free mass (0.86 ± 1.63 vs 1.03 ± 0.94 kg; $p = 0.07$) after 3 months of treatment with both aGLP1. Side effects were gastrointestinal and transient/comparable between groups.

Conclusions: subcutaneous semaglutide 0.5 mg and subcutaneous liraglutide 3 mg are effective treatments for reducing weight safely among PwO in a real-world scenario at short term and without a negative impact on fat-free mass. Moreover, low doses of semaglutide were similar to liraglutide 3 mg in reducing bodyweight at short term.

Keywords:

Obesity. Overweight.
Liraglutide. Semaglutide.
Nutrition.

INTRODUCCIÓN

La obesidad es una enfermedad crónica, progresiva y recurrente, responsable directa o indirectamente de la muerte anual de 2,8 millones de personas según la Organización Mundial de la Salud (OMS). Es la enfermedad endocrino-metabólica más frecuente y, a día de hoy, afrontamos una creciente epidemia mundial de obesidad. Actualmente hay más de 670 millones de personas con obesidad. Las estimaciones futuras sugieren que cerca de 1 billón de personas sufrirá obesidad en el año 2030 (1,2).

Un objetivo de pérdida de peso del 5-10 % es clínicamente significativo porque reduce los factores de riesgo cardiovascular y mejora algunas comorbilidades en las personas con obesidad (PwO) (3-5). Sin embargo, pueden ser necesarias pérdidas de peso mayores, iguales o superiores al 10 % en aquellos con un IMC igual a o mayor de 35 kg/m² o con alto riesgo de desarrollar complicaciones relacionadas con la obesidad (3,5). El estudio Look AHEAD demostró que el grupo de intervención intensiva mediante modificaciones del estilo de vida solo consiguió reducciones inferiores al 10 % de su peso corporal después de 1 año (6). Por tanto, las intervenciones sobre el estilo de vida podrían no ser suficientes para conseguir una pérdida ponderal significativa que consiga una mejoría de las comorbilidades relacionadas con la obesidad y que, además, reduzca el riesgo cardiovascular, debiéndose considerar el tratamiento farmacológico adyuvante a esta mejora del estilo de vida.

En este sentido, la liraglutida en dosis de 3 mg, en el momento de la realización de este estudio, era el único análogo de GLP-1 (aGLP-1) aprobado para el tratamiento de la obesidad en España. En el ensayo SCALE, en donde se comparó el efecto de la liraglutida en dosis de 3 mg en PwO durante 56 semanas con el de un placebo, el 63,2 % de los pacientes, frente al 27,1 % del

grupo del placebo perdieron un 5 % de su peso corporal, y en el 33,1 % de los pacientes frente al 10,6 % del grupo del placebo, dicha pérdida de peso llegó al 10 % del peso corporal. Sin embargo, casi dos tercios de los pacientes no lograron la pérdida de peso deseada con la combinación de liraglutida 3 mg con la modificación intensiva del estilo de vida (7,8).

Por otro lado, los estudios STEP demostraron la eficacia y la seguridad de la semaglutida en dosis de 2,4 mg/semana para reducir el peso corporal de forma dosis-dependiente en PwO con y sin diabetes (9-11). Previamente, el programa de desarrollo clínico SUSTAIN ya había demostrado la eficacia y la seguridad de la semaglutida en dosis de 1 mg en PwO y diabetes de tipo 2 frente a un placebo tras 30 semanas de tratamiento (12). Además, el ensayo STEP 8 demostró la superioridad de la semaglutida en dosis de 2,4 mg frente a la liraglutida en dosis de 3 mg, al objetivarse una reducción del 15,8 % del peso con semaglutida 2,4 mg frente a una reducción del 6,4 % en el grupo tratado con liraglutida 3 mg (11). Recientemente, y después de la realización de este trabajo, se ha aprobado el uso de la semaglutida para el tratamiento de la obesidad en España.

En España, en los últimos dos años, la falta y/o el suministro irregular tanto de liraglutida como de semaglutida ha obligado a adaptar la terapia farmacológica a la disponibilidad de estos fármacos. Además, ambos fármacos no están financiados por la Administración, hecho que dificulta el acceso a ellos. Por otro lado, la semaglutida a cualquier dosis resulta más económica que la liraglutida a dosis de 3 mg, y esto puede ser un factor relevante a la hora de la prescripción del fármaco por parte del facultativo según la capacidad económica del paciente.

Nuestro objetivo fue comparar los efectos de la semaglutida en dosis de 0,5 mg frente a la liraglutida en dosis de 3 mg, en PwO, sobre los parámetros antropométricos y de composición corporal en la práctica clínica diaria durante 4 meses.

MATERIAL Y MÉTODOS

POBLACIÓN Y MUESTRA DEL ESTUDIO

Este estudio observacional y retrospectivo incluyó a 179 pacientes que asistieron a dos clínicas de obesidad. Estos pacientes no lograron alcanzar o mantener una pérdida de peso significativa a pesar de las intervenciones en el estilo de vida, que comprendían una dieta hipocalórica adaptada y un mínimo de 150 minutos de ejercicio por semana. Tras un proceso de toma de decisiones compartido a fondo, que involucró al paciente, en el que se repasó la información comprensible sobre los posibles beneficios y daños del uso de semaglutida y liraglutida, estas se prescribieron a criterio del facultativo y de modo consensuado con el paciente, incluyéndose finalmente un total de 179 PwO. La falta y/o el suministro irregular tanto de liraglutida como de semaglutida condicionó la elección de la farmacoterapia disponible y, dado que la semaglutida a cualquier dosis resulta más económica que la liraglutida a dosis de 3 mg, este fue un factor relevante a la hora de la prescripción del fármaco por parte del facultativo según la posibilidad económica del paciente.

Los criterios de elegibilidad fueron los siguientes: a) pacientes mayores de 18 años, con IMC igual o superior a 27 kg/m² y con comorbilidades relacionadas con la obesidad, o con IMC igual o superior a 30 kg/m²; b) pacientes sin antecedentes personales de carcinoma medular de tiroides, ni de pancreatitis aguda o crónica; c) pacientes que pudieran entender la información proporcionada y capaces de mantener un seguimiento regular; y d) pacientes que dieran su consentimiento para participar en el estudio. Este estudio se llevó a cabo de acuerdo con la Declaración de Helsinki de la Asociación Médica Mundial. Se obtuvo el consentimiento informado de todos los sujetos antes de la participación en el estudio.

INTERVENCIÓN

El asesoramiento dietético incluyó una dieta cuantitativa y estructurada adaptada, con una reducción promedio de 500 kcal/día de la tasa metabólica basal (TMB) calculada mediante la ecuación de Harris Benedict (para varones: $TMB = 88,362 + (13,397 \times \text{peso en kg}) + (4,799 \times \text{altura en cm}) - (5,677 \times \text{edad en años})$; para mujeres: $TMB = 447,593 + (9,247 \times \text{peso en kg}) + (3,098 \times \text{altura en cm}) - (4,330 \times \text{edad en años})$) y ajustada a la actividad física. Mediante recordatorios dietéticos de 24 horas y un seguimiento estrecho, se monitorizó la adherencia a las pautas nutricionales. Además, se prescribió un mínimo de 150 minutos de ejercicio aeróbico por semana. Mediante acelerómetros y/o el registro de la actividad física por parte del paciente, se monitorizó el seguimiento de las recomendaciones de actividad física. En cuanto a la titulación de la semaglutida, los pacientes comenzaron con una dosis de 0,25 mg por semana durante las primeras dos semanas y, dependiendo de la tolerancia y los efectos secundarios, principalmente gastrointestinales, esta dosis se

tituló hasta 0,5 mg después de dos semanas de tratamiento. En cuanto a la titulación de la liraglutida, los pacientes comenzaron con una dosis de 0,6 mg diarios durante la primera semana para pasar a 1,2 mg diarios durante la segunda semana y 1,8 mg diarios durante la tercera semana; dependiendo de la tolerancia y los efectos secundarios, principalmente gastrointestinales, esta dosis se tituló hasta 3 mg de forma paulatina y siguiendo la ficha técnica. El tiempo promedio para alcanzar las dosis objetivo fue de 4-6 semanas, dependiendo de la tolerancia individual de cada paciente. Los pacientes fueron evaluados al inicio y al cabo de tres meses desde el inicio de la semaglutida o la liraglutida.

PARÁMETROS ANTROPOMÉTRICOS

La altura y el peso se midieron con cada participante en ropa interior sin zapatos. El índice de masa corporal (IMC) se calculó como el peso dividido por la altura al cuadrado. Para la determinación del porcentaje de masa grasa (MG) corporal y de la masa magra se realizó el análisis de composición corporal por la técnica de la bioimpedancia eléctrica en un equipo bicompartimental (TANITA MC 580M[®], Biológica Tecnología Médica SL, Tokio, Japón). El porcentaje de masa libre de grasa (MLG), el índice de grasa visceral (IGV) y el porcentaje de agua corporal total (ACT) también se calcularon mediante el equipo bicompartimental TANITA. Para ello se concertó una cita a fin de que las participantes cumplieran las recomendaciones necesarias para un correcto análisis (es decir, no comer alimentos desde 3 horas antes de la medición; no beber nada desde 30 minutos antes; no realizar deporte o actividad física moderada o intensa desde 12 horas antes; no beber café, té, coca cola o cualquier otra bebida estimulante o energética desde 4 horas antes; no ingerir bebidas alcohólicas desde 24 horas antes; no fumar desde 30 minutos antes; y comunicar si tomaba algún fármaco que pudiera causar retención de líquidos). La pérdida de peso significativa se definió como una reducción de más del 5 % del peso basal.

ANÁLISIS ESTADÍSTICO

Los análisis estadísticos se realizaron utilizando el programa IBM[®] SPSS[®] Statistics Versión 21.0. Los análisis iniciales fueron descriptivos e incluyeron el cálculo de la media, la mediana y la desviación estándar para las variables continuas, y las frecuencias para las variables categóricas. La distribución de la muestra se analizó mediante la prueba de Kolmogorov-Smirnov.

El principal resultado en este estudio fueron la pérdida de peso y la composición corporal después de tres meses de tratamiento con semaglutida o liraglutida. En los resultados secundarios se comparan las diferencias de composición corporal entre ambos grupos. La pérdida de peso y los cambios de la composición corporal se compararon utilizando el ANOVA para medidas repetidas. Para todas las comparaciones estadísticas se asumió una p de dos lados < 0,05 como significativa.

RESULTADOS

De las 179 pacientes incluidas, 99 (55,3 %) iniciaron tratamiento con semaglutida y a 80 pacientes (44,7 %) se les prescribió liraglutida. No se evidenciaron diferencias significativas entre los dos grupos en cuanto a la edad ($45,4 \pm 10,5$ vs. $46,1 \pm 10,6$ años; $p = 0,6$) o el porcentaje de mujeres incluidas en los grupos (87 % vs. 91 %; $p = 0,9$).

El peso inicial y el IMC fueron significativamente mayores en el grupo de pacientes que iniciaron tratamiento con semaglutida ($97,2 \pm 21,1$ vs. $90,7 \pm 21,8$ kg y $34,8 \pm 6,7$ vs. $31,6 \pm 7,9$ kg/m²; $p < 0,001$ y $p = 0,004$, respectivamente). Al tener en cuenta los parámetros de composición corporal al inicio del estudio, tanto la masa grasa en kilogramos como el porcentaje de masa grasa fueron significativamente mayores en el grupo de pacientes tratados con semaglutida en comparación con aquellos tratados con liraglutida ($42,4 \pm 15$ vs. $34,8 \pm 16,1$ kg y $42 \pm 7,8$ vs. $38,4 \pm 11,8$ %; $p < 0,001$ y $p = 0,02$). Del mismo modo, la masa magra fue significativamente más baja en el grupo de

tratamiento con semaglutida ($31,6 \pm 7,6$ vs. $45,7 \pm 15,5$ kg; $p < 0,001$). Estos datos se muestran en la tabla I.

Como se muestra en las tablas II y III, después de tres meses de tratamiento con los respectivos aGLP-1, ambos grupos experimentaron reducciones significativas del peso y mejoras de los parámetros de composición corporal.

Cuando comparamos la evolución de los parámetros antropométricos entre los dos grupos tras tres meses de tratamiento, tanto la pérdida de peso ($-5,3 \pm 4,2$ vs. $-5,7 \pm 1,6$ kg; $p = 0,4$) como el porcentaje de pérdida de peso ($5,9 \pm 2,8$ vs. $6,2 \pm 2,2$ %; $p = 0,2$) fueron comparables. Además, tanto la pérdida de masa grasa en kilos ($-2,7 \pm 5,3$ vs. $-1 \pm 4,2$ kg; $p = 0,3$) como el porcentaje de pérdida de masa grasa ($-1,6 \pm 1,7$ vs. $-1,1 \pm 1,7$ %; $p = 0,8$) fueron similares entre los dos grupos. Asimismo, la pérdida de masa magra también fue comparable entre los dos grupos (-0.86 ± 1.6 vs. $-1.03 \pm 0,9$ kg; $p = 0,3$). Estos datos se muestran en la tabla IV.

No se observaron diferencias entre los dos grupos con respecto a los efectos secundarios gastrointestinales ni en las interrupciones del tratamiento.

Tabla I. Parámetros basales demográficos, antropométricos y de composición corporal en el grupo de pacientes tratados con liraglutida 3 mg y el grupo de pacientes en tratamiento con semaglutida 0,5 mg

	Grupo con liraglutida (n = 80)	Grupo con semaglutida (n = 99)	p
Edad (años)	46,1 ± 10,6	45,4 ± 10,5	0,6
Sexo (mujer, %)	91	87	0,9
Peso inicial (kg)	90,7 ± 21,8	97,2 ± 21,1	< 0,001
IMC inicial (kg/m ²)	31,6 ± 7,9	34,8 ± 6,7	0,004
MG inicial (kg)	34,8 ± 16,1	42,4 ± 15	< 0,001
MG inicial (%)	38,4 ± 11,8	42 ± 7,8	0,02
MM inicial (kg)	45,7 ± 15,5	31,6 ± 7,6	< 0,001

Los datos se expresan en % o media ± desviación estándar. IMC: índice de masa corporal; MG: masa grasa; MM: masa muscular.

Tabla II. Cambios en los parámetros antropométricos y de composición corporal tras tres meses de tratamiento con liraglutida 3 mg

Grupo liraglutida (n = 56)	Basal	3 meses	p
Peso (kg)	90,7 ± 21,8	80,1 ± 18,4	< 0.0001
IMC (kg/m ²)	31,6 ± 7,9	31,1 ± 6,1	< 0.0001
Masa grasa (%)	38,4 ± 11,8	35,1 ± 15,3	0,05
Masa grasa (kg)	34,8 ± 16,1	31,5 ± 17,8	0,05
Masa magra (kg)	45,7 ± 15,5	47,1 ± 18	0,9

Los datos se expresan en % o media ± desviación estándar. IMC: índice de masa corporal.

Tabla III. Cambios en los parámetros antropométricos y de composición corporal tras tres meses de tratamiento con semaglutida 0,5 mg

Grupo semaglutida (n = 99)	Basal	3 meses	p
Peso (kg)	97,2 ± 21,1	91,4 ± 19,6	< 0.0001
IMC (kg/m ²)	34,8 ± 6,7	32,7 ± 6,2	< 0.0001
Masa grasa (%)	42 ± 7,8	39,8 ± 8,8	0,01
Masa grasa (kg)	42,4 ± 15	38 ± 14,1	0,01
Masa magra (kg)	31,6 ± 7,6	30,4 ± 6	0,05

Los datos se expresan en % o media ± desviación estándar. IMC: índice de masa corporal.

Tabla IV. Cambios en los parámetros antropométricos y de composición corporal tras 3 meses de tratamiento con liraglutida 3 mg frente a semaglutida 0,5 mg

	Grupo con liraglutida (n = 80)	Grupo con semaglutida (n = 99)	p
Cambio en el peso (kg)	-5,7 ± 1,6	-5,3 ± 4,2	0,5
Porcentaje de pérdida de peso (%)	5,9 ± 2,8	6,2 ± 2,2	0,2
Cambio en masa grasa (%)	-1,6 ± 1,7	-1,1 ± 1,7	0,8
Cambio en masa grasa (kg)	-1 ± 4,2	-2,7 ± 5,3	0,3
Cambio en masa magra (kg)	1,03 ± 0,9	-0,86 ± 1,6	0,3
Cambio en el IMC	-1,03 ± 0,9	-2,7 ± 2,4	0,07

Los datos se expresan en media ± desviación estándar o %. IMC: índice de masa corporal.

DISCUSIÓN

Los resultados de nuestro estudio mostraron que la pérdida de peso y la modificación de la composición corporal en las pacientes que iniciaron tratamiento con liraglutida a dosis máximas o semaglutida a dosis medias fueron comparables (Fig. 1).

La obesidad es una enfermedad crónica, compleja, multifactorial y recidivante que se asocia a múltiples comorbilidades metabólicas, mecánicas y psicológicas, y que reduce significativamente la calidad de vida, además de incrementar el riesgo de desarrollar un evento cardiovascular. El primer escalón terapéutico son las modificaciones del estilo de vida, que comprenden una reducción del aporte calórico diario, así como la práctica de un ejercicio físico regular. Sin embargo, pese a la adopción de estos hábitos, un porcentaje importante de PwO no alcanzan una pérdida de peso significativa o en ellas se produce un estancamiento de la pérdida de peso, habitualmente a partir de los 6-8 meses desde el inicio de la intervención, con el riesgo progresivo de recuperación ponderal. Es por ello que la adyuvancia farmacológica se considera el segundo escalón terapéutico al que muchos pacientes deberán recurrir (3-5). Desde la aparición de los aGLP-1 como fármacos antiobesidad se ha visto un cam-

bio significativo en la mejoría de las comorbilidades relacionadas con la obesidad e incluso una reducción de la enfermedad cardiovascular (7-10,13-15).

La pérdida de peso en el grupo tratado con liraglutida 3 mg fue comparable a los resultados del estudio SCALE, en donde se evidenció una disminución media del peso de 5,24 kg a las 56 semanas de tratamiento. De hecho, en la mayoría de los estudios incluidos en el programa SCALE, más del 50 % de los pacientes incluidos habían perdido más del 5 % de su peso corporal (7,8,16). Además, estos resultados se confirmaron en estudios en condiciones de vida real. Entre estos, Ferrari y cols. observaron una reducción ponderal de hasta el 7,1 % en 93 PwO italianas tratadas con liraglutida 3 mg (17). Otro estudio coreano mostró una pérdida de peso media del 5,85 % (18). Wharton y cols., en Canadá, obtuvieron una pérdida de hasta el 7,1 % tras el tratamiento con liraglutida 3 mg durante 6 meses (19).

En el programa de desarrollo clínico de la semaglutida en dosis de 1 mg/semana en pacientes con obesidad y diabetes, la semaglutida comportó una reducción media de 3,74 kg. Posiblemente, nuestra mayor pérdida de peso se debiera a que los pacientes del brazo de tratamiento con semaglutida tenían un peso inicial mayor y, al igual que con cualquier otra variable

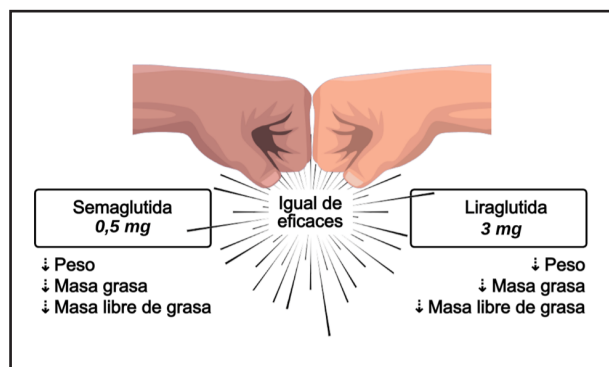


Figura 1.

Resumen gráfico de los resultados.

biológica, la pérdida de peso es superior cuanto mayor es el peso inicial. Los diferentes estudios STEP (*the Semaglutide Treatment Effect in People with obesity*) evaluaron el efecto, la seguridad y el perfil de tolerabilidad de la semaglutida a dosis de 2,4 mg una vez a la semana para obtener la aprobación regulatoria de este análogo de GLP-1 de acción prolongada para el control del peso, independientemente de la diabetes de tipo 2 (10). La pérdida de peso media en los ensayos STEP fue del 17 % (10). Nosotros obtuvimos una pérdida de peso media de alrededor del 5 %, porcentaje similar al logrado entre las PwO incluidas en el programa STEP cuando estaban en la semana 16, en donde la dosis media era de 1 mg, a pesar de que la dosis fue menor en nuestro estudio (9). En una subpoblación de los ensayos STEP se realizó una DEXA al inicio y al final del tratamiento con semaglutida. Al igual que los resultados obtenidos en nuestra serie, la masa grasa total se redujo significativamente y la proporción de masa corporal magra en relación con la masa corporal total aumentó en el grupo de la semaglutida (9). Sin embargo, los datos de composición corporal en estos estudios son anecdóticos.

Previamente ha habido ensayos clínicos que han comparado la eficacia de la liraglutida en comparación con la semaglutida a diferentes posologías. En el SUSTAIN-10 (*Semaglutide Unabated Sustainability in Treatment of Type 2 Diabetes*) se compararon la eficacia y la seguridad de la semaglutida en dosis de 1 mg/semana frente a la liraglutida en dosis de 1,2 mg/día durante 30 semanas. La pérdida de peso media con la semaglutida a dosis de 1 mg fue de 5,8 kg frente a una reducción ponderal de 1,9 kg con la liraglutida a dosis de 3 mg ($p < 0,0001$) (20). O'Neil y cols., en un estudio comparativo, evidenciaron la superioridad de semaglutida 0,2 mg al día frente a liraglutida 3 mg al día en PwO sin diabetes (21).

Sin embargo, posiblemente, su uso fuera de la indicación oficial condicionó una falta de stock de estos fármacos de forma escalonada y a nivel mundial, con el consiguiente impacto negativo sobre la evolución ponderal, la calidad de vida y las comorbilidades de estos PwO. Por ello, es importante disponer de evidencia científica en la vida real que compare estos diferentes aGLP-1, y a diferentes dosis, en cuanto a eficacia y seguridad en caso de potenciales desabastecimientos futuros.

Somos conscientes de que nuestro estudio tiene diversas limitaciones puesto que, a día de hoy, los aGLP1 no están financiados por el sistema sanitario español, por lo que aquellos pacientes que disponen de medios económicos para autofinanciárselos posiblemente tengan un nivel sociocultural mayor, sabiendo que ello puede sesgar la muestra al dejar sin esta posibilidad terapéutica a las personas de nivel cultural inferior, donde la prevalencia de la obesidad es significativamente mayor. Del mismo modo, la asignación arbitraria por parte del facultativo de la semaglutida o la liraglutida puede también conllevar sesgos, ya que los pacientes tratados con semaglutida tenían unos parámetros antropométricos basales mayores, presuponiéndose que dicho fármaco tiene una eficacia superior. El uso de recordatorios dietéticos de 24 horas depende de la memoria de los pacientes, lo que puede generar inexactitudes y no representar sus hábitos alimentarios a largo plazo. Además, los pacientes pueden subestimar o sobreestimar su ingesta, introduciendo un sesgo en los datos obtenidos.

En cuanto a la actividad física, aunque los acelerómetros son útiles, no siempre captan adecuadamente ciertas actividades, como el ciclismo o los ejercicios de baja intensidad, y su uso continuo puede verse afectado por la adherencia de los pacientes. Los registros autoinformados también son susceptibles de sesgos de memoria y pueden no reflejar con precisión el nivel de actividad real. También, la duración del estudio es corta y aunque pese a ello se obtuvieron resultados significativos, desconocemos el efecto de ambos fármacos una vez alcanzada la fase de meseta del peso. Sin embargo, el disponer de datos en condiciones de vida real y que reflejan la práctica clínica diaria, especialmente tras haber vivido una época de desabastecimiento de esta clase de fármacos, siendo necesario a veces cambiar de uno a otro de forma brusca por este motivo, permite que, en caso de necesidad, exista evidencia científica sobre la eficacia similar con estas dosis determinadas. Por otro lado, la obesidad es una enfermedad basada en la adiposidad y, frecuentemente, el IMC puede sobreestimar o infraestimar la adiposidad, por lo que la composición corporal debería estar presente en el manejo de los pacientes con obesidad. Sin embargo, la mayoría de los ensayos clínicos aleatorizados y de los estudios en condiciones de vida real carecen de dicha información, por lo que consideramos una de las principales fortalezas de nuestro estudio el aportar parámetros de composición corporal que complementan el tradicional uso del peso y del IMC.

En conclusión, en condiciones de vida real, la semaglutida a dosis de 0,5 mg a la semana y la liraglutida a dosis de 3 mg al día son tratamientos eficaces y comparables para reducir el peso de forma segura en las PwO, a corto plazo y sin condicionar un impacto negativo sobre la masa magra.

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Trabajo Original

Obesidad y síndrome metabólico

Relationship between serum omentin-1 levels and nascent metabolic syndrome in Caucasian patients with obesity

Relación entre los niveles séricos de omentina-1 y el síndrome metabólico incipiente en pacientes caucásicos con obesidad

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Abstract

Background and aims: omentin-1 might present a potential role in metabolic syndrome (MS). The aim of our investigation was to evaluate the relationship between omentin-1 and nascent MS.

Methods: we carried out a cross-sectional study in 606 obese subjects. Adiposity parameters, blood pressure, fasting blood glucose, insulin levels, insulin resistance (HOMA-IR), triglyceride and glucose index (TyG), lipid profile, C-reactive protein, omentin-1, and prevalence of nascent MS were determined.

Results: 307 subjects had MS (49.2 %) and 299 did not show MS (50.8 %). Subjects without MS have higher omentin-1 levels (delta: 78.0 ± 13.8 ng/ml; $p = 0.01$). A negative correlation was observed between omentin-1 and adiposity parameters, glucose, insulin, HOMA-IR, TyG index and triglycerides in both groups. And a positive correlation was observed with HDL-cholesterol. BMI (OR = 1.17, 95 % CI = 1.09-1.31; $p = 0.02$), HOMA-IR (OR = 5.21, 95 % CI = 1.69-21.11; $p = 0.01$) and omentin-1 (OR = 0.95, 95 % CI = 0.94-0.97; $p = 0.02$) remained in the final model as predictors of MS. The cut-off point according to the Youden index was 372.45 ng/ml of omentin-1, to predict MS.

Conclusions: Caucasian patients with obesity had clearly lower serum omentin-1 levels in the presence of nascent MS. An inverse correlation was demonstrated with adiposity parameters, insulin resistance and triglycerides. And a direct correlation with HDL-cholesterol was reported.

Keywords:

Insulin resistance. Nascent metabolic syndrome. Obesity. Omentin-1.

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Data availability statement: all data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethical statement: all patients provided written and informed consent, and the protocol complied with the Declaration of Helsinki as well as with local institutional guidelines. It was approved by the Ethics Committee (code of registration 06/2021).

Conflicts of interest: there are no conflicts of interest related to the study design or its results.

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Resumen

Antecedentes y objetivos: la omentina-1 podría tener un papel potencial en el síndrome metabólico (SM). El objetivo de nuestra investigación fue evaluar la relación entre la omentina-1 y el SM incipiente.

Métodos: realizamos un estudio transversal en 606 sujetos obesos. Se determinaron los parámetros de adiposidad, la presión arterial, la glucemia en ayunas, los niveles de insulina, la resistencia a la insulina (HOMA-IR), el índice de triglicéridos y glucosa (TyG), el perfil lipídico, la proteína C-reactiva, la omentina-1 y la prevalencia del SM incipiente.

Resultados: 307 sujetos tenían SM (49,2 %) y 299 no presentaban SM (50,8 %). Los sujetos sin SM tienen niveles más altos de omentina-1 (delta: $78,0 \pm 13,8$ ng/ml; $p = 0,01$). Se observó una correlación negativa entre la omentina-1 y los parámetros de adiposidad, la glucosa, la insulina, el HOMA-IR, el índice TyG y los triglicéridos en ambos grupos. Se observó una correlación positiva con el colesterol HDL. EL IMC (OR = 1,17, IC 95 % = 1,09-1,31; $p = 0,02$), el HOMA-IR (OR = 5,21, IC 95 % = 1,69-21,11; $p = 0,01$) y la omentina-1 (OR = 0,95, IC 95 % = 0,94-0,97; $p = 0,02$) permanecieron en el modelo final como predictores del SM. El punto de corte según el índice de Youden fue 372,45 ng/ml de omentina-1 para predecir el SM.

Conclusiones: los pacientes caucásicos con obesidad tenían niveles séricos de omentina-1 claramente más bajos en presencia de SM incipiente. Se demostró una correlación inversa con los parámetros de adiposidad, resistencia a la insulina y triglicéridos. Y se detectó una correlación directa con el colesterol HDL.

Palabras clave:

Resistencia a la insulina.
Síndrome metabólico
incipiente. Obesidad.
Omentina-1.

INTRODUCTION

Obesity is an important health problem with huge dimensions (1), leading to a metabolic dysfunction. The adipose tissue is a storage organ, but the role of adipose tissue as an endocrine organ has emerged (2). Adipokines are secreted by different cells of this tissue such as adipocytes, macrophages, mast cell and stromal vascular. These adipokines could be related with the pathogenesis of insulin resistance, hypertension, dyslipemia and other cardiovascular risk factors related with obesity (3) and in this context, omentin-1 is one of them.

Omentin-1 is a 32 kDa protein that is secreted by stromal vascular cells in visceral adipose tissue, and it is expressed in other tissues such as lung, heart and placenta (4). This adipokine is a beneficial molecule that improve insulin-stimulated glucose uptake and triggers Akt pathway, which produces downstream effects such as glucose metabolism (5). Circulating omentin-1 correlated negatively with anthropometric parameters such as weight, body mass index (BMI), waist circumference and biochemical parameters (fasting insulin, HOMA-IR and leptin) and positively with high density lipoprotein cholesterol (HDL-C) and adiponectin levels (6).

Metabolic syndrome (MS) is a constellation of risk entities related with obesity, including glucose intolerance or diabetes *mellitus*, abdominal obesity, hyperlipidemia and high blood pressure levels (7). MS is considered a polygenic and multifactorial disorder due to interaction of numerous genes with environmental factors and in this context, adipose tissue develops an important role in the presence of this entity (8). Adipose tissue dysregulation and altered secretion of different adipokines are presented in this syndrome (9,10). Moreover, few studies have evaluated the relationship between MS and circulating levels of omentin-1 in obese patients without cardiovascular events (11-13), this type of MS without cardiovascular events or diabetes *mellitus* is called nascent MS. For example, Jialal et al. (12) reported lower levels of omentin-1 in patients with MS than in patients without MS. This study was realized in a small sample of 75 subjects, of which 30 had nascent MS. In other small sample of 93 adults, Vu et al. (13) reported an association between this adipokine and

MS only in males. These preliminary findings have not been evaluated in large samples of patients that represent the wide range of patients with obesity.

The aim of our investigation was to evaluate the potential relationship between circulating omentin-1 levels with nascent MS and its components in an important sample of Caucasian patients with obesity.

MATERIALS AND METHODS

SUBJECTS AND PROCEDURE

This cross-sectional study was performed in a population of 606 Caucasian patients with obesity (20 to 70 years) of age remitted to our Nutritional Unit in a Health Area of the Castilla y León Autonomous Community in Spain. Consecutive volunteers with body mass index (BMI) ≥ 30 kg/m² were included. The inclusion criteria for the study protocol were the following — body mass index ≥ 30 kg/m² and an age in the range 20-70 years. Exclusion criteria were any of the next conditions: diabetes *mellitus*, cardiovascular events, chronic kidney disease, chronic liver disease, heart failure, malignant tumours and history of alcoholism, or use of medications that potentially influenced weight or metabolic parameters (statins, fibrates and drugs against diabetes *mellitus* or hypertension). Finally, all patients provided their written and informed consent, and the protocol complied with the Declaration of Helsinki as well as with local institutional guidelines. It was approved by the hospital's Ethics Committee (code of registration 06/2021).

Demographic and clinical characteristics of all patients were recorded in the hospital registry system. The parameters of the present study included sociodemographic data, classical anthropometric parameters (weight, height, body mass index (BMI) and waist circumference), total fat mass (FM) by bioimpedance, blood pressure, and biochemical assessment. During the baseline visit 15 ml of venous blood after an 8 hour overnight fast were aliquoted in ethylenediaminetetraacetic acid (EDTA)-coated tubes for biochemical analysis. The Adult Treatment Panel III

(ATPIII) criteria: elevated fasting glucose or treatment for diabetes *mellitus*, elevated triglycerides (> 150 mg/dl), low HDL cholesterol < 40 mg/dl (males) or < 50 mg/dl (females), elevated systolic or diastolic blood pressure ($> 130/85$ mmHg) and increased waist circumference (> 88 cm in females and > 102 cm in males) were used to diagnosis nascent MS. Patients meeting at least 3 of these above-mentioned criteria were included in the MS+ group and those not meeting these criteria in the MS- group.

ANTHROPOMETRIC PARAMETERS AND BLOOD PRESSURE

Height and weight measurements were performed while patients were wearing light clothes and no shoes. Body height (cm) was determined using a standard height measurement scale (Omrom, LA, CA, USA) and body weight was measured using digital scales (Omrom, LA, CA, USA). Body mass index (BMI) was calculated using the formula (weight (kg) / height² (m)). Waist circumference was measured at the nearest 0.1 cm just above the ilium with a flexible standard tape (Omrom, LA, CA). Body fat mass was determined by impedance with an accuracy of 50 g (14) (EFG BIA 101 Anniversary, Akern, It).

Finally, systolic and diastolic blood pressures were measured two consecutive times on the right arm after 10 minutes rest at the heart level with and automated monitor (Omrom, LA, CA, USA), and the average of both measures was calculated.

BIOCHEMICAL PROCEDURES

Serum biochemistry analyses for glucose, insulin, C-reactive protein (CRP), total cholesterol, HDL-cholesterol, triglyceride, and interleukine-6 were realized using the COBAS INTEGRA 400 analyser (Roche Diagnostic, Basel, Switzerland). LDL cholesterol was calculated using Friedewald's equation (LDL cholesterol = total cholesterol - HDL cholesterol - triglycerides / 5) (15). Based on these parameters, the homeostasis model assessment for insulin resistance (HOMA-IR) was obtained using these values (glucose (mmol/L) x insulin (IU/L) / 22.5) (16). The triglyceride glucose index (TyG) was calculated using the formula: $\ln(\text{fasting TG (mg/dl)} \times \text{fasting blood glucose (mg/dl)} / 2)$ (17).

STATISTICAL ANALYSIS

All statistical data were analyzed using the SPSS ver.23 (IBM) software (SPSS Inc. Chicago, IL). Sample size ($n = 600$) was calculated to find a difference in omentin-1 levels greater than 50 ng/ml between the two groups of patients (MS- vs. MS+). The normality of the variables was tested using the Kolmogorov-Smirnov test. Mean \pm standard deviation was used to express continuous variables. Categorical variables were presented as percentages. Continuous variables were compared with Student's t-test (for normally distributed variables) or the

Mann-Whitney U-test (for non-normally-distributed variables). Differences between categorical variables were determined using the Chi-squared test. The relationship between omentin-1 levels and other variables was evaluated using Pearson's correlation analysis. A multivariate logistic regression analysis was performed using a backward stepwise method to identify independent variables for MS. The Receiver Operation Characteristic Curve for MS was used to determine the best cutoff point of omentin-1 in predicting MS. And the cutoff points were elucidated by two methods: the area under the curve (AUC) that had the best specificity and sensitivity values for the test in question, and the Youden index as (sensitivity + specificity) - 1). p -values below 0.05 were considered statistically significant.

RESULTS

A total of 606 Caucasian patients with obesity were evaluated, 150 males (24.8 %) and 456 females (75.3 %) with an average age of 49.3 ± 13.3 years (range: 31-68). A total of 307 subjects had MS (49.2 %) and 299 did not show MS (50.8 %). Mean age in the metabolic syndrome (MS+) group was higher (50.6 ± 3.9 years vs 45.9 ± 6.2 years; $p = 0.02$) than in the non-metabolic syndrome group (MS-). The proportions of females were higher in both groups (MS+ group, 24.7 % males vs 75.3 % females; $p = 0.01$, and MS- group, 24.6 % males vs 75.4 % females; $p = 0.02$). No differences in the percentages of both groups were detected.

The basic demographic and clinical characteristics of the population are showed in table I. We reported statistical differences (delta; p -values) between both groups in BMI (3.1 ± 0.2 kg/m²; $p = 0.02$), body weight (8.8 ± 2.1 kg; $p = 0.03$), body fat mass (5.0 ± 0.2 kg; $p = 0.03$) and waist circumference (11.6 ± 2.5 cm; $p = 0.02$). All these parameters were higher in MS+ group than MS- group. Systolic blood pressure (6.3 ± 2.6 mmHg; $p = 0.01$) and diastolic blood pressure (6.5 ± 2.1 mmHg; $p = 0.02$) were higher in the MS+ group than in the MS- group, too.

Laboratory findings according to MS group are summarized in table II. We observed higher levels in the MS+ group than in the MS- group in the following parameters (delta; p -values): fasting glucose (16.0 ± 2.9 mg/dL; $p = 0.01$), HDL-cholesterol (-3.5 ± 0.3 mg/dl; $p = 0.03$), triglycerides (31.1 ± 4.5 mg/dl; $p = 0.01$), insulin levels (4.1 ± 0.4 UI/L; $p = 0.02$), HOMA-IR (1.8 ± 0.3 units; $p = 0.03$), omentin-1 levels (78.0 ± 13.8 ng/ml; $p = 0.01$) and TyG index (0.50 ± 0.01 mg/dl; $p = 0.02$). Total cholesterol, LDL-cholesterol, and CRP levels were similar in both groups.

Table III shows the percentage of each metabolic syndrome criterion in the MS+ group vs the MS- group. As expected, the percentages of central obesity, hypertriglyceridemia, low-HDL cholesterol, hypertension and hyperglycemia were higher in the MS+ group than in the MS- group. Omentin-1 levels according to the number of MS criteria decreased as the number of criteria were aggregated (0 criteria, 715.4 ± 13.2 ng/ml; 1 criterion, 533.5 ± 12.2 ng/ml; 2 criteria, 520.6 ± 11.1 ng/ml; 3 criteria,

511.8 ± 9.1 units; 4 criteria, 488.1 ± 8.2 units, and 5 criteria, 452.1 ± 8.1 ng/ml; $p = 0.001$).

Table IV describes correlations between different parameters and omentin-1 levels. A negative correlation was observed between omentin-1 and adiposity parameters, glucose, insulin, HOMA-IR, TyG index and triglycerides in both groups. And a positive correlation was observed between omentin-1 and HDL-cholesterol, too.

The multivariate logistic regression analysis was performed including variables with $p < 0.25$ between groups in the univariate analysis but not showing collinearity and excluding variables

used as criteria of MS. BMI (OR = 1.17, 95 % CI = 1.09-1.31; $p = 0.02$), HOMA-IR (OR = 5.21, 95 % CI = 1.69-21.11; $p = 0.01$) and omentin-1 (OR = 0.95, 95 % CI = 0.94-0.97; $p = 0.02$) remained in the final model as independent predictors of MS.

The ROC curve of the omentin-1 for MS is shown in figure 1. The area under the curve (AUC) according to ATPIII criteria showed a value of 0.721 (0.694-0.792; $p = 0.001$). The cut-off point according to the Youden index was 372.45 ng/ml of omentin-1 to predict MS, with a sensitivity and specificity of 80.9 % and 70.2 %, respectively.

Table I. Basic demographic and clinical characteristics of the Caucasian patients with obesity

Parameters	All population $n = 606$	MS- group $n = 307$	MS+ group $n = 299$	p
Age	49.3 ± 13.3	49.0 ± 12.1	49.8 ± 7.3	0.62
BMI	36.3 ± 1.4	34.2 ± 0.9	37.9 ± 0.4	0.02
Weight (kg)	94.7 ± 6.1	90.1 ± 7.1	98.9 ± 5.9	0.03
Fat mass (kg)	38.6 ± 9.1	36.3 ± 2.1	41.3 ± 1.2	0.03
WC (cm)	110.1 ± 4.1	105.2 ± 3.1	116.8 ± 2.9	0.02
SBP (mmHg)	126.8 ± 2.3	120.5 ± 3.1	128.9 ± 2.8	0.01
DBP (mmHg)	81.9 ± 3.1	75.5 ± 4.1	83.8 ± 3.2	0.02

BMI: body mass index; DBP: diastolic blood pressure; SBP: systolic blood pressure; WC: waist circumference. Statistical differences between groups ($p < 0.05$).

Table II. Laboratory findings of Caucasian patients with obesity (mean ± SD)

Parameters	All population $n = 606$	MS- group $n = 307$	MS+ group $n = 299$	p
Fasting glucose (mg/dl)	100.2 ± 4.1	93.0 ± 2.9	109.3 ± 2.1	0.01
Total cholesterol (mg/dl)	203.4 ± 11.8	200.8 ± 11.2	210.8 ± 12.2	0.29
LDL-cholesterol (mg/dl)	124.6 ± 12.9	122.4 ± 7.9	132.8 ± 5.9	0.18
HDL-cholesterol (mg/dl)	52.1 ± 2.1	55.4 ± 1.4	52.0 ± 1.2	0.03
Triglycerides (mg/dl)	125.1 ± 8.0	110.4 ± 9.5	141.1 ± 10.3	0.01
Insulin (mU/l)	13.9 ± 1.1	12.4 ± 0.9	16.4 ± 0.7	0.02
HOMA-IR	3.4 ± 0.3	2.9 ± 0.5	4.7 ± 0.3	0.02
CRP (mg/dl)	5.9 ± 0.7	5.8 ± 0.8	6.1 ± 1.9	0.12
Omentin-1 (ng/ml)	510.1 ± 13.4	521.2 ± 15.8	443.8 ± 12.9	0.02
TyG	4.61 ± 0.3	4.50 ± 0.2	4.99 ± 0.1	0.02

HOMA-IR: homeostasis model assessment of insulin resistance; CRP: C-reactive protein; TyG: triglyceride glucose index. Statistical differences between groups ($p < 0.05$).

Table III. Metabolic syndrome and components of metabolic syndrome in Caucasian patients with obesity

Parameters	All population n = 606	MS- group n = 307	MS+ group n = 299	p
Percentage of MS	49.2 %	0 %	100 %	0.01
Percentage of central obesity	73.4 %	53.9 %	93.3 %	0.01
Percentage of hypertriglyceridemia	9.4 %	3.9 %	12.3 %	0.02
Low HDL-cholesterol	28.0 %	12.7 %	43.4 %	0.03
Percentage of hypertension	45.7 %	14.9 %	76.9 %	0.02
Percentage of hyperglycaemia	23.4 %	7.1 %	40.2 %	0.01

The following cutoff points were used for the criteria of: central obesity (waist circumference > 88 cm in females and > 102 in males), hypertension (systolic BP > 130 mmHg or diastolic BP > 85 mmHg or specific treatment), hypertriglyceridemia (triglycerides > 150 mg/dl or specific treatment) or hyperglycaemia (fasting plasma glucose > 110 mg/dl). Statistical differences between groups (p < 0.05).

Table IV. Correlation analysis of omentin with other parameters

Parameters	All population n = 606	MS- group n = 307	MS+ group n = 299
Age (years)	r = 0.17, p = 0.23	r = 0.23, p = 0.22	r = 0.18, p = 0.31
glucose (mg/dL)	r = 0.11, p = 0.41	r = 0.12, p = 0.43	r = 0.10, p = 0.33
LDL-cholesterol (mg/dL)	r = 0.06, p = 0.52	r = 0.08, p = 0.43	r = 0.07, p = 0.52
HDL-cholesterol (mg/dL)	r = 0.30, p = 0.01	r = 0.28, p = 0.01	r = 0.33, p = 0.01
Triglycerides (mg/dl)	r = -0.29, p = 0.02	r = -0.31, p = 0.02	r = -0.27, p = 0.03
Insulin (U/L)	r = -0.32, p = 0.02	r = -0.29, p = 0.02	r = -0.35, p = 0.01
HOMA-IR	r = -0.36, p = 0.02	r = -0.27, p = 0.03	r = 0.40, p = 0.01
TyG index	r = -0.35, p = 0.02	r = -0.28, p = 0.02	r = 0.39, p = 0.01
Weight (kg)	r = -0.21, p = 0.01	r = -0.15, p = 0.02	r = -0.24, p = 0.02
Fat mass (kg)	r = -0.17, p = 0.03	r = -0.15, p = 0.03	r = -0.21, p = 0.02
Waist circumference (cm)	r = -0.28, p = 0.001	r = -0.21, p = 0.003	r = 0.34, p = 0.002

CRP: C-reactive protein; HOMA-IR: homeostasis model assessment. Statistical differences between groups (p < 0.05).

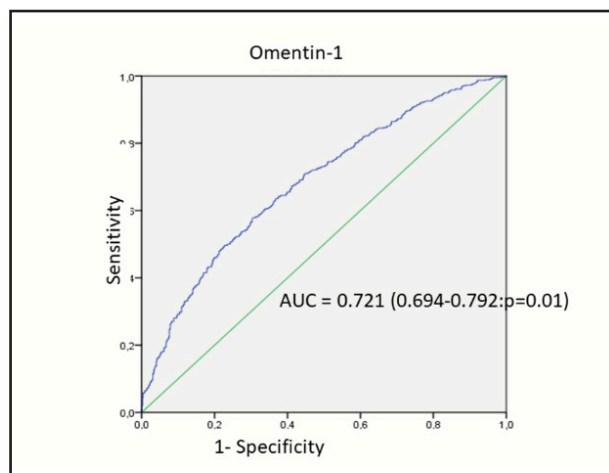


Figure 1. ROC curve of omentin-1 for metabolic syndrome according to the ATPIII criteria.

DISCUSSION

In our study, patients with obesity and nascent MS had significantly lower levels of omentin-1 compared with patients without MS. In all patients omentin-1 levels showed a significant negative correlation with insulin resistance as estimated by HOMA-IR and TyG index, adiposity parameters and triglyceride levels. A positive correlation with HDL-cholesterol was observed, too.

In small previous studies, Jialal et al. (12) showed that the adipose tissue of patients ($n = 45$) with nascent MS secreted lower omentin-1 levels than the adipose tissue of patients ($n = 30$) without MS. To our knowledge, this is the first study to validate these findings in an important sample of Caucasian patients with obesity, and to give a cut-off value of omentin-1 to predict nascent MS. Similar to our study, other study demonstrated lower levels of omentin-1 in patients with nascent MS compared with patients without MS (18). This work was carried out in a different sample than ours, composed of a sample of 110 Turkish patients with MS, all with high blood pressure. In other small sample of 93 adults, Vu et al. (13) reported an association between this adipokine and MS only in males. In comparison with these above-mentioned investigations, decreased circulating omentin-1 in subjects with MS in our study were more pronounced. This relationship has also been found in studies carried out with obese adolescents (19), but in the literature there are also studies that have demonstrated a lack of difference in the levels of omentin-1 depending on the presence or absence of MS (20). These contradictory results depended on age, gender distribution, average BMI, ethnic diversity, study design, exclusion and inclusion criteria, heterogeneity or predominance of MS components, and measurements techniques.

In addition to the difference in omentin-1 levels depending on the presence of MS in our obese patients, we also demonstrated a significant inverse correlation between insulin resistance estimated as TyG index and HOMA-IR. It has been postulated that omentin-1 contributes to insulin sensitivity through the modulation of protein kinase (Akt/protein kinase B). In one study, HOMA-IR was related to decreased circulating omentin-1 levels (21), and these results were replicated with TyG, too (12). Another design showed that weight loss with different hypocaloric diets produced parallel significant decreased values of omentin-1 and insulin resistance (22).

In addition, we reported that levels of omentin-1 were inversely correlated with adiposity parameters (BMI, fat mass and waist circumference). Obesity is a well-known chronic low-grade inflammatory condition and may change circulating adipokine levels secondary to adipocyte dysregulation in visceral adipose tissue. This increase of visceral adipose tissue has been related with a decrease in omentin-1 gene expression (23). However, there are discrepancies between studies investigating this relationship and some of them failed to detect this correlation (24). These inconsistencies raise the question of whether omentin-1 levels are regulated by the obesity status or by the inflammation process triggered by obesity.

The positive correlation between HDL cholesterol and omentin-1 has been previously reported in different studies (25). A potential explanation for this association is that dysregulation of omentin-1 may adversely affect insulin signaling and regulation, thereby modifying HDL production (26). Some studies have explained the potential protective role of omentin-1 concentrations against coronary artery disease through this association with HDL-cholesterol (27).

There were some limitations to our study. First, the study has been designed in Caucasian adults with obesity, so the data are not generalizable to younger subjects, overweight patients, or other ethnicities. Secondly, the design as a cross-sectional design (transversal) does not allow to extract causality. Third, we did not directly measure the visceral distribution of fat, only indirect parameters such as waist circumference were used. Fourth, patients with diabetes *mellitus* were not included. However, patients with impaired glucose tolerance may have been enrolled in this design as oral a glucose tolerance test was not carried out as routine screening test, and this fact may affect the findings. Finally, physical activity has not been evaluated, and it has a potential role in omentin-1 levels (28). The strengths of our study were that we studied a representative population of obese patients with a median age of predominantly females.

The results from our design showed that Caucasian patients with obesity had clearly lower serum omentin-1 levels in the presence of nascent MS. An inverse correlation was demonstrated with adiposity parameters, insulin resistance and triglycerides, with direct correlation with HDL-cholesterol. All this allows to consider that omentin-1 may play a partial role in the development of MS and may be a predictive marker of MS and metabolic health status, too (29).

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Trabajo Original

Valoración nutricional

Heuristic evaluation of body mass index with bioimpedance data in the Mexican population

Evaluación heurística del índice de masa corporal con datos de bioimpedancia en la población mexicana

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Abstract

Introduction: given the problematic battle against cardio-metabolic diseases and the increase in computational power, different applications are being developed to help estimate overweight and obesity in the population.

Objectives: to evaluate the body mass index (BMI) formula (kg/m^2), taking body fat measured by bioimpedance as a reference and comparing it with variations of the same form obtained by applying algebraic transformation rules using an artificial intelligence heuristic search method.

Material and methods: an artificial intelligence heuristic method was applied to search for the formula that most accurately calculates people's body fat percentage. The formula was generated from body mass and stature, variables used to estimate BMI. Thousands of formulas involving body mass and stature were generated from BMI using transformation rules with algebraic variations and increased and decreased constants.

Results: body mass, stature, and body fat percentage data set from 142 female and 150 male participants were used. Body mass and stature were used to classify participants into two classes based on body fat percentage (excessive or adequate, with cutoff points of 30 % for women and 15 % for men). The Youden index guided the search algorithm by evaluating candidate formulas to generate new ones. Among the formulas with the maximum value of the Youden index, $\text{Body mass}^{1.1} / \text{Stature}^{2.9}$, is proposed as the best candidate as an alternative formula to apply instead of the BMI conventional formula.

Conclusions: although BMI showed a high Youden index, the AI algorithm found that the $W^{1.1} / H^{2.9}$ formula is even more efficient in assessing body fat in men and women.

Keywords:

Anthropometry. Best first search. Mathematical algorithms.

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Resumen

Introducción: ante la problemática batalla contra las enfermedades cardiometabólicas y el aumento del poder computacional, se están desarrollando diferentes aplicaciones que ayuden a estimar el sobrepeso y la obesidad en la población.

Objetivos: evaluar la fórmula del índice de masa corporal (IMC) (kg/m^2), tomando como referencia la grasa corporal medida por bioimpedancia y comparándola con variaciones de la misma forma obtenidas aplicando reglas de transformación algebraica mediante un método de búsqueda heurística de inteligencia artificial.

Material y métodos: se aplicó un método heurístico de inteligencia artificial para buscar la fórmula que calcule con mayor precisión el porcentaje de grasa corporal en las personas, que se generó a partir de la masa corporal y la estatura, variables utilizadas para estimar el IMC. Se generaron miles de fórmulas que involucran la masa corporal y la estatura a partir del IMC utilizando reglas de transformación con variaciones algebraicas y constantes aumentadas y disminuidas.

Resultados: se utilizó un conjunto de datos de masa corporal, estatura y porcentaje de grasa corporal de 142 mujeres y 150 hombres participantes. La masa corporal y la estatura se utilizaron para clasificar a los participantes en dos clases según el porcentaje de grasa corporal (excesiva o adecuada, con puntos de corte del 30 % para mujeres y del 15 % para hombres). El índice de Youden guió el algoritmo de búsqueda evaluando fórmulas candidatas para generar otras nuevas. Entre las fórmulas con el valor máximo del índice de Youden, Masa corporal^{1.1} / Estatura^{2.9}, se propone como la mejor candidata como fórmula alternativa para aplicar en lugar de la fórmula convencional del IMC.

Conclusiones: aunque el IMC mostró un índice de Youden alto, el algoritmo de IA encontró que la fórmula Masa corporal^{1.1} / Estatura^{2.9} es aún más eficiente para evaluar la grasa corporal en hombres y mujeres.

Palabras clave:

Antropometría. *Best first search*. Algoritmos matemáticos.

INTRODUCTION

Body mass index (BMI) is a recognized anthropometric evaluation to estimate, to varying degrees, to determine calorie-nutritional problems and to classify individuals with or without risk of metabolic diseases according to their body mass-for-stature ratio (1). It is used systematically to estimate undernutrition, overweight, and obesity and is crucial in determining public health policy. The elegant and simple formula allows a straightforward interpretation of an individual's calorie-nutritional status: $\text{BMI} = \text{body mass (kg)} / \text{stature (m)}^2$.

While it is a paradigm that BMI estimates the proportion of fat mass in both men and women (2), it provides a good measure of risk for heart disease, high blood pressure, dyslipidemias, type 2 diabetes, gallstones, respiratory problems, and certain types of cancer (3). Even in women, BMI values $\geq 25 \text{ kg}/\text{m}^2$ are associated with endocrine diseases such as hyperandrogenic syndrome (4). Its widespread application has allowed comparisons of health over time in different regions and population subgroups. However, BMI has limitations; it does not directly measure body fat, and factors such as age, gender, ethnicity, and muscle mass can influence the relationship between BMI and body fat (5). For example, BMI can classify muscular individuals as overweight or obese, especially in athletes, due to the higher muscle density compared to fat mass (6). In addition, BMI does not capture information about the distribution of fat mass at different sites in the body (2). Despite these limitations, BMI remains a valuable tool for assessing potential disease risk when used with other indicators, such as waist girth, body composition (fat mass, muscle mass, bone mass), lifestyles, and genetic and hereditary factors (7). However, new anthropometric indices are suggested to be developed that more readily estimate body fat, especially central adiposity. Such indices should be equally simple to apply and understand (5). Thus, the need arises to develop accurate equations that optimize the assessment of nutritional status and risks associated with disease, considering the biological and environmental factors described above. Such a task is complex and requires the si-

multaneous analysis of a large amount of data, where artificial intelligence (AI) and mathematical algorithms can help us.

Mathematical algorithms are increasingly important in diagnosing and treating obesity, which is relevant to medicine (8). In this sense, AI can help identify patterns of obesity among variables that are invisible to the naked eye but clinically significant (9).

Classical search engine techniques (chatbots) and traditional applications are still helpful in finding algebraic formulas that relate and provide optimal or near-optimal estimates among multiple variables. These search methods have the characteristic that the search space is explicit, i.e., they generate possible solutions that are automatically evaluated by the heuristic function predefined by the programmer but which, in turn, are directly observable by the researcher. Such is the case of BMI, which is used to find relationships between weight and height that estimate obesity. Using an equation, BMI expresses a particular way of relating two independent variables, body mass, and stature, allowing the estimation of overweight relative to body fat. Since BMI does not correctly estimate body fat in different populations (10), we wonder if there are variations of the BMI formula that assess obesity more accurately in most populations. AI can help in this search if the algebraic transformation rules and the heuristic function that guides them are defined.

Therefore, this work aimed to evaluate the BMI formula (kg/m^2), taking body fat measured by bioimpedance as a reference and comparing it with variations of the same form obtained by applying algebraic transformation rules using an AI heuristic search method.

METHODS

ETHICS AND PARTICIPANT ELIGIBILITY

All participants were informed of the study's purpose and procedures. Their acceptance was formalized through informed consent, and their anonymity and confidentiality were strictly

enforced. This study was carried out following the Declaration of Helsinki and was approved by the Universidad Autónoma de Ciudad Juárez (UACJ) Review Board (Reference number: CBE. ICB/062.09-15).

Participant eligibility, anthropometric measurements, and electric bioimpedance evaluations have been published in detail (11).

SEARCH SPACE

The “Best First Search” (BFS) method was used to generate a search space of alternative formulas to the BMI by applying 14 transformation rules starting from the BMI formula as the initial node, i.e., all evaluated formulas start from successive transformations of the BMI. The algebraic transformation rules applied were the same as in Murguía-Romero et al. (12): the increase or decrease of the stature exponent (by one-tenth),

the increase or decrease of the body mass exponent, the change of the body mass share from base to exponent, the change of the stature share from base to exponent, the increase of a constant multiplying body mass as an exponent, the increase of a regular multiplying stature as exponent, the change of the equation as quotient to a multiplication, subtraction or addition (Fig. 1).

The heuristic function to guide the search was the accuracy of the formula concerning the percentage of body fat measured by bioimpedance. The cutoff points for deciding excessive body fat, measured as the percentage of total fat, were 15 % for men and 30 % for women, corresponding to the average values of total fat measured by bioimpedance in the participants.

Sensitivity, specificity, and their 95 % errors are described, as well as the Youden index and its counterpart, the overall accuracy of the equation.

The BFS algorithm was programmed in Prolog language and ran independently for women and men. A search space of at

```
% Prolog rules
rule(r10_exp_h_increment, W/H ^ Exp_h, W/H^Exp_h1):-
    number(Exp_h),
    Exp_h < 3,
    Exp_h1 is Exp_h + 0.1.
rule(r11_exp_w_increment, W^Exp_w/ H, W^Exp_w1/H):-
    number(Exp_w),
    Exp_w < 2,
    Exp_w1 is Exp_w + 0.1.
rule(r20_w_as_exponent, W ^ Exp_w /H^N, 1.1^(W*1)/H^N):-
    number(Exp_w).
rule(r21_h_as_exponent, W / H^Exp, W / 2^(H*2)):-
    number(Exp).
rule(r31_w_increment_exp, Base^(W*N)/H, Base^(W*N1)/H):-
    number(Base),
    var(W),
    N < 2,
    N1 is N + 0.1.
rule(r32_h_increment_exp, W/Base^(H*N), W/Base^(H*N1)):-
    number(Base),
    var(H),
    N < 4,
    N1 is N + 0.1.
rule(r33_decess_exp, W/Base^(H*N), W/Base^(H*N1)):-
    number(Base),
    var(H),
    N > 1,
    N1 is N - 0.1.
rule(r40_w_base_inc, Base^(W*N) / H, Base1^(W*N)/H):-
    number(Base),
    Base < 4,
    Base1 is Base + 0.1.
rule(r41_w_base_dec, Base ^ (W*N)/H, Base1^(W*N)/H):-
    number(Base),
    Base > 0.1,
    Base1 is Base - 0.1.
rule(r42_h_increase_base, W/Base^ H, W/Base1^H):-
    number(Base),
    Base < 3,
    Base1 is Base + 0.1.
rule(r43_h_drecrement_base, W/Base^H, W/Base1^H):-
    number(Base),
    Base > 1,
    Base1 is Base - 0.1.
rule(r51_multiply, W/H,W*H).
rule(r52_substract, W / H, W - H).
rule(r52_add, W / H, H + W).
```

Figure 1.

Applied transformation rules to the generation of BMI variant formulae.

least 70,000 formulae was generated. In addition to its algebraic structure, each formula's sensitivity (and its error), specificity (and its error), Youden index, and precision were obtained.

RESULTS

This study used data on body mass, stature, and body fat percentage measured by bioimpedance in 142 women and 150 men (Table I).

The BFS search method evaluated 70,955 BMI formula variants for women and 303,095 for men (Table II). Thus, formulas with a maximum sensitivity of 87 % for women and 79 % for men were obtained. It should be noted that the BFS algorithm is guided by the heuristic function, which in this case was sensitivity, so the search tree does not represent the totality of possible formulae when applying the defined algebraic transformation rules (Fig. 1).

The formulas with the highest Youden index (0.77 for women and 0.60 for men) are mostly algebraic in structure:

$$W^a / b^{H^c}$$

where W is the body mass (kg), and H is the stature (m), with a, b, and c constants. The maximum value was presented by a total

of 328 and 40 formulas for females and males, respectively, of which almost all have the above algebraic structure, except the following three formulae for females:

$$W / H^{2.6}$$

$$W / H^{2.7}$$

$$W^{1.1} / H^{2.9}$$

And the following three formulas for men:

$$W / H^{2.6}$$

$$W^{1.1} / H^{2.8}$$

$$W^{1.1} / H^{2.9}$$

The formula $W^{1.1} / H^{2.9}$ has two essential characteristics: a) it is expected for women and men, and b) it has the same algebraic structure as BMI; only the values of the exponents change, so it was chosen as the possible formula for BMI, and with which its efficiency as a classifier is compared (Fig. 2, Table III).

Comparing the efficiency of the formula $W^{1.1} / H^{2.9}$ with the BMI (Table III) shows that the parameters are generally very similar. For example, the difference in sensitivity is 1 % in women and 4 % in men; in specificity, 0 % (women) and 1 % (men). The difference in the Youden Index is meager, 0.01 (women) and 0.04 (men). In general, the differences in the efficiency parameters of these two formulas are higher in men than in women. Sensitivity was lower than specificity in BMI and in all variant formulae explored.

Table I. Anthropometric characteristics of the participants

Statistics	Women				
	Average	SD	Minimum	Maximum	Total data (n)
Age, yrs	21.1	4.0	17	46	143
Weight, kg	64.8	13.1	40.53	117.1	143
Stature, cm	160.3	5.0	149	171	143
BMI, kg/m ²	25.2	4.5	16.6	42.0	143
WG, cm	76.5	10.1	54.8	104.8	143
Body fat, %	30.6	6.1	18.3	47.4	143
	Men				
	Average	SD	Minimum	Maximum	Total data (n)
Age, yrs	21.9	3.4	16	37	151
Weight, kg	72.4	11.8	47.77	113.58	151
Stature, cm	172.4	6.7	154	189	151
BMI, kg/m ²	24.4	3.9	17.3	40.9	151
WG, cm	80.5	8.8	64.5	109.6	151
Body fat, %	15.3	5.0	5.3	34.1	150

SD: standard deviation; BMI: body mass index; WG: waist girth.

Table II. Example of formulas generated in the BFS search space. The first 15 formulas with BMI as the starting node apply the rules in figure 1

Search generation order	Formula	Sensitivity %	Specificity %	Errors 95 %	Errors 95 %	Youden Index	Accuracy %
Women							
1	W/H^2	86	90	24	18	0.76	88
2	$W/H^{2.1}$	83	91	24	16	0.75	87
3	$W^{1.1}/H^2$	86	90	22	16	0.76	88
4	$W^{1.1}/H^2$	79	86	49	22	0.65	82
5	$W/2^{2H}$	85	91	24	18	0.76	88
6	$W*H^2$	75	79	69	33	0.53	77
7	W^2-H	80	83	52	23	0.63	82
8	W^2+H	80	83	52	23	0.63	82
9	$W^{1.1}/H^{2.1}$	86	90	22	18	0.76	88
10	$W^{1.2}/H^2$	86	89	21	16	0.74	87
11	$W^{1.1}/2^{2H}$	87	90	24	18	0.77	89
12	$W^{1.1}*H^2$	75	79	66	33	0.53	77
13	$W^2-H^{1.1}$	80	83	52	23	0.63	82
14	$W^2+H^{1.1}$	80	83	52	23	0.63	82
15	$W^{1.2}/2^{2H}$	86	90	22	16	0.76	88
Men							
1	W/H^2	76	80	77	45	0.55	78
2	$W/H^{2.1}$	77	81	77	42	0.58	79
3	$W^{1.1}/H^2$	76	78	77	46	0.54	77
4	$W^{1.1}/H^2$	69	71	84	61	0.39	70
5	$W/2^{2H}$	77	81	76	42	0.58	79
6	$W*H^2$	61	65	87	81	0.26	63
7	W^2-H	64	70	87	68	0.34	67
8	W^2+H	64	70	87	68	0.34	67
9	$W/H^{2.2}$	77	81	77	45	0.58	79
10	$W^{1.1}/H^{2.1}$	76	78	76	45	0.54	77
11	$W^{1.1}/H^{2.1}$	69	71	84	61	0.39	70
12	$W*H^{2.1}$	59	65	87	82	0.23	62
13	$W^{2.1}-H$	64	70	87	68	0.34	67
14	$W^{2.1}+H$	64	70	87	68	0.34	67
15	$W/H^{2.3}$	76	81	77	44	0.57	78

W: body weight (kg); H: stature (m).

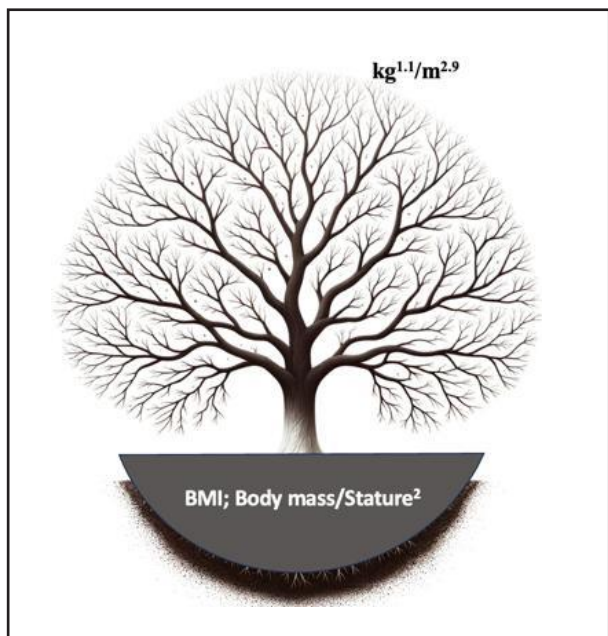


Figure 2. Representative structure of the applied heuristics in the search for the formula that best calculates fat percentage (body mass in kg^{1.1} / stature in m^{2.9}). The formula was generated from BMI.

Table III. Efficiency characteristics of the BMI formulae and one found with maximum sensitivity

Formula	Women			Men		
	BMI	W ¹ /H ^{2.9}	Difference	BMI	W ^{1.1} /H ^{2.9}	Difference
Sensitivity	86 %	87 %	1 %	76 %	79 %	3 %
Specificity	90 %	90 %	0 %	80 %	81 %	1 %
error s95	24 %	22 %	-1 %	77 %	73 %	-4 %
error e95	18 %	15 %	-3 %	45 %	46 %	1 %
Youden Index	0.76	0.77	0.01	0.55	0.60	0.04
Accuracy	88 %	89 %	1 %	78 %	80 %	2 %

BMI: body mass index; W: body weight (kg); H: stature (m).

DISCUSSION

To our knowledge, this is the first work that performs a search for alternative formulas to BMI (kg/m²) using the “Best First Search” algorithm, a classical AI heuristic technique with a combinatorial approach to economically find optimal formulas from preceding nodes (13, 14). The formulas found here are variants of the BMI based on algebraic transformation rules, each generated from precursor branches, confirming a broad tree-like search space whose common root or trunk is the BMI. This work provides new knowledge in two respects. First, how the equation production system is defined, consisting of the transformation rules, the initial state of BMI (kg/m²), and the heuristic that guides the search for new formulas to detect obesity (12); it could serve as an exam-

ple in the search for new classifiers of health status, such as the already known atherogenic indices of waist-hip, hypertriglyceridemia-waist, glucose-insulin, among others (1, 15). Secondly, this work provides further insight into the properties of BMI in terms of its efficiency as a classifier of obesity-related health status (1). In this regard, the most important findings are that BMI is 10 % more sensitive in women than in men (86 % for women, 76 % for men), much higher than the sensitivity reported (~ 51 %) by Sommer et al. (16), and optimal when compared to its algebraic variants analyzed here. Regarding specificity, it is higher than sensitivity (90 % and 80 % for females and males, respectively) in all variants explored and slightly lower than those already reported (~ 96 %) (16). The differences may be due to the different methods used to calculate fat percentages between authors (16).

There is no doubt that BMI is a good discriminator of individuals' caloric-nutritional status, where values above 25 kg/m² are related to cardiovascular diseases, dyslipidemias, and insulin resistance (1). However, the $W^{1.1} / H^{2.9}$ formula outperforms BMI as a classifier of fat percentage in both women and men and has the highest values for efficiency parameters among the many variants evaluated.

Murguía-Romero et al. (12), in a similar study and with the same methodology, compared BMI with other formulas and its relationship with metabolic syndrome. They found that the Ponderal Index is only 0.8 % more sensitive than BMI for classifying individuals at risk of metabolic syndrome. Similarly, we found two equations close to the weight index ($Weight / Height^{2.9}$), with only 1 % and 2 % more accurate than BMI for detecting obesity.

Coincidentally, the formulae $W^{1.1} / H^{2.9}$ are very similar to the Ponderal Index ($body\ mass / stature^3; kg/m^3$), an index used to assess caloric-nutritional status in pregnant women, neonates, and infants and its associations with possible cardiovascular and metabolic complications (17). Ayatollahi (18) confirmed its usefulness as an indicator of fat mass in adolescents, like us, in people 17-46 years of age. However, BMI is still erroneously considered the best classification of the obesity degree (19). The low use of the Ponderal Index as an indicator of calorie-nutritional status in adolescents and adults may be because, to date, no cutoff points related to metabolic and cardiovascular diseases have been established for this index. In addition, BMI is a relatively more straightforward formula than the weight index.

The present analysis uses a dataset of 292 participants (142 women and 150 men) with total fat percentage measured by bioelectrical impedance as the independent variable. Thus, the results can be improved by increasing the number of participants, subdividing by age group, and taking visceral fat percentage instead of total fat percentage as the independent variable. Another way to improve the analysis is to increase the search space and evaluate an even more significant number of people. However, no more efficient formulas than those found here will likely be seen, as the algorithm (BFS) is very efficient.

AI-powered tools are effective in decision-making and digital health interventions for weight loss (9). AI can personalize diets and exercise programs to suit individual needs by analyzing large amounts of clinical data: blood, images, medications, stomach bacteria, reactions to certain foods, and lifestyles, among others. AI can also be used to predict and treat obesity in adults. For example, AI algorithms have been developed to predict when people will drop out of weight loss programs (20). As we are currently experiencing with ChatGPT, AI can also act as a behavioral coach, encouraging patients to follow a healthier lifestyle.

Despite advances in AI, it is essential to recognize that human interaction remains valuable in treating obesity. Research shows that AI-powered weight loss apps are most effective when used with support from healthcare professionals (21), as they can offer more personalized weight loss advice and empathetic doctor-patient interactions.

LIMITATIONS

This analysis uses data from 143 and 150 female and male participants, respectively, so it was impossible to obtain adequate resolution to differentiate between many formulas for which the maximum value of the Youden index was obtained. Studies that involve data from more participants may yield more precise results. For the same reason, no cutoff points were proposed for the candidate formula that exceeds the BMI in the Youden index, and it was not possible to evaluate the formulas by age groups.

CONCLUSIONS

The BMI showed a Youden index close to the formulas with the highest value, corroborating its importance in evaluating health with body mass. Although the AI algorithm found that the $W^{1.1} / H^{2.9}$ formula is even more efficient in assessing body fat in men and women. In summary, AI has a great potential to aid in diagnosing and treating obesity and can be a valuable tool for nutritionists and exercise physiologists. While AI offers solutions and support to patients with obesity, it is essential to combine it with the support of healthcare professionals to obtain the best results in weight loss and obesity treatment.

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Trabajo Original

Valoración nutricional

Do nutritional assessment scores have a relationship with transthyretin levels? *¿Las puntuaciones de la evaluación nutricional tienen relación con los niveles de transtiretina?*

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Abstract

Background and aims: nutritional screening tools assess factors like weight loss, BMI, food intake, and disease severity to determine a patient's nutritional risk and needed care. Plasma transthyretin is a practical measurement used to assess nutritional evolution due to its rapid response to food intake. This study examines the relationship between nutritional scores, transthyretin protein levels, and the possibility of death.

Methods: the sample consisted of 302 patients hospitalized in the wards or intensive care unit of a public teaching hospital, using parenteral nutrition as the primary source of nutrition. Five nutritional screening tools were applied, and patient charts were verified for transthyretin levels.

Results: from the sample, 260 were adults, and 42 were children, with a mean age of 48.3 years. When evaluating the patient's outcome in relation to the scores, the Malnutrition Universal Screening Tool proved to be better at predicting death (p -value = 0.02). None of the scores were related to transthyretin levels, showing that lower transthyretin values did not influence nutritional risk.

Conclusion: we believe early identification of nutritional risk through nutritional scores is necessary for better nutritional monitoring to minimize unfavorable outcomes. This study corroborates the more recent concept that transthyretin is not useful for determining unfavorable outcomes in hospitalized patients with a severe inflammatory process. In clinical practice, identifying a patient at nutritional risk according to the Malnutrition Universal Screening Tool and promoting adequate nutritional monitoring may reduce mortality.

Keywords:

Transthyretin. Nutrition assessment. Nutritional scores.

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Resumen

Antecedentes y objetivos: las herramientas de detección nutricional evalúan factores de riesgo como: pérdida de peso, índice de masa corporal, ingesta de alimentos y gravedad de la enfermedad. Así, estos factores establecen el riesgo nutricional del paciente y, en consecuencia, definen el nivel de atención requerido. Una medida práctica, con una vida media de 48-72 horas, es la transtiretina plasmática, que se ha utilizado para evaluar la evolución nutricional de los pacientes, debido a su rápida respuesta a la ingesta de alimentos. El objetivo de este estudio fue evaluar si los puntajes nutricionales están relacionados con los niveles de proteínas del paciente, en este caso evaluados por transtiretina y su asociación con la posibilidad de muerte.

Métodos: la muestra consistió en 302 pacientes hospitalizados en las salas o la unidad de cuidados intensivos de un hospital público docente, utilizando nutrición parenteral como fuente primaria de nutrición. Se aplicaron cinco herramientas de detección nutricional y se verificaron los registros de los pacientes para determinar los niveles de transtiretina.

Resultados: de la muestra, 260 eran adultos y 42 eran niños, con una edad media de 48,3 años. Al evaluar el resultado del paciente en relación con las puntuaciones, la Herramienta de detección universal de desnutrición demostró ser mejor para predecir la muerte (valor $p = 0,02$). Ninguna de las puntuaciones se relacionó con los niveles de transtiretina, lo que demuestra que los valores más bajos de transtiretina no influyeron en el riesgo nutricional.

Conclusión: creemos que la identificación temprana del riesgo nutricional a través de puntajes nutricionales es necesaria para un mejor seguimiento nutricional, con miras a minimizar los resultados desfavorables. Sobre todo, este estudio corrobora el concepto más reciente de que la transtiretina no es útil para determinar resultados desfavorables en pacientes hospitalizados con un proceso inflamatorio severo. Por lo tanto, identificar al paciente en riesgo nutricional según la Malnutrition Universal Screening Tool y promover un seguimiento nutricional adecuado puede reducir potencialmente la mortalidad.

Palabras clave:

Transtiretina. Evaluación nutricional. Puntajes nutricionales.

INTRODUCTION

Malnutrition will bring changes in body composition, damaging physical and mental functions and worsening the patient's clinical outcome. One of the greatest difficulties in nutritional assessment is performing it on hospitalized patients. Identifying nutritional risk early through nutritional scores is necessary for better nutritional monitoring, adequate nutritional action, and potentially reducing unfavorable outcomes in this population, especially critically ill patients (1).

Nutritional screening tools assess risk factors such as weight loss, Body Mass Index (BMI), low dietary intake, and severity of the underlying disease. These factors are necessary for establishing the patient's nutritional risk and, subsequently, defining the level of attention they will need (2). There are several scores proposed for this purpose, and the most used are the Malnutrition Universal Screening Tool (MUST), the Mini Nutritional Assessment (MNA), Nutrition Screening 2002 (NRS 2002), Nutrition Risk in the Critically Ill Score (NUTRIC Score), and Strong Kids — for pediatric patients.

The MUST evaluates three pillars for diagnosis: BMI, unintentional weight loss, and the effect of acute illness on nutritional intake.³ The MNA (Guigoz *et al.*, 1996) is a nutritional screening tool designed for older adults over 65 years old. It comprises 18 questions: weight loss, BMI, number of meals a day, mobility, presence of neurological disease, and even the older adults' perception of their health (4).

Another widely used tool in the hospital environment is the NRS 2002, which analyzes the severity of the patient's disease. It has been validated for use in all adult hospitalized patients, including older adults, as it considers an age greater than 70 years old relevant for nutritional risk. Nutritional intervention is then established according to the score obtained (5).

One of the greatest nutritional assessment difficulties is performing it on critically ill patients; therefore, the NUTRIC score was developed. The criteria for this tool are age, severity scores

(The Acute Physiology and Chronic Health Evaluation II - APACHE II and The Sequential Organ Failure Assessment — SOFA), number of comorbidities, days of hospitalization before admission to the ICU, and interleukin-6 (IL-6) levels (if available) (6).

In children and adolescents, the Strong Kids tool can be used and is composed of objective questions, such as the presence of serious illness or major surgery, food intake, diarrhea or vomiting, and weight stability (7).

One biomarker that is very practical to measure due to its short half-life (48-72 hours) is plasma transthyretin (TTR). It has been used to assess the nutritional evolution of patients due to its rapid response to food intake. However, its applicability in relation to the prognosis of hospitalized patients has not been reported (8).

Considering that clinical nutritional evaluation and assessment are essential for the management of hospitalized patients and that death is undoubtedly an inverse outcome, the present study aimed to assess whether patients at nutritional risk classified according to nutritional scores would have lower levels of protein plasma levels, assessed by TTR levels and whether there were any associations with the possibility of death (9).

MATERIALS AND METHODS

STUDY DESIGN

A cross-sectional prospective study was developed. The total sample consisted of 338 patients, of which 36 were excluded due to not signing the Informed Consent Form (ICF), an ethical criterion indispensable for the development of studies involving human beings, leaving a total of 302 patients included in the study at a public teaching hospital, which is a quaternary care hospital. Data were collected in the first 72 hours after starting Parenteral Nutrition (PN). Specific studies in this population are essential because it is a frequently used type of nutrition among critically ill patients.

The use of PN as the primary source of nutrition was the criterion for inclusion in the sample. Not filling out the ICF by the patient or their legal guardian (in cases of unconscious and pediatric patients) was the exclusion criterion for this sample. Those under 18 years of age who could sign were asked to fill out an Assent Form.

ETHICAL ASPECTS

This study was approved by the Research Ethics Committee of the State University of Campinas under number 2.676.452.

ASSESSMENT OF NUTRITIONAL STATUS

Weight and height were used to calculate the BMI in adults, according to the World Health Organization (WHO) 2000 classification (10). Weight was measured using a Plena[®] digital scale with a maximum capacity of 150 kg, and height was measured with a vertical metal stadiometer ranging from 20 cm to 220 cm. When it was impossible to weigh or measure the patient, the data obtained from reading the medical records or from that reported by them or their family member were used. If a patient was older than six years and was restricted to bed, the height estimated by the formula of Chumlea *et al.* was employed, where the knee height (KH) in centimeters is used in the predetermined equations (11). For restricted children, those under six years of age, height/length was measured using a horizontal wooden stadiometer.

For children and adolescents, the WHO (2006 and 2007) curves were used to classify the nutritional status, where the Z-score values were adopted. The Z-score was calculated using the WHO Anthro and WHO Anthro plus software (12).

For the nutritional classification of older adults, those with a BMI between 23 and 28 kg/m² were considered eutrophic. Those below 23 kg/m² were considered malnourished, and those above 28 kg/m² were considered obese (13).

NUTRITIONAL RISK ASSESSMENT

To determine nutritional risk, the researchers applied nutritional screening tools, and the questions were directed to the patients themselves when they had health conditions to answer or to a family member if the patients were unconscious or were from the pediatric population. The screening tools were applied according to the target population, as described below:

In eligible patients, the following tools were applied:

- Adults: MUST (3), NRS 2002 (5).
- Critical adults: MUST, NRS 2002 and NUTRIC (6).
- Older adults: MUST, NRS 2002 and MNA (4).
- Critical older adults: MUST, NRS 2002, MNA and NUTRIC.
- Children: Strong Kids (14).

According to the answers given, each of these nutritional scores generates a nutritional risk classification, which are: low risk, moderate/medium risk, high risk.

LABORATORY EVALUATION

Laboratory tests were collected by health professionals responsible for the patient and sent to the Laboratory of Clinical Pathology at *Hospital de Clínicas* (HC), where the samples were processed according to the standards required for each test. To determine TTR levels, nephelometry was used. The reference value adopted as suitable for TTR was greater than 20 mg/dL, the HC standard (15).

STATISTICAL ANALYSIS

An evaluation of the normality of the sample variables was carried out to determine the tests that would be applicable. With this, it was established that the chi-square test or the Fisher's exact and Fisher-Freeman-Halton tests would be used when indicated to assess the association between two qualitative variables. Data were processed using the Statistical Package for the Social Sciences 16.0 software (SPSS Inc., Chicago, IL, USA). The significance level adopted was 5 %.

RESULTS

The sample consisted of 302 patients, 260 of whom were adults and 42 children, aged between 0.7 and 93.7 years, with a mean age of 48.3 years old; the characterization of the sample is described in table I. NRS 2002 presented the highest percentage of high nutritional risk, followed by MUST (Table II). When assessing the patient's outcome in relation to the scores, MUST proved to be better at predicting death, *p*-value = 0.02 (Table III). None of the scores were related to TTR, showing that lower TTR values did not influence nutritional risk (Table IV).

Table I. Characterization of the sample

Variables (n = 302)	Frequency	Percentage
<i>Sex</i>		
Female	116	38.4
Male	186	61.6
<i>Age</i>		
0 to 19 years	42	13.9
Above 19 years	260	86.1
<i>Outcome</i>		
Discharged	235	77.8
Death	67	22.2
<i>Hospitalization unit</i>		
ICU	96	31.8
Ward	206	68.2
<i>Reason for PN referral</i>		
GIT surgery	187	61.9
BMT	16	5.3
ILEO	99	32.8

GIT: gastrointestinal tract; BMT: bone marrow transplantation; ILEO: includes abdominal distention, metabolic disorders, and systemic infectious response syndrome.

Table II. Nutritional classification of the sample in relation to BMI and distribution of high nutritional risk according to NRS 2002, MUST, MNA for the older adults, NUTRIC, and Strong Kids

Variables	n	%
<i>Nutritional status according to BMI</i>		
Malnourished	82	27.7 %
Eutrophic	122	41.2 %
Overweight/Obese	92	31.1 %
Total	296	100 %
<i>Nutritional classification scores – High risk</i>		
NRS 2002 (n = 233)	208	89.3
MUST (n = 260)	189	72.7
NUTRIC (n = 50)	9	18
MNA (n = 51)	18	35.3
Strong Kids (n = 39)	28	71.8

NRS 2002: Nutrition Risk in the Critically Ill Score; MUST: Malnutrition Universal Screening Tool; NUTRIC: Nutrition Risk in the Critically ill Score; MNA: Mini Nutritional Assessment.

Table III. Outcome in relation to the NRS 2002, MUST, MNA of the older adults, NUTRIC, and Strong Kids scores

		Death (n/%)	Discharged (n/%)	p-value*
Nutritional risk				
MUST (n = 260)	High risk	54/28.6	135/71.4	0.002
	Intermediate risk	3/6.3	45/93.8	
	Low risk	3/13	20/87	
Nutritional risk				
NRS 2002 (n = 233)	Serious risk	46/22.1	162/77.9	0.809
	Moderate risk	5/20	20/80	
	Low risk	0	0	
Nutritional risk				
Strong Kids (n = 39)	High risk	4/14.3	24/85.7	1.0
	Intermediate risk	1/9.1	10/90.9	
Nutritional risk				
NUTRIC (n = 50)	High risk	3/33.3	6/66.7	0.429
	Low risk	10/24.4	31/75.6	
Nutritional risk				
MNA (n = 51)	Malnourished	9/50	9/50	0.188
	Risk of malnutrition	7/26.9	19/73.1	
	Normal nutritional status	1/14.3	6/85.7	

NRS 2002: Nutrition Risk in the Critically ill Score; MUST: Malnutrition Universal Screening Tool; NUTRIC: Nutrition Risk in the Critically ill Score; MNA: Mini Nutritional Assessment. *Chi-squared test for probability.

Table IV. Transthyretin level in relation to NRS 2002, MUST, MNA for the older adults, NUTRIC, and Strong Kids

	NRS 2002		Moderate risk	Serious risk		Total	p-value
Transthyretin	Adequate	<i>n</i> %	0 0.0 %	12 100 %		12 100 %	
	Inadequate	<i>n</i> %	16 12.2 %	115 87.8 %		131 100 %	
	Total	<i>n</i> %	16 11.2 %	127 88.8 %		143 100 %	0.361*
	MUST		Low risk	Intermediate risk	High risk	Total	
Transthyretin	Adequate	<i>n</i> %	1 6.3 %	2 12.5 %	13 81.3 %	16 100 %	
	Inadequate	<i>n</i> %	11 7.5 %	28 19.2 %	107 73.3 %	146 100 %	
	Total	<i>n</i> %	12 7.4 %	30 18.5 %	120 74.2 %	162 100 %	0.896 [†]
	MNA		Normal	Risk of malnutrition	Malnourished	Total	
Transthyretin	Adequate	<i>n</i> %	0 0.0 %	0 0.0 %	0 0.0 %	0 0.0 %	
	Inadequate	<i>n</i> %	3 10 %	15 50 %	12 40 %	30 100 %	
	Total	<i>n</i> %	3 10 %	15 50 %	12 40 %	30 100 %	NA
	NUTRIC		High risk	Low risk		Total	
Transthyretin	Adequate	<i>n</i> %	0 0.0 %	2 100 %		2 100 %	
	Inadequate	<i>n</i> %	6 21.4 %	22 78.6 %		28 100 %	
	Total	<i>n</i> %	6 20 %	24 80 %		30 100 %	1.00*
	Strong Kids		High risk	Intermediate risk		Total	
Transthyretin	Adequate	<i>n</i> %	2 100 %	0 0.0 %		2 100 %	
	Inadequate	<i>n</i> %	14 63.6 %	8 36.4 %		22 100 %	
	Total	<i>n</i> %	16 66.7 %	8 33.3 %		24 100 %	0.540*

*Fisher's exact test bilateral probability; [†]Fisher-Freeman-Halton exact test bilateral probability. NA: not applicable statistical test.

NRS 2002: Nutrition Risk in the Critically Ill Score; MUST: Malnutrition Universal Screening Tool; NUTRIC: Nutrition Risk in the Critically ill Score; MNA: Mini Nutritional Assessment.

DISCUSSION

Although the scores are not intended to define outcomes, it was observed that those with a higher nutritional risk, according to the MUST, had a higher risk of death (p -value = 0.002). Another observation of the present study is that no relationship was identified between TTR levels and nutritional risk. This corroborates new evidence that TTR does not reflect the nutritional status of individu-

als suffering from an acute inflammatory process (16). This is the reality of many hospitalized patients, especially those needing PN.

The MUST was observed to be more useful in predicting death than the NRS 2002. Rabito *et al.* showed that the risk ratio for mortality was 2.34 times higher in patients classified as at nutritional risk, according to the MUST. Some differences were observed between the MUST and NRS 2002 tools in relation to nutritional risk classification, and can be explained by the lower BMI cutoff point in the MUST

compared to the NRS 2002 (19). Gomes-Neto *et al.* also found an association between high nutritional risk according to MUST and higher mortality, even after adjustments for age, sex, ward, and hospitalization in the six months before baseline ($p = 0.02$) (20).

Vries *et al.*, in their study, identified that NUTRIC was useful in predicting the mortality of patients within 28 days of hospitalization and was superior to MUST when compared (17). As for Strong Kids, NUTRIC, and MNA, the sample was probably too small to determine any difference.

Of the adult assessment scores, MUST is an effective tool for nutritional screening of the patient by identifying weight loss and low food intake. A recent study ($N = 430$) found that among patients with a BMI ≥ 25 kg/m², only 5 % were classified as at nutritional risk according to MUST versus 36 % according to the Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF) score. This difference occurred because the PG-SGA SF also considers the functionality of the gastrointestinal tract (nausea, dysphagia, and diarrhea). Therefore, a more comprehensive evaluation of the patient is necessary to consider different criteria aiming at the best nutritional diagnosis (18).

On the other hand, Liu *et al.*, in patients with COVID-19, when comparing the various nutritional assessment scores — NRS 2002, MNA, Nutrition Risk Index (NRI), and MUST — observed that the only score not identified as a good predictor of prognosis was the MUST. The authors attributed this finding to the fact that the cardinal points of MUST are BMI, unintentional weight loss, and acute disease state, unlike other tools that consider other aspects. Another critical issue was that all the patients included in the study were in severe conditions, which already classified them as having high nutritional risk, according to MUST. Patients classified as having a higher nutritional risk were also observed to have significantly worse clinical outcomes (21).

The NRS 2002 considers weight loss, food intake, BMI, age, and disease severity as criteria for nutritional risk. Luca *et al.* evaluated which of the score components had the most significant influence on mortality and length of stay, that is, the part related to nutrition or the severity of the disease. Findings show that of the 21,855 patients evaluated, both aspects of nutrition and severity were associated with more extended hospital stays and higher odds of all-cause mortality. However, nutrition had a greater impact on length of stay, while severity had a greater association with mortality. Therefore, the potentially modifiable aspect, nutritional aspects, should be addressed since they can influence shorter hospital stays and mortality (22).

In a study that evaluated the use of the NRS 2002 and the implementation of a standardized nutritional policy in hospitalized patients — with surgical sepsis, the length of hospital stay decreased by 17 days compared to the period before the study. However, it is noteworthy that the NRS 2002 is not as sensitive when the patient has chronic malnutrition, where weight loss and decreased food intake have been gradual over several years of the disease (23).

Zhao *et al.* observed in patients infected with SARS-CoV-2 that those with higher scores according to the NRS 2002 score were hospitalized for longer periods and died more. In logistic regres-

sion models, for each increase of 1 unit in the NRS 2002 score, there was a 1.23-fold increase in mortality (p -value = 0.026). COVID-19 caused a critical inflammatory state in patients, with changes in procalcitonin, interleukins, CRP, albumin, and TTR. In this case, low levels of TTR correlated negatively with NRS 2002, suggesting the use of TTR as a valuable nutritional marker. Patients at higher nutritional risk benefited from early nutritional therapy (24).

It is noteworthy that once the inflammatory status of critical patients returned to normal, TTR values tended to increase again; however, this is not necessarily associated with nutrition. Adjusting the nutritional offer in this group can reduce oxidative stress and improve the immune response, which could promote their recovery from the clinical situation, but no direct association has been established (16).

Although some authors use TTR as a prognostic marker, our findings indicate its use was ineffective for this purpose. In their systematic review ($n = 2104$), Akbar *et al.* showed that lower TTR values were associated with worsening of the clinical picture (mortality, ICU admission, or use of mechanical ventilation) in patients with COVID-19. For each 1 mg/dL reduction of TTR, there was a 1 % increase in clinical worsening (OR: 0.992 [0.987, 0.997], $p = 0.004$, I²: 81.70 %). It is known that in COVID-19, the inflammatory cascade is intensely activated, which causes the disease to worsen. The increase in the release of inflammatory cytokines decreases the production of TTR, and its increase can be used as a negative marker in these patients. The authors corroborated that TTR could be a modest predictor of prognosis in patients with COVID-19. This way, using TTR could be associated with other laboratory parameters to increase its performance (25).

Nutritional risk was high in the population of the present study, which is expected since these are critically ill patients. Maintaining and/or recovering nutritional status is essential for hospitalized patients. Chada *et al.* point out that patients who received inadequate energy and protein supply had higher mortality in 28 days when compared to those with adequate supply. It is clear that a proper nutritional intake, i.e. > 80 % supply of dietary needs, can reduce the length of hospital stay and reduce mortality in patients at high or low nutritional risk (26).

Most evaluated children were classified as high nutritional risk according to the Strong Kids score, and none at low risk. Similar findings were identified in the study by Shaaban *et al.*, where 80.4 % of children < 3 years old were classified as having moderate or severe nutritional risk. It was also observed that those with the worst Strong Kids classification scores had worsened clinical status and longer hospital stays, suggesting that this tool could predict outcomes. Identifying the nutritional risk in children is essential to improve nutritional strategies to prevent and/or treat malnutrition, thus reducing the length of hospital stay and unfavorable outcomes (27).

One limitation of this study was that applying all the score criteria to the entire sample was not always possible. However, this was only the case for a small portion of the sample, so it did not influence the study's general findings. Another point of limitation

is that this study was carried out in a teaching hospital and may not represent the reality of all public hospitals in the country.

CONCLUSION

We believe that early identification of nutritional risk through nutritional scores is necessary for better nutritional monitoring, adequate nutritional action, and, potentially, to minimize the unfavorable outcomes in this population. Above all, this study corroborates the recent concept that TTR is not useful for determining unfavorable outcomes in hospitalized patients with a severe inflammatory process. Furthermore, we identified the MUST score as a valuable tool in predicting the outcome of death among these patients. Therefore, promoting the recovery of nutritional status can potentially reduce mortality. More studies in this area are needed, interventional studies where strategies to promote the recovery of the nutritional status are carried out, and the follow-up of the nutritional score and TTR values, verifying if there is a direct association between them after an intervention period.

Furthermore, when evaluating the score data, the MUST was useful in predicting mortality; however, we believe a multicenter study is welcome to corroborate this conclusion.

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Trabajo Original

Valoración nutricional

Exploring the link between the Naples prognostic score and the cardio-ankle vascular index

Explorando el vínculo entre la puntuación pronóstica de Nápoles y el índice vascular cardio-tobillo

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Abstract

Background: the Naples Prognostic Score is a novel scoring system designed to provide a comprehensive assessment of patients' inflammation and nutritional status.

Aim: our aim was to investigate the correlation between the Naples Prognostic Score and arterial stiffness, a factor known to be linked with heart failure and acute coronary syndrome.

Materials and methods: this prospective study included 142 consecutive patients without a history of cardiovascular disease, inflammatory disease, immunological disease, malignancy, or comorbid conditions other than hypertension. Patients were categorized into two groups based on their Naples Prognostic Scores: Group 1 (score of 0-2) and Group 2 (score of 3 or 4). Arterial stiffness was assessed using the Cardio-Ankle Vascular Index (CAVI) measured with the VaSera VS-1000 device. CAVI values were compared between the groups.

Results: the mean age of the patients was 54 ± 9 years. Group 1 comprised 114 (80.3 %) patients, while Group 2 comprised 28 (19.7 %) patients. There were no significant differences in demographic data between the groups ($p > 0.005$). Additionally, there were no statistically significant differences between Group 1 and Group 2 regarding left CAVI (7.92 ± 1.45 vs. 8.72 ± 1.85 ; $p = 0.295$), right CAVI (7.89 ± 1.52 vs. 8.67 ± 1.34 ; $p = 0.332$), or left or right ankle brachial index ($p > 0.005$).

Conclusions: despite previous studies indicating a significant association between the Naples Prognostic Score and heart failure or acute coronary syndrome, our study did not observe a significant correlation between this score and arterial stiffness assessed by CAVI.

Keywords:

Naples Prognostic Score.
Arterial stiffness. Cardio-Ankle Vascular Index.
Inflammation.

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Resumen

Antecedentes: la puntuación pronóstica de Nápoles es un nuevo sistema de puntuación diseñado para proporcionar una evaluación integral de la inflamación y el estado nutricional de los pacientes.

Objetivo: nuestro objetivo fue investigar la correlación entre la puntuación pronóstica de Nápoles y la rigidez arterial, un factor que se sabe que está relacionado con insuficiencia cardíaca y síndrome coronario agudo.

Materiales y métodos: este estudio prospectivo incluyó a 142 pacientes consecutivos sin antecedentes de enfermedad cardiovascular, enfermedad inflamatoria, enfermedad inmunológica, malignidad o afecciones comórbidas distintas de la hipertensión. Los pacientes se clasificaron en dos grupos según sus puntuaciones pronósticas de Nápoles: Grupo 1 (puntuación de 0-2) y Grupo 2 (puntuación de 3 o 4). La rigidez arterial se evaluó utilizando el índice vascular cardio-tobillo (CAVI) medido con el dispositivo VaSera VS-1000. Los valores de CAVI se compararon entre los grupos.

Resultados: la edad media de los pacientes fue de 54 ± 9 años. El grupo 1 comprendía 114 (80,3 %) pacientes, mientras que el Grupo 2 comprendía 28 (19,7 %) pacientes. No hubo diferencias significativas en los datos demográficos entre los grupos ($p > 0,005$). Además, no hubo diferencias estadísticamente significativas entre el Grupo 1 y el Grupo 2 con respecto al CAVI izquierdo ($7,92 \pm 1,45$ frente a $8,72 \pm 1,85$; $p = 0,295$), CAVI derecho ($7,89 \pm 1,52$ frente a $8,67 \pm 1,34$; $p = 0,332$) o índice braquial del tobillo izquierdo o derecho ($p > 0,005$).

Conclusiones: a pesar de que estudios previos indicaron una asociación significativa entre la puntuación pronóstica de Nápoles y la insuficiencia cardíaca o síndrome coronario agudo, nuestro estudio no observó una correlación significativa entre esta puntuación y la rigidez arterial evaluada por CAVI.

Palabras clave:

Puntuación pronóstica de Nápoles. Rigidez arterial. Índice vascular cardio-tobillo. Inflamación.

INTRODUCTION

Arterial stiffness, a hallmark of vascular aging and pathology, plays a pivotal role in the development and progression of cardiovascular disease (1). It represents one of the earliest stages of the atherosclerotic process, a pathological condition characterized by a decrease in the artery's ability to expand and contract in response to pressure changes (2). This condition typically increases with age, serving as an indicator of arteriosclerosis, and is exacerbated by various factors such as obesity, diabetes, smoking, and inflammation (3). In cases of vascular inflammation, stimulated white blood cells may adhere to the vascular endothelial intima, leading to capillary leukostasis, vascular damage, and increased arterial stiffness (4).

Several white blood cell indices, including the neutrophil-to-lymphocyte ratio (NLR) (5), the monocyte-to-lymphocyte ratio (LMR) (6), and low albumin levels (7,8), have been linked to arterial stiffness in previous studies. The Naples Prognostic Score (NPS), developed as a multifaceted assessment tool, incorporates various biomarkers to provide a comprehensive snapshot of an individual's health status. By integrating parameters such as serum albumin, total cholesterol, neutrophil-to-lymphocyte ratio, and lymphocyte-to-monocyte ratio, this scoring system aims to capture both inflammatory and nutritional components (9). Previous research has correlated the NPS with the severity of coronary artery disease (10).

The Cardio-Ankle Vascular Index serves as a non-invasive measure of arterial stiffness, evaluating vascular health from the aorta to the ankle. Elevated CAVI values have been associated with increased cardiovascular risk, including hypertension, coronary artery disease, and stroke. Thus, CAVI holds promise as a valuable prognostic tool in cardiovascular risk assessment (11). Studies have demonstrated that CAVI assessment in asymptomatic patients is a valuable method for assessing both arterial stiffness and the risk of subclinical coronary atherosclerosis (12). Our study is the first in the literature and we aimed to investigate the relationship between NPS with arterial stiffness and coronary atherosclerosis-related CAVI values, which have been shown to be associated with inflammation and coronary artery disease.

MATERIALS AND METHODS

Between January and April 2024, we consecutively enrolled non-geriatric patients into the study. Exclusion criteria comprised a history of atherosclerotic heart disease and/or myocardial infarction other than arterial hypertension, heart failure (left ventricular ejection fraction < 50 %), moderate to severe valvular disease, renal insufficiency (estimated glomerular filtration rate < 50 ml/min/1.73 m²), a history of arrhythmia, diabetes *mellitus*, peripheral arterial disease, severe anemia (hemoglobin < 10 g/dL), active infection, immunological disease, and malignancy potentially impacting the NPS evaluation. Patients were stratified into two groups based on their NPS values and compared in terms of arterial stiffness evaluated by CAVI and ankle brachial index (ABI).

EVALUATION OF ARTERIAL STIFFNESS

Arterial stiffness was assessed by measuring CAVI using a portable VaSera VS-1000 (Fukuda-Denshi Company, Ltd., Tokyo, Japan). CAVI, a reliable index of arterial stiffness, comprises functional stiffness independent of blood pressure. Electrodes were affixed to the upper arm and ankles in the supine position, with the patient's head centrally positioned. Following a 10-minute rest period, electrography, phonocardiography, pressure, and waveforms of the brachial and ankle arteries were recorded.

EVALUATION OF THE NPS

The NPS value was determined by summing the scores obtained from the following biochemical and hematological parameters: serum albumin (mg/dl) (≥ 4 g/dL, 0 points; < 4 g/dL, 1 point), total cholesterol (> 180 mg/dl, 0 points; ≤ 180 mg/dl, 1 point), NLR (≤ 2.96 , 0 points; > 2.96 , 1 point), and LMR (> 4.44 , 0 points; ≤ 4.44 , 1 point). Referencing a previous study (13), patients were categorized into two groups: NPS 0-2 (Group 1) and NPS 3 and 4 (Group 2).

ETHICAL CONSIDERATIONS

This study adhered to the principles outlined in the Declaration of Helsinki, and approval was obtained from the local ethics committee (Ethic number: 2024/85). Verbal and written informed consent was obtained from all patients prior to study commencement.

STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS 22.0 for Windows (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean ± standard deviation, while categorical variables were expressed as numbers and percentages. Normally distributed quantitative variables were compared between groups using the independent-samples t-test, and categorical variables were compared using the chi-squared test. A probability value of $p < 0.05$ was considered statistically significant.

RESULTS

The mean age of the 142 patients enrolled in the study was 54 ± 9 years. Among them, 50 (35.2 %) were male, and 92 (64.8 %) were female. Group 1 comprised 114 (80.2 %) patients, while Group 2 consisted of 28 (19 %) patients. No significant differences were observed between the two groups in terms of demographic or laboratory data, including gender, body mass index, systolic blood pressure, diastolic blood pressure, ejection fraction, plasma glucose, creatinine, estimated glomerular filtration rate, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglyceride values ($p > 0.005$). The mean NPS score was calculated to be 1.45 ± 0.38 for Group 1 and 2.28 ± 1.27 for Group 2. Detailed demographic, laboratory, and clinical characteristics are summarized in table I.

No statistically significant differences were found between Group 1 and Group 2 in terms of left CAVI (7.92 ± 1.45 vs. 8.72 ± 1.85 ; $p = 0.295$), right CAVI (7.89 ± 1.52 vs. 8.67 ± 1.34 ; $p = 0.332$), left ABI (1.08 ± 0.15 vs. 1.05 ± 0.15 , $p = 0.744$), or right ABI (1.10 ± 0.15 vs. 1.14 ± 0.17 ; $p = 0.858$) ($p > 0.005$) (Table II).

Table I. Demographic data and laboratory results of the study groups

Parameters	NPS Group 1 (Score 0-2) (n = 114, 80.3 %)	NPS Group 2 (Score 3 and 4) (n = 28, 19.7 %)	p-value
Age (years)	55 ± 7	51 ± 9	0.318
Female (%)	80 (70.2 %)	12 (42.9 %)	0.055
Male (%)	34 (29.8 %)	16 (57.1 %)	
BMI (kg/m ²)	28 ± 3	26 ± 2	0.690
SBP (mmHg)	133 ± 2	129 ± 3	0.312
DBP (mmHg)	83 ± 3	80 ± 2	0.456
EF (%)	61 ± 4	60.3 ±	0.407
HT (%)	38 (28 %)	9 (32 %)	0.589
Glucose (mg/dl)	94 ± 4	98 ± 11	0.614
Creatinine, (mg/dl)	0.79 ± 0.12	0.76 ± 0.13	0.314
eGFR, mL/min/1.73 m ²	87 ± 6	92 ± 13	0.316
LDL (mg/dl)	112 ± 35	103 ± 22	0.230
HDL (mg/dl)	48 ± 11	44 ± 8	0.366
Triglyceride (mg/dl)	170 ± 15	159 ± 12	0.315
Total cholesterol (mg/dl)	185 ± 19	169 ± 21	0.001
Albumin (g/dl)	4.3 ± 0.4	4.1 ± 0.5	0.017
Hemoglobin (g/dl)	14.2 ± 2.1	13.2 ± 1.1	0.412
WBC (/μL)	7.4 ± 1.7	7.2 ± 1.3	0.814
Neutrophils (/μL)	4.1 ± 1.2	3.8 ± 1.4	0.442
Lymphocytes (/μL)	2.4 ± 0.5	2.6 ± 0.2	0.814
Monocytes (/μL)	0.5 ± 0.02	0.4 ± 0.02	0.825
NPS	1.45 ± 0.38	2.28 ± 1.27	0.001

Numerical data are expressed as mean ± standard deviation and categorical data as percentages (%). BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HT: hypertension; EF: ejection fraction; eGFR: estimated glomerular filtration rate; LDL: low-density lipoprotein; HDL: high-density lipoprotein; WBC: white blood cell; NPS: Naples prognostic score.

Table II. Comparison of the CAVI and ABI values of the study groups

Parameters	NPS Group 1 (Score 0-2) (n = 116, 81.2%)	NPS Group 2 (Score 3 and 4) (n = 26, 18.8 %)	p-value
L-CAVI	7.92 ± 1.45	8.72 ± 1.85	0.295
L-ABI	1.08 ± 0.15	1.05 ± 0.15	0.744
R-CAVI	7.89 ± 1.52	8.67 ± 1.34	0.332
R-ABI	1.10 ± 0.15	1.14 ± 0.17	0.858

CAVI: cardio-ankle vascular index; ABI: ankle-brachial index; NPS: Naples prognostic score.

DISCUSSION

Our study represents the first investigation into the relationship between arterial stiffness, vascular inflammation, and NPS. We found no significant difference between patient groups with high and low NPS values in terms of CAVI, indicating that NPS did not exhibit a significant relationship with arterial stiffness.

CAVI, a parameter utilized for assessing arterial stiffness, has proven to be a valuable method for evaluating arterial stiffness in asymptomatic patients (11,13). The NPS, on the other hand, is a novel scoring system that provides a comprehensive reflection of inflammatory and nutritional status, comprising four parameters: serum albumin, total cholesterol, NLR, and LMR (14).

Previous studies have indicated associations between cholesterol (15), serum albumin, and increased albuminuria in urine (16) with increased arterial stiffness. For instance, Cheng et al. found higher arterial stiffness in albuminuric patients (17). Similarly, increased NLR has been linked to arterial stiffness in prior research (18). The association of NPS score with different diseases has been evaluated and it has been shown that high NPS is associated with the prognosis of ST segment elevation myocardial infarction, myocardial ischemia, the prognosis of transcatheter aortic valve replacement and heart failure-related mortality (HF). Oguz et al. reported significantly higher mortality in patients with a high NPS among hospitalized heart failure patients (19). Ender et al., in a study of 499 patients with acute ST-elevation myocardial infarction, observed that the SYNTAX score increased with higher NPS at admission, indicating a relationship between NPS and the severity of coronary artery disease (10). However, Eyüp et al., in an assessment of 1,138 patients undergoing coronary computed tomographic angiography, did not find a clear benefit of NPS in predicting coronary artery severity (20). According to Unkun et al., in her study, she showed that a high NPS score can be used as a predictor of ischemia in myocardial perfusion scintigraphy (21). Guven et al. mortality was found to be higher and significantly higher in patients with a high NPS score performed TAVR (22).

Arterial stiffness is a component of the chronic process of atherosclerosis (23). The lack of a significant correlation between NPS and CAVI values in our study may be attributed to the chronic nature of arterial stiffness, as seen in the study by Eyüp et al.

(19). The clinical stability of our patient group and limited variability in albumin, neutrophil, lymphocyte, and monocyte counts could also contribute to this finding. Furthermore, the negative relationship between low total cholesterol levels in NPS and arterial stiffness, which develops over time, may diminish the predictive value of NPS in acute clinical conditions such as acute heart failure (19) and acute coronary syndrome (10). Nonetheless, we believe that the rapid and effective changes in the laboratory parameters comprising NPS will enhance its significance in evaluating treatment and follow-up in patient groups.

LIMITATIONS

Our study had several limitations. Firstly, it was a single-center study with a relatively small sample size, further reduced by the non-routine use of CAVI testing. Additionally, while we utilized NLR and LMR, we were unable to identify unknown comorbidities that could affect these values based on high-sensitivity C-reactive protein and procalcitonin, specific inflammation markers.

CONCLUSIONS

This study is the first to examine the relationship between NPS and arterial stiffness. We found no significant association between NPS and CAVI values in arterial stiffness.

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Trabajo Original

Epidemiología y dietética

Adherence to the Mediterranean diet and risk of stroke in a Chilean population: a case-control study

Adherencia a la dieta mediterránea y riesgo de infarto cerebral en una población chilena: estudio de casos y controles

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Abstract

Introduction: Ñuble is the region of Chile with the highest stroke incidence rates in the country. The aim was to estimate the association between adherence to the MED diet and the first ischemic stroke in adult patients living in the Ñuble region.

Methods: a case-control hospital-based study. The cases ($n = 89$) were patients with first ischemic stroke, and controls ($n = 178$) were admitted to the same hospital during the same month the cases were recruited. We selected two controls for one case and paired them for sex and age (± 5 years). We used the food frequency questionnaire and the adherence Mediterranean diet questionnaire. A descriptive analysis of the variables and a conditional logistic regression to determine the association between variables.

Results: 71 % of the sample was ≥ 65 years old and 64 % were male. Cases smoked (11.2 %), consumed at least one drink per month (41.6 %), and had a diagnosis of hypertension (76.4 %) more frequently than controls. In the model adjusted for all variables, it is observed that those who are in quartile 2 of adherence (6-7 points) are 42 % less likely to have a cerebral infarction compared to those who have a lower score ($p < 0.005$).

Conclusions: our findings suggest that moderate adherence to a Mediterranean diet, defined by the PREDIMED score and adjustment for other variables, reduces the probability to first ischemic stroke.

Keywords:

Stroke. Mediterranean diet. Case-control. Dietary pattern.

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Resumen

Objetivo: estimar la asociación entre la adherencia a la dieta Mediterránea y un primer accidente cerebrovascular isquémico en adultos de la región de Ñuble.

Métodos: estudio de casos y controles con base hospitalaria. Los casos ($n = 89$) fueron pacientes con primer accidente cerebrovascular (ACV) isquémico, y los controles ($n = 178$) fueron ingresados en el mismo hospital durante el mismo mes en que se reclutaron los casos. Se seleccionaron dos controles para un caso y se emparejaron por sexo y edad (± 5 años). Se utilizó el cuestionario de frecuencia de consumo de alimentos y el cuestionario de adherencia a dieta mediterránea. Se realizó un análisis descriptivo y una regresión logística condicional para determinar la asociación entre variables.

Resultados: el 71 % de la muestra tenía ≥ 65 años y el 64 % eran hombres. Los casos fumaban (11,2 %), consumían al menos una bebida al mes (41,6 %) y tenían diagnóstico de hipertensión arterial (76,4 %) con mayor frecuencia que los controles. En el modelo ajustado por todas las variables, se observa que aquellos que se encuentran en el cuartil 2 de adherencia (6-7 puntos) tienen un 42 % menos de probabilidades de sufrir un infarto cerebral en comparación con los que tienen una puntuación más baja ($p < 0,005$).

Conclusiones: nuestros hallazgos sugieren que la adherencia moderada a una dieta mediterránea, definida por la puntuación PREDIMED y el ajuste por otras variables, reduce la probabilidad de un primer ACV isquémico.

Palabras clave:

Accidente cerebrovascular.
Dieta mediterránea.
Casos y controles. Patrón dietético.

INTRODUCTION

Stroke is an important leading cause of death and disability worldwide, the third leading cause of disability-adjusted life-years. The absolute number of strokes continues to increase due to an aging population, with an estimated total of 6.24 million deaths annually (1,2). About 90 % of the risk of stroke is preventable and attributable to modifiable risk factors such as smoking, dyslipidemia, high blood pressure, alcohol consumption, sedentary lifestyle, obesity, and poor eating habits, according to the INTERSTROKE study (3). An unhealthy diet was attributed to stroke at 19 % (11-30 %) (4).

Diet influences the onset of stroke through different mechanisms: effect on blood pressure, blood lipids, coagulation process, oxidative stress, inflammatory processes, endothelial function, glycemic and insulin homeostasis, gut microbiota, and body weight (5). The main mechanism by which diet can influence the etiopathogenesis of stroke is by the atherosclerotic process, mainly produced by fat metabolism.

Different dietary interventions have been implemented to reduce the incidence of stroke while controlling for risk factors such as high blood pressure, obesity, diabetes *mellitus*, and dyslipidemia (6,7). Evidence has shown a protective effect on stroke associated with the Dietary Approaches to Stop Hypertension (DASH) and the Mediterranean diet (MED). Both dietary patterns are characterized by a higher intake of fruits and vegetables, whole grains, legumes, and olive oil, and a moderate intake of dairy products. Lastly, the MED diet added a moderate intake of red wine and nuts (8-10).

In prospective cohort studies, the MED diet has reduced mortality and the risk of cancer, cardiovascular disease, metabolic syndrome, stroke, and neurodegenerative diseases (9,11-17). The beneficial effect of the MED diet is probably due to the additive effect of its nutritional components and not the effect of each food alone (18). On the other hand, the MED diet forms part of the primary prevention of stroke guidelines (19). In a systematic review and meta-analysis, the MED diet had a protective role against stroke, reducing the risk between 10 % (RR = 0.90; 95 % CI, 0.87-0.93) and 36 % (RR = 0.64; 95 % CI, 0.87-0.93) (20). Furthermore, high adherence to the MED diet reduced

27 % (RR = 0.73; 95 % CI, 0.59-0.91) for unspecified stroke and 18 % (RR = 0.82; 95 % CI, 0.73-0.92) for ischemic stroke (9).

The third cause of death in Chile is stroke, accounting for 7.3 % of all deaths in 2019 (21) and a population-estimated incidence of 140 per 100,000/year; that result was moderate incidence. The age-standardized mortality rate of stroke for the year 2015 in Chile (34.4 per 100,000 inhabitants) (22) doubles that of developed countries such as the United States (21.9 per 100,000 inhabitants) and Canada (16.4 per 100,000 inhabitants). In the central-southern regions of Chile, the stroke mortality and case-fatality rates are higher than in the northern and southern regions. The region of Ñuble, located in the central plains of Chile, is a region with low income; 30.6 % lived in rural areas, with 16.1 % living below the poverty line according to income, and 80 % of the population is affiliated with the public health system. Ñuble have incidence rate Stroke of 163.4 (95 % CI, 152.9-174.6) was also higher than the GBD age-adjusted incidence rate of 108 (95 % CI, 100.4-116) for Chile in 2017 (23).

The aim was to estimate the association between adherence to the MED diet and first ischemic stroke in adult living in the Ñuble region.

MATERIALS AND METHODS

A paired case-control hospital-based study (1:2) by sex and age was carried out in adults over 45 years and hospitalized at the Herminda Martín Hospital in Chillán, Ñuble Region of Chile.

CASES

The cases were patients admitted to the Hospital Herminda Martín in Chillán between August 2018 and February 2019 for a first ischemic stroke, which according to the International Statistical Classification of Diseases and Related Problems with Health (ICD-10) corresponds to the code I63 evaluated by the neurologist using the National Institutes of Health Stroke Scale (NIHSS) score. Patients with confirmed hemorrhagic stroke by Computed Tomography (CT) scan and/or Diffusion Weighted Magnetic Resonance Imaging (DWI-MRI) or admitted to the hospital for a cause

of non-vascular stroke or with a previous history of any vascular accident or patients with stage IV renal failure or on dialysis, celiac, with any intolerance and /or food allergies, or patients who have modified their diet in the last two weeks were excluded.

The cases were recruited 72 hours after being admitted to the hospital and consecutively until the sample size was completed. For cases that presented a decreased communication capacity, which prevented them from responding to the study questionnaire, the collaboration of a next of kin, defined as the husband or wife or couple, immediate relative, or anybody living in the same house as the case, was utilized.

CONTROLS

For reaching comparability between groups, the controls were patients admitted to the same hospital during the same month the cases were recruited. Controls corresponded to patients hospitalized for any disease unrelated to diet or vascular diseases, and the same exclusion criteria were applied in selecting cases. Diagnosis information was obtained through clinical records, and it was checked that the cases did not have stroke events during the hospital stay. All controls were recruited from surgery (56.7 %), general medicine (8.5 %), and the traumatology department (34.4 %) of the hospital. Two controls were consecutively selected for each case (1:2) and matched by sex and age (\pm 5 years).

SAMPLE SIZE

The sample size was 89 cases and 178 controls, considering an error $\alpha = 0.05$, a power of 80 %, and a minimum OR associated with the diet of 2.3.

VARIABLES

Socio-demographic, clinical, and anthropometric characteristics

A semi-structured questionnaire was administered to cases and controls, including socio-demographic information, tobacco use, alcohol, and physical activity. The history of arterial hypertension and type 2 diabetes *mellitus* confirmed by medical diagnosis was collected from clinical records.

Food habits

Food habits were measured through a validated Food Frequency Questionnaire (FFQ) of 149 foods. The questionnaire included regular consumption foods in Chile; this instrument was applied to patient or next of kin with trained nurses during the hospital stay by face-to-face interview. The frequency of consumption of

each food included in the questionnaire was asked and recorded based on monthly, weekly, and daily intake.

Adherence to Mediterranean diet

The Spanish version of the Questionnaire of Adherence to the Mediterranean diet-MEDAS measured adherence to a Mediterranean diet to the local Chilean terms (24). The MEDAS is a 14-point questionnaire validated and used in the PREDIMED study to assess adherence to a Mediterranean diet pattern; 12 items are related to the dimension frequency of food consumption, and two items are related to food intake habits considered characteristic of the Spanish Mediterranean diet. Each question ranged from 0 to 1, obtaining a final score between 0-14 points (25,26). Higher scores were associated with higher adherence. That questionnaire was applied to the Chilean population, and the cultural translation was carried out: the word "ration" was changed to "portion"; the phrase "piece of fruit" for "units of fruit" and "carbonated drinks" for "soda drinks."

The adherence to the Mediterranean diet was classified into three categories (26): Low (0-3 points), Medium (4-7 points), and High (8-14 points). In addition, we measured by quartile score (p25, p50 and p75).

STATISTICAL ANALYSES

A descriptive analysis of the variables was performed using absolute frequencies and proportions, the normality of the variables was evaluated with the Shapiro Wilk test. A conditional logistic regression was performed to determine the association between the individual components of the Mediterranean diet and the risk of a first stroke while adjusting for age, sex, diabetes *mellitus*, tobacco use (current smoker), alcohol consumption (at least one drink/month), and educational level.

We investigated the association between adherence to the Mediterranean diet and the risk of stroke using conditional logistic regression while adjusting for age, sex, diabetes *mellitus*, tobacco use (current smoker), alcohol consumption (at least one drink/month), and educational level. We used a linear regression model to evaluate the relationship between adherence to the Mediterranean Diet when the measurement was a continuous variable and the risk of stroke. All statistical analyses were performed with Stata 12.0. An alpha error < 0.05 was considered significant.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This research was carried out following the guidelines of the Declaration of Helsinki. Each participant signed their informed consent and was approved by the Scientific Ethics Committee of the Herminda Martín of Chillan's Hospital.

RESULTS

Table I shows the distribution of cases and controls according to socio-demographic, clinical, and behavioral variables. The average age of the sample was 71.8 ± 13.97 SD and 64 % were male. Cases smoked (11.2 %) more frequently than controls, and consumed at least one drink per month (41.6 %) and had a diagnosis of hypertension (76.4 %) or diabetes *mellitus* (41.6 %) more frequently than controls. No significant statistical differences were observed between cases and controls.

Table II shows the association between the individual components of the Mediterranean diet and the risk of stroke. It is observed that the cases consumed in lower proportion olive oil (12.4 %), vegetables (84.3 %), legumes (58.4 %), and white meats (40.4 %) compared to the controls. It was consuming commercial pastry less than three times a week that reduced by 70 % the probability of having a first stroke (OR = 0.30; 95 % CI, 0.079-0.98) after adjusting for age, sex, educational level, alcohol consumption, tobacco consumption, and diagnosis of diabetes *mellitus*. An inverse relationship was observed between

stroke and higher consumption of olive oil (OR = 0.76; 95 % CI, 0.36-1.59), vegetables (OR = 0.75; 95 % CI, 0.34-1.68), legumes (OR = 0.83; 95 % CI, 0.48-1.43), nuts (OR = 0.60; 95 % CI, 0.20-1.75), and white meats (OR = 0.67; 95 % CI, 0.38-1.19) as well as stroke and lower consumption of red meat (OR = 0.91; 95 % CI, 0.31-2.60), animal fat (OR = 0.74; 95 % CI, 0.37-1.51), and sugar-sweetened beverages (OR = 0.90; 95 % CI, 0.32-2.61), such as sodas and store-bought juices that include added sugars. However, none of these associations were statistically significant.

Table III shows a more significant protective effect when the adherence to the Mediterranean diet was greater, without reaching statistical significance. In the model adjusted for all variables, it is observed that those who are in quartile 2 of adherence (6-7 points) are 42 % less likely to have a cerebral infarction compared to those who have a lower score ($p < 0.005$). In the linear regression model, for each point that increases adherence according to the MEDAS questionnaire, the probability of having a cerebral infarction decreased by 8 % (OR = 0.92; 95 % CI, 0.76-1.11). The mean MEDAS score is 6.1 (SD = 1.5).

Table I. Description of sample

Variables	Cases (n = 89) n/%	Controls (n = 178) n/%	p-value
<i>Age</i>			
≤ 55 y	17 (19.1)	26 (14.6)	0.570
56-64 y	10 (11.2)	25 (14)	
≥ 65 y	62 (69.7)	127 (71.4)	
<i>Sex</i>			
Men	57 (64)	114 (64)	1.000
Women	32 (36)	64 (36)	
<i>Educational level</i>			
≤ 8 y	61 (68.5)	128 (71.9)	0.691
9-12 y	24 (27)	40 (22.5)	
≥ 13 y	4 (4.5)	10 (5.6)	
<i>Tobacco</i>			
Never	68 (77.5)	149 (83.7)	0.162
Currently	10 (11.2)	9 (5.1)	
Have quit smoking	11 (12.3)	20 (11.2)	
<i>Alcohol</i>			
Never	52 (58.4)	127 (71.3)	0.064
At least once a month	37 (41.6)	51 (28.7)	
<i>Physical activity</i>			
Yes	3 (3.4)	5 (2.8)	0.254
No	86 (96.6)	173 (97.2)	
<i>Arterial hypertension</i>			
Yes	68 (76.4)	129 (72.5)	0.491
No	21 (23.6)	49 (27.5)	
<i>Diabetes mellitus</i>			
Yes	37 (41.6)	63 (35.4)	0.325
No	52 (58.4)	115 (64.6)	

Table II. Odds ratios and confidence interval 95% for stroke by individuals' components of Mediterranean diet

Components	Cases n (%)	Controls n (%)	OR* (95 % CI)	OR† (95 % CI)
Use olive oil as the principal source of fat	11 (12.4)	28 (15.9)	0.76 (0.36-1.59)	0.60 (0.28-1.31)
Consume > 2 spoons of olive oil per day	9 (10.1)	27 (15.3)	0.64 (0.29-1.40)	0.55 (0.25-1.26)
Consume ≥ 2 portions of vegetables per day	75 (84.3)	153 (86.9)	0.75 (0.34-1.68)	0.77 (0.33-1.77)
Consume < 3 portions of fruits per day	83 (93.2)	167 (94.8)	1.33 (0.47-3.74)	1.50 (0.50-4.54)
Consume < 1 portions of red meat per day	81 (91)	161 (91.4)	0.91 (0.31-2.60)	0.73 (0.24-2.24)
Consume < 1 portion of butter per day	75 (84.3)	141 (80.1)	0.74 (0.37-1.51)	0.75 (0.36-1.57)
Consume < 1 portion of sugar-sweetened beverage per day	84 (94.4)	165 (93.7)	0.90 (0.32-2.61)	0.77 (0.25-2.39)
Consume ≥ 3 glasses of wine per week	8 (8.9)	14 (7.9)	0.87 (0.37-2.08)	0.95 (0.34-2.08)
Consume ≥ 3 portions of legumes per week	52 (58.4)	111 (62.4)	0.83 (0.48-1.43)	0.79 (0.44-1.41)
Consume < 3 portions of fish or seafood per week	88 (98.8)	171 (96.1)	3.99 (0.45-35.0)	4.42 (0.49-39.9)
Consume < 3 portions of commercial sweets or pastries per week	86 (96.6)	176 (98.8)	0.34 (0.09-1.28)	0.30 (0.079-0.98)
Consume > 1 portions of nuts per week	7 (7.8)	9 (5.1)	0.60 (0.20-1.75)	0.64 (0.21-1.95)
Consume chicken or turkey	36 (40.4)	86 (48.3)	0.67 (0.38-1.19)	0.70 (0.39-1.26)
Consume cooked vegetables, pasta, rice or other dishes prepared with olive oil	7 (7.9)	17 (9.6)	0.81 (0.33-2.00)	0.79 (0.32-1.99)

*Adjustment by year and sex. †Adjustment by year, sex, educational level, alcohol, tobacco, and diabetes mellitus type 2.

Table III. Odds ratios and confidence interval 95% for stroke by Mediterranean diet adherence score

Mediterranean diet adherence	Cases n (%)	Controls n (%)	OR (95 % CI)*	OR (95 % CI)†
<i>Quartils</i>				
Q1 (0-5 score)	39	58	Ref	Ref
Q2 (6-7 score)	39	89	0.64 (0.36-1.13)	0.58 (0.32-0.98)
Q3 (8-11 score)	11	29	0.55 (0.23-1.28)	0.50 (0.20-1.19)
<i>PREDIMED score</i>				
Low (0-4 score)	7	17	Ref	Ref
Moderate (5-7 score)	71	130	1.30 (0.48-3.50)	1.40 (0.49-3.98)
High (8-14 score)	11	29	0.90 (0.26-3.14)	0.94 (0.26-3.44)
Score (continuous)			0.94 (0.78-1.13)	0.92 (0.76-1.11)

*Adjustment by sex and year. †Adjustment by sex, year, educational level, tobacco, alcohol consumption, and diabetes mellitus type 2.

DISCUSSION

In this case-control hospital-based study, 15 % of participants strongly adherence to the Mediterranean diet. This result is concordant with the previous Chilean cross-sectional study (27). Furthermore, regular adherence to the Mediterranean diet is associated with a lower probability of the first ischemic stroke in the Ñuble population after adjustment by confounding variables. These results are consistent with previous retrospective and prospective studies, which reported a lower risk of stroke with high adherence to a Mediterranean diet pattern (28-30). All authors in two systematic reviews chose the Mediterranean diet to reduce stroke or CVD risk and mortality rates. Moreover, six meta-analyses were conducted, choosing that high adherence to the MEDAS diet was associated with decreased stroke risk, overall mortality, and cardiovascular disease incidence or mortality. This study will likely not achieve a significant statistic between high adherence and the risk of ischemic stroke by sample size (31,32).

We have not observed significant associations between individual components of the MEDAS diet and stroke, indicating a synergic effect between individual components. Therefore, it is necessary to analyze the MEDAS pattern overall (33).

Reductions in blood pressure and slight reductions in blood lipids mediate the protective effect of the MEDAS diet. Other probable mechanisms are related to the anti-inflammatory effect of all the foods that make up the Mediterranean diet pattern (34-36). For this reason, the nutrients of interest for public health, due to the protective and beneficial effect on people's cardiovascular health, are fiber, potassium, calcium, and vitamin D. Its main mechanisms are lipid-lowering capacity and blood pressure regulation. However, the low consumption of fruits, vegetables, low-fat dairy products, and whole grains in Chile has led to their consumption not exceeding half of the recommendations (37).

In this case-control study, the mean MEDAS score was 6 (SD = 1.5), which is similar to the found in 368 stroke patients in cross-sectional study (mean 6 SD = 2.3) (27) and similar to the mean 5.7 (SD = 1.6) found in a validation study that used a self-applicable questionnaire for a Chilean Mediterranean dietary index (38) and higher than found in intervention study in 96 Chilean workers (39) whom had a basal score of 4.8 (SD = 1.4) and post dietary intervention the score increase to 7.4 (SD = 1.5).

Chile has a Mediterranean climate and is a producer of the foods that make up the Mediterranean diet, however, there are structural and economic barriers that hinder access and availability of these foods for the population. Evidence supports that the Mediterranean diet is an effective primary prevention strategy for ischemic stroke (28-30), therefore, it would be important to implement public policies that facilitate access to foods from the Mediterranean diet such as fish, olive oil, nuts to the population.

The strengths of this study are that using the PREDIMED questionnaire to assess adherence to the Mediterranean diet allowed us to compare with other studies on the same topic carried out in other countries for its international validation. However, 28 other scores evaluate the same pattern (40). Furthermore, in Chile, the research related to exploring the relationship between diet and

diseases is incipient; for that reason, this study is a contribution. This study is carried out in Ñuble, one of the six regions in Chile in which 20 % or more of the population is classified as poor according to the multidimensional poverty index; in this line, Ñuble is similar to many underserved populations in Latin America and other regions in the world.

Limitations of this observational study do not allow for establishing causal relationships, and, likely, some results do not reach the significance statistics probably due to sample size. On the other hand, the fact that participants are from the same hospital limits external validity. There may exist recall bias, but when we contrast the MEDAS diet answer with the FFQ, the results are concordant. Finally, this study did not use biochemical parameters (For example, inflammatory markers) as adjustment variables, which could have been interesting to include.

Our findings suggest that moderate adherence to a Mediterranean diet, defined by the PREDIMED score and adjustment for other variables, reduces the probability to first ischemic stroke but more local research with higher sample size is needed to complement our results. Evidence shows that changing dietary habits and improving adherence to the Mediterranean diet decrease cardiometabolic risk factors and stroke in high-risk populations, but it is unclear whether it could be used as a population-level primary prevention strategy (41,42).

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Trabajo Original

Epidemiología y dietética

Reliability of the New Index of Global Food Quality and its relationship with sociodemographic variables and physical activity levels in the Chilean population *Confiability del Nuevo Índice de Calidad Global de Alimentación y su relación con variables sociodemográficas y niveles de actividad física en la población chilena*

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Abstract

Introduction: surveys play a crucial role in evaluating the quality of food in populations, especially in healthcare settings, helping identify important characteristics of food descriptions and improving efficiency in the collection and management of data in dietary surveys.

Objective: the primary aim of this study was to analyze the internal consistency of the New Index of Global Food Quality (NIGFQ) instrument and assess its applicability to sociodemographic variables and levels of physical activity (IPAQ-S) in a specific region of Chile.

Methods: a descriptive, comparative, and correlational study that utilizes the online platform of Google Forms for data collection using the New Index of Global Food Quality (NIGFQ) and IPAQ-S instruments, in addition to considering sociodemographic variables, in a sample of 1,331 participants from the metropolitan region of Chile.

Results: the study shows an improvement in the reliability of the GQIN (Cronbach's alpha: 0.63 to 0.71). Findings reveal significant inverse correlations between fruits ($r = -0.31$; $p \leq 0.05$) and legumes ($r = -0.34$; $p \leq 0.05$) with body mass.

Conclusions: it is concluded that values above 52.5 points are considered healthy on the new evaluation scale of the index, supported by statistical reliability tests. Similarly, the components of the adjusted New Index of Global Food Quality, particularly fruits and vegetables in greater proportion, show a beneficial relationship with daily consumption in reducing body mass index and body weight.

Keywords:

Nutrition. Diet. Surveys.
Metabolic task. Reliability.

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Resumen

Introducción: las encuestas desempeñan un papel crucial en la evaluación de la calidad de los alimentos en las poblaciones, especialmente en entornos de atención médica, ayudando a identificar características importantes de las descripciones de alimentos y mejorando la eficiencia en la recopilación y gestión de datos en encuestas dietéticas.

Objetivo: el objetivo principal de este estudio fue analizar la consistencia interna del instrumento Nuevo Índice de Calidad Global de Alimentación (ICGA) y evaluar su aplicabilidad a variables sociodemográficas y niveles de actividad física (IPAQ-S) en una región específica de Chile.

Métodos: estudio descriptivo, comparativo y correlacional que utiliza la plataforma en línea de Google Forms para la recopilación de datos utilizando los instrumentos ICGA e IPAQ-S, además de considerar variables sociodemográficas, en una muestra de 1,331 participantes de la región metropolitana de Chile.

Resultados: el estudio muestra una mejora en la confiabilidad del ICGA (alfa de Cronbach: 0,63 a 0,71). Los hallazgos revelan correlaciones inversas significativas entre frutas ($r = -0,31$; $p \leq 0,05$) y legumbres ($r = -0,34$; $p \leq 0,05$) con el peso corporal.

Conclusiones: se concluye que los valores por encima de 52,5 puntos se consideran saludables en la nueva escala de evaluación del índice, respaldados por pruebas estadísticas de fiabilidad. De manera similar, los componentes del Nuevo Índice de Calidad Alimentaria Global ajustado, en particular las frutas y verduras en mayor proporción, muestran una relación beneficiosa con el consumo diario en la reducción del índice de masa corporal y el peso corporal.

Palabras clave:

Nutrición. Dieta. Encuestas.
Tarea metabólica.
Confiabilidad.

INTRODUCTION

In the world, more than 821 million people suffer from hunger due to factors such as demographic growth, urbanization, climate change, and the excessive use of natural resources and ecosystems, among others (1). Despite agricultural food systems and recommendations from the Food and Agriculture Organization (FAO) of the United Nations, the current demands for food for the global population are not being met (2).

Currently, various methods exist to assess the quality of food, using self-perception of the consumer and in the literature, several methodologies comprehensively address the quality of the diet in a population (3). Among them, the Healthy Eating Index (HEI), developed by the Center for Nutrition Promotion of the United States Department of Agriculture in 1995, is recommended. Its main objective is to determine the degree of adherence of the U.S. population to the Dietary Guidelines (4).

To analyze eating behaviors, various surveys have been used, such as consumption trends or 24-hour recall (5), where dietary consumption, specific food groups, and nutrients are analyzed. Additionally, the degree of adherence to intake recommendations for the population is measured (5). To achieve a comprehensive diagnosis of nutrition, in recent years, various global diet quality indices have been developed. These are constructed from algorithms that determine how healthy the dietary pattern is (6). The proposed indices are based on current nutritional knowledge and the dietary guidelines of a specific country, allowing for the identification of key dietary risk factors associated with non-communicable chronic diseases (7).

Surveys play a crucial role in evaluating the quality of food in populations, especially in healthcare settings (8). They also help identify important characteristics of food descriptions, improving the efficiency of data collection and management in dietary surveys (5). These surveys often use anthropometric and food consumption indicators such as food records and 24-hour dietary recalls, commonly used to assess nutritional and health status (9). Consumers also rely on surveys to assess the quality, safety, and environmental impact of food, with freshness, taste, and appearance being key factors (10).

The caloric content of foods, due to their varied contents, has been on the rise, leading to overweight and obese in individuals furthermore, malnutrition is considered, evident in various social classes across all countries, and when combined with physical inactivity, it is associated with a deterioration of physical health and the development of cardiovascular diseases (11).

In Latin America, which is composed of 33 countries with approximately 650 million people, of which 42.5 million are children aged 0 to 19 years, and there is a prevalence of those classified as overweight and obese, which is becoming a public health burden due to the consequences of non-communicable chronic diseases (NCDs) affecting the population of all ages and genders (12). This public health problem results in an increase in economic health costs and has a growing incidence in all regions of the countries (13).

The purpose of this study was to assess the reliability of the survey titled "Proposal for a New Index of Global Food Quality (NIGFQ)," originally developed by Ratner et al. (2017) within the Chilean context and adapted from Kennedy et al. (1996). This assessment involved a comparison with similar research conducted in various populations (14). Specifically, the study aimed to analyze the internal consistency of the instrument. Furthermore, it evaluated the applicability of the index to different sociodemographic variables and levels of physical activity within a specific population from the Chile region.

MATERIALS AND METHODS

PROCEDURES

This study is considered descriptive, comparative, and correlational because it determines relationships or effects between the study variables. For data collection, the study utilized the online platform of Google Forms, accessible through the following link (<https://tinyurl.com/mrmdkykh>). The application of instruments took place from June 1st to July 12th, 2020, with the inclusion criterion being the acceptance of informed consent and voluntary participation. The self-perceived survey remained online for

42 days, and the response time ranged from approximately 8 to 15 minutes. The instrument included sociodemographic variables, the International Physical Activity Questionnaire (IPAQ-S), and New Index of Global Food Quality.

The sociodemographic variables included in the study were: gender, age, height, weight, geographical origin, socioeconomic level, as well as questions from IPAQ-S and GFQI. After the specified dates, the results were downloaded into Excel spreadsheets, tabulated, and examined to initiate the statistical procedure. Participants who did not complete the survey in its entirety or those with higher levels of outliers were excluded from the study.

The study was approved by the Ethical-Scientific Evaluation Committee of the Santiago Campus of the Universidad Mayor, dated June 29, 2020. The analysis of the documentation considered the recommendations and norms contained in the following legal bodies and international declarations, specifically related to the proposed research type: Law No. 19.628 "On the Protection of Privacy," dated August 18, 1999. Circular No. A15/15 dated April 18, 2013, from the Ministry of Health of Chile, providing guidelines on obtaining consent from individuals participating in scientific research.

The study adhered to the Declaration of Helsinki of the World Medical Association, on ethical principles for medical research involving human participants, in its version approved at the 64th General Assembly in October 2013.

For the data collection protocol, two surveys with open, closed, and alternative questions were used. This was based on the study by Ratner et al. (2017), along with sociodemographic questions and the International Physical Activity Questionnaire IPAQ-S, in its Spanish version.

To conduct the analysis of this research, a factorial design was employed, comprising five study variables:

1. Gender factor, divided into two levels (male and female).
2. Body mass index (BMI) factor, subdivided into three levels (underweight, normal, and overweight).
3. Quality of food factor, three levels (unhealthy, needs changes, and healthy).
4. Physical Activity factor, subdivided into three levels (low, moderate, and high).
5. Age category factor, subdivided into three levels (18 years to > 30 years).

PARTICIPANTS

A total of 1,331 participants enrolled in the study from various communities in the Metropolitan Region, from both rural and urban areas. Inclusion criteria such as not having pathologies, being self-sufficient, and being 18 years old were applied. A total of 93 surveys were excluded due to lack of information or incompleteness, resulting in a total of 1,238 study participants. (51.29 % female, 48.71 % male). The age range varied from 18 to 65 years, (mean 30.2 ± 8.6 years).

The sample selection utilized social media platforms such as Facebook and Instagram, where the link and invitation to partic-

ipate were openly and publicly shared, following the concept of "Snowball Sampling" proposed by Atkinson & Flint (2001).

To characterize the population segmentation, social indicators were considered goods or attributes whose value is primarily expressed in relation to occupation, education, and family composition. These indicators included marital status, level of education, occupation, number of people in the household, and classification in relation to average income.

BODY MASS INDEX EVALUATION

To assess the body condition, self-reports of total mass (kg) and height (cm) were requested to calculate the body mass index (BMI) and classify the participants' status according to global health parameters. The use of self-reported information (total mass and height) was employed, as it is a variable already validated with good reliability (15). In the guidelines for this evaluation, it should be considered that the difference between self-reported and actual mass should not exceed 2.4 kg, and for height, a variation not exceeding 3.5 cm, demonstrating a high degree of accuracy in the self-reports of these parameters (16).

NEW INDEX OF GLOBAL FOOD QUALITY

To measure the quality of nutrition, a questionnaire called the New Index of Global Food Quality was administered to university students in a national sample, following the dietary guidelines of the Ministry of Health in Chile (17). The instrument consists of 14 questions, divided into two sections: the first comprises 10 multiple-choice questions regarding eating habits, and the second part includes 4 questions with responses based on the frequency of food consumption. The questionnaire is composed of three sections, distributed into 12 variables, each with six possible responses ranging from 1 to 10. The ideal score, according to dietary guidelines, is 10, while the least healthy score is 1. Establishing the maximum score with all 12 variables studied at 120, it was classified according to the following criteria: healthy: 90-120 points; needs changes: 60-89 points; unhealthy: < 60 points.

LEVELS OF PHYSICAL ACTIVITY

This assessment was conducted through self-reporting of physical activity (PA) and sedentary time over the past 7 days, as determined by the abbreviated version of the IPAQ (International Physical Activity Questionnaire). The data were reported in minutes per day (min/day) for each of the domains, and to estimate the total physical activity (PA) performed, the reported time was adjusted by the metabolic equivalent (METs), which corresponds to 3.3 METs for light intensity (walking), 4 METs for moderate, and 8 METs for vigorous intensity. The total Physical Activity was reported as the sum of METs for each intensity. Additionally,

the IPAQ-SF algorithm was used to transform continuous data into categorical data (low, moderate, and high physical activity). The results were calculated as the weekly metabolic equivalent for exercises and tasks in minutes (MET-minutes/week). Everything was done according to the scoring protocols and recommendations for physical activity levels in IPAQ, which are low (< 600 MET-minutes/week), moderate (> 600 MET-minutes/week), and high (> 3000 MET-minutes/week) to determine the values according to METS.

CATEGORIZATION AND INCLUSION CRITERIA

To characterize the population segmentation, social indicators were considered goods or attributes whose value is primarily expressed in relation to occupation, education, and family members comprising the family group. The calculation of the sample was based on the representativeness of the participants under study, from a universe characterized mainly by the metropolitan region (Santiago, Chile). The sample size was calculated using the equation for finite populations through a sample calculator (<https://www.netquest.com/en/panel/sample-calculator/statistical-calculators>) with a universe population of 5,455,464 individuals; 2,756,945 males (50.4 %) and 2,698,519 females (49.7 %), the sample size was determined. The calculation considered a confidence level of 95 %, using a margin of error of 5 %. The following inclusion and exclusion criteria were applied:

1. Being under 18 years old.
2. Having disabilities associated with reduced mobility (musculoskeletal injuries).
3. Having pathologies and/or being pregnant.
4. Being under pharmacological treatment.
5. Having any physical or mental disability.

STATISTICAL ANALYSIS

All analyses were conducted using Jamovi Software® version 1.6. Sociodemographic data and results are presented as percentages for qualitative variables through contingency tables and as mean \pm standard deviation for quantitative variables. The normality and homogeneity of variance of the data were verified using the Kolmogorov-Smirnov test and Levene's test. Subsequently, the interaction between variables was analyzed through the analysis of variance (ANOVA) with a mixed component, complemented with Tukey's post hoc tests to identify significant differences between groups. Multivariate analysis of variance (MANOVA) was conducted to explore in-depth the variables that compose eating habits. Effect size measurement followed Cohen's proposal (1997). Spearman's correlation was used to identify relationships between variables. The internal consistency of the instrument was evaluated using the Cronbach's Alpha test with a significance level of $p \leq 0.05$ in all analyses.

RESULTS

RELIABILITY AND SCORING CRITERIA

The reliability of the proposed instrument for the New Index of Global Food Quality, composed of 14 questions, was assessed through the calculation of the Cronbach's alpha coefficient, yielding a value of 0.63. This result is considered undesirable according to the criteria established by (18). To enhance the internal consistency of the instrument, an additional analysis focused on seven specific variables was conducted: vegetables, fruits, milk and dairy products, legumes, fish, sugar, and fried foods, determined by the variables that showed an increase in the Cronbach's coefficient when added or removed. The resulting Cronbach's alpha coefficient for these variables was 0.71, indicating good internal consistency (19). The research findings revealed a maximum possible score of 70 points for the index. A new classification based on percentiles (25, 50, and 75) was established, dividing scores into the following ranges:

Score (points)	Classification
52.5 to 70	Healthy
40 to 52.4	Needs improvement
< 40	Unhealthy

POPULATION CHARACTERISTICS (χ^2)

The sociodemographic data of the participants were categorized by gender and presented in terms of number and percentages for nominal and ordinal variables. For continuous data, mean and standard deviation values were provided (Table I).

No significant differences or associations were found between gender and the values of morphological information, BMI, physical activity level, age category and eating habits ($p > 0.05$).

Significant inverse correlations were found in almost all components of the new food quality index when compared to mass and BMI (Table II) with coefficients ranging from small ($r = 0.1$ to 0.29) to moderate ($r = 0.3$ to 0.5) according to Hopkins (2002).

Trivial ($r = 0.0$ to 0.1) and small (0.1 to 0.3) positive and inverse correlations were identified between the New Index of Global Food Quality and body composition variables (Table III). The scale of correlation coefficients was determined according to the proposed classification by Hopkins (2002).

In table IV the results are reported according to the eating habits vs. study variable (sex, marital status, education level, socioeconomic status, BMI level, self-perceived overweight, physical activity level, and age category) and analyzed using the MANOVA test (Pillai's Trace) and ANOVA (Tukey).

The disparity in educational levels reveals a significant impact, with a large effect size (ES: 1.46). When contrasting both levels, an unhealthy trend is observed in individuals without higher education. The identified differences in socioeconomic status highlight a large effect size between low and high levels (ES: 1.0).

Table I. Sociodemographic values according to gender and morphological variables, marital status, educational level, socioeconomic status, BMI, physical activity, age category, eating habits

Morphological information	Male	Female
Sex	603 (48.7 %)	635 (51.2 %)
Age (years)	29.8 ± 8.61	30.5 ± 8.6
Height (cm)	170.4 ± 8.38	169.4 ± 8.25
Weight (kg)	71.8 ± 13.0	72.0 ± 12.8
BMI (kg·m ⁻¹)	24.6 ± 3.55	24.9 ± 3.42
METs	1751 ± 1375	1697 ± 1465
<i>Marital status</i>		
Married	285 (23.0 %)	330 (26.7 %)
Single	318 (25.7 %)	305 (24.6 %)
<i>Education level</i>		
College graduate	348 (57.7 %)	393 (61.9 %)
Non- College graduate	255 (42.3 %)	242 (38.1 %)
<i>Socioeconomic status</i>		
Low income	132 (19.5 %)	110 (17.3 %)
Middle income	432 (71.6 %)	478 (75.3 %)
Hight income	39 (6.5 %)	47 (7.4 %)
<i>BMI level</i>		
Underweight	40 (6.7 %)	28 (4.4 %)
Normal weight	269 (44.9 %)	297 (46.9 %)
Overweight	290 (48.4 %)	308 (48.7 %)
<i>Self-perceived overweight</i>		
No	542 (49 %)	565 (51 %)
Yes	61 (46.6 %)	70 (53.4 %)
<i>Physical activity level</i>		
Low active	115 (19.1 %)	137 (21.6 %)
Moderately active	409 (67.8 %)	409 (64.4 %)
Very active	79 (13.1 %)	89 (14.0 %)
<i>Age category (years)</i>		
18 to 25	216 (17.4 %)	191 (15.4 %)
25 to 30	180 (14.5 %)	207 (16.7 %)
> 30	207 (16.7 %)	237 (19.1 %)
<i>Global Food Quality Index</i>		
Unhealthy	274 (45.4 %)	277 (43.7 %)
Needs changes	168 (27.9 %)	194 (30.6 %)
Healthy	161 (26.7 %)	163 (25.7 %)

BMI = body mass index.

Likewise, concerning body mass index (BMI), a significant difference is observed, especially between low and overweight levels (ES: 1.0). Cohen's results show that disparities in self-perception of overweight have a small effect (ES: 0.3). Regarding levels of physical activity, a small effect size is notable, especially between low and very active activity levels (ES: 0.31). Similarly, age presents large effects when comparing ages 18 to 25 with those over 30 years old (21).

Table II. Correlations between body composition and Components of the Global Food Quality Index

	Body mass		BMI	
Vegetables	-0.316	†	-0.155	†
Fruits	-0.345	†	-0.221	†
Milk	-0.198	† ^o	-0.071	*
Legumes	-0.147	†	-0.211	†
Fish	-0.040		-0.145	†
Sugar	-0.109	†	0.009	
Fried foods	-0.244	†	-0.173	†

**p* < 0.05; †*p* < 0.001.

DISCUSSION

The fundamental objectives of this research were established with two main purposes. Firstly, the aim was to validate the reliability of the instrument used, the New Index of Global Food Quality. Secondly, a detailed analysis of the overall NIGFQ was undertaken, considering its comparison and relationship with sociodemographic variables and levels of physical activity in a representative sample of the Chilean population. To facilitate a more comprehensive understanding of the manuscript, the discussion was structured into two sections, allowing for a detailed analysis of the findings achieved throughout this study.

RELIABILITY OF THE NEW INDEX OF GLOBAL FOOD QUALITY

Four similar studies have been identified with variations in some variables, wherein no evidence of reliability testing is apparent. It is pertinent to address this gap found in the literature for a better understanding of the results. Numerous studies have explored the reliability of surveys in assessing food quality, emphasizing the importance of this factor in response reliability. An illustrative example comes from a study revealing that satisfaction surveys with food service for patients in medical settings are generally valid and of acceptable quality. In this context, food quality emerged as a key predictor of overall satisfaction (8).

Table III. Correlations between the Global Food Quality Index and body composition variables

	GFQI		METs		AGE		BMI		Body mass	
GFQI	—									
METS	0.123	‡	—							
AGE	-0.070	*	0.028		—					
BMI	-0.174	‡	-0.159	‡	0.241	‡	—			
Body mass	-0.284	‡	-0.074	†	0.289	‡	0.846	‡	—	

* $p < 0.05$; † $p < 0.01$; ‡ $p < 0.001$; GFQI: Global Food Quality Index; METs: metabolic equivalents.

Table IV. Results are reported according to the eating habits vs. study variable (sex, marital status, education level, socioeconomic status, BMI level, self-perceived overweight, physical activity level, and age category) and analyzed using the MANOVA test (Pillai's Trace) and ANOVA (Tukey)

	Vegetables	Fruits	Legumes	Milk	Fish	Fried	Sugar	GFQI#
<i>Sex</i>								
Female	6.3 ± 2.5	4.4 ± 3.1	8.1 ± 1.98	5.2 ± 3.56	6.5 ± 3.0	5.6 ± 2.2	6.9 ± 2.7	43.3
Male	6.1 ± 2.8	4.3 ± 3.3	8.4 ± 1.69	5.0 ± 3.67	6.5 ± 3.1	5.4 ± 2.0	7.0 ± 2.5	43
<i>Marital status</i>								
Married	6.3 ± 2.8	4.4 ± 3.2	8.1 ± 2.2	5.6 ± 3.5	6.5 ± 3.1	5.8 ± 2.2	6.6 ± 2.9	43.2
Single	6.2 ± 2.6	4.4 ± 3.2	8.5 ± 1.3	4.7 ± 3.7	6.6 ± 3.1	5.3 ± 2.0	7.4 ± 2.3	43.2
<i>Education level</i>								
College graduate	7.5 ± 2.3	5.7 ± 3.3	8.3 ± 2.2	7.1 ± 2.9	6.2 ± 3.5	6.0 ± 2.4	7.5 ± 2.8	48.3*
Non-college graduate	4.4 ± 2.2	2.4 ± 1.8	8.3 ± 1.2	2.2 ± 2.3	7.1 ± 2.1	4.8 ± 1.4	6.2 ± 2.3	35.4*
<i>Socioeconomic status</i>								
Low income	5.3 ± 2.9	4.8 ± 3.3	8.3 ± 1.9	5.4 ± 3.9	6.1 ± 3.8	5.2 ± 2.0	6.3 ± 3.0	41.4 ^a
Middle income	6.4 ± 2.6	4.0 ± 3.1	8.3 ± 1.8	4.8 ± 3.5	6.7 ± 2.9	5.5 ± 2.1	7.1 ± 2.5	42.8 ^b
High income	7.4 ± 2.0	7.1 ± 2.7	8.6 ± 2.5	7.7 ± 2.7	6.4 ± 2.7	7.2 ± 2.6	7.8 ± 2.5	52.2 ^{ab}
<i>BMI level</i>								
Underweight	8.0 ± 1.99	8.0 ± 2.3	9.7 ± 0.7	8.3 ± 3.1	5.8 ± 4.3	6.0 ± 2.0	6.7 ± 2.6	52.8 ^{cd}
Normal weight	6.1 ± 2.9	4.5 ± 3.4	8.2 ± 2.0	4.8 ± 3.4	6.8 ± 2.9	5.8 ± 2.3	6.8 ± 2.9	43.4 ^e
Overweight	6.0 ± 2.4	3.8 ± 2.7	8.2 ± 1.6	5.0 ± 3.6	6.3 ± 2.9	5.1 ± 1.8	7.1 ± 2.3	41.9 ^d
<i>Self-perceived overweight</i>								
No	6.0 ± 2.7	4.2 ± 3.2	8.4 ± 1.8	4.8 ± 3.5	6.8 ± 2.7	5.5 ± 2.0	6.8 ± 2.6	42.8*
Yes	7.7 ± 2.2	5.1 ± 3.2	7.8 ± 2.1	7.7 ± 3.1	3.8 ± 3.9	5.5 ± 2.8	8.3 ± 2.2	46.1*
<i>Physical activity levels</i>								
Low	5.6 ± 2.8	4.3 ± 2.9	8.0 ± 2.1	4.8 ± 3.7	5.4 ± 3.5	5.5 ± 2.1	7.3 ± 2.8	41 ^{ef}
Moderate	6.3 ± 2.6	4.3 ± 3.2	8.4 ± 1.5	5.2 ± 3.6	7.0 ± 2.6	5.5 ± 2.1	6.8 ± 2.5	43.6 ^e
Very active	6.7 ± 2.8	4.8 ± 3.2	8.3 ± 2.5	5.6 ± 3.3	6.0 ± 3.8	6.0 ± 2.3	7.1 ± 2.8	44.3 ^f
<i>Age category (years)</i>								
18 to 25	7.1 ± 2.1	2.5 ± 5.0	7.5 ± 2.5	5.5 ± 3.9	7.5 ± 2.5	5.0 ± 0.0	7.5 ± 2.5	44.1 ^g
26 to 30	7.1 ± 2.1	2.5 ± 5.0	7.5 ± 2.5	4.8 ± 3.3	7.5 ± 0.0	5.0 ± 0.0	7.5 ± 2.5	43.8 ^h
> 30	5.0 ± 4.6	2.5 ± 6.5	7.5 ± 2.5	5.0 ± 3.5	7.5 ± 6.5	5.0 ± 0.0	7.5 ± 2.5	41.8 ^{gh}

Superscript characters or symbols indicate significant differences ($p \leq 0.05$); BMI: body mass index; #GFQI: Global Food Quality Index.

Other studies have developed specific indices, such as the Main Meal Quality Index, demonstrating its internal validity and reliability in assessing the nutritional quality of meals (22). Similarly, Kang & Namkung (2022) contributed to the landscape by creating and validating a scale to measure service quality in fresh food delivery platforms. This tool addresses crucial factors such as information quality and delivery, and they examined the reliability and validity of a simplified food frequency questionnaire, concluding that it was acceptable for use in epidemiological studies in adults undergoing physical examinations. In our study, 14 variables that make up the food quality index were analyzed, and the analyses did not yield reliability values. Considering the literature, the number of questions was reduced to seven, improving the Cronbach's alpha (24).

Regarding the reliability assessment, it is essential to highlight the crucial role of the Cronbach's alpha test. However, its interpretation and application can be complex, as the survey design characteristics may influence the reliability of scores, leading to mixed results (25). Furthermore, the literature warns against overreliance on Cronbach's alpha, as it does not always reflect the instrument's quality (26). While other studies have developed a system to assess questionnaire reliability using Cronbach's alpha (27). Although Cronbach's alpha remains a widely used measure of reliability in psychometric tests, it is crucial to recognize that a value higher than 0.70 indicates good reliability (19). Despite its limitations, Cronbach's alpha maintains its relevance, with reported average coefficients ranging between 0.70 and 0.82 (28). However, addressing misconceptions about this test, including its origin by Cronbach, its equivalence to reliability, and the assumption that a high value indicates internal consistency, is crucial (29).

APPLICABILITY TO OTHER STUDY VARIABLES

The findings of our study align with the majority consulted in scientific literature, where results indicate that a smaller percentage of the studied population, both in males (26.7 %) and females (25.7 %), exhibit a healthy diet (Table I). Simultaneously, higher values are observed in the need for changes or the presence of an unhealthy diet (17,30). It is noteworthy that these results may vary significantly by region, with Western and Latin American regions showing higher scores for healthy dietary patterns, while Asia and Sub-Saharan Africa obtained the highest scores for unhealthy dietary patterns (31). Another study has examined these differences in more detail, finding variations in the intake of food groups and diet quality scores among different ethnic groups (32). However, data gaps were identified, particularly in the coverage of specific and sensitive nutrition interventions (33).

The relationships identified in our study (Tables II and III) indicate that the consumption of fruits and vegetables is associated with a decrease mass and the risk factor for NCDs due to normal BMI values. The results show that both males and females fall within a non-risk index (18.5 to 24.9). Scientific literature has demonstrated a complex relationship between food quality and

weight and body mass index (BMI). It has been found that diets rich in carbohydrates, especially those with a low glycemic load and high consumption of whole grains, are associated with lower BMI (34). Furthermore, it has been observed that better diet quality in early and middle childhood is associated with increased height, weight, and fat-free mass index, but not with body adiposity (35). Similarly, it has been found that food security is a significant determinant of diet quality, especially in impoverished urban environments (36). Additionally, it has been demonstrated that higher diet quality can mitigate the genetic predisposition to obesity, emphasizing the importance of a healthy diet in obesity prevention (37).

Analyzing the differences revealed by the ANOVA test (Table IV), we are particularly struck by the unhealthy eating habits that individuals with no university education may exhibit. The research consistently shows that educational level significantly influences nutrition quality because older adults with lower educational levels rely on different sources for nutrition information, potentially leading to poorer dietary choices (38). Similarly, higher educational levels have consistently been demonstrated to be associated with better nutrition, linked to healthier food choices such as increased consumption of fruits, vegetables, and fish. This underscores the importance of incorporating nutritional education into school curricula (39), highlighting the role of education in promoting healthy eating habits and overall well-being.

We believe that our proposal could have a positive impact on instruments assessing food quality due to a reduced number of components and demonstrated reliability through statistical tests. Further research is expected to corroborate these results by replicating the study and thereby reinforcing the support for the proposed data. In addition to nutrition, we consider the importance of healthy lifestyle habits, coupled with variables such as physical activity levels, to reduce risk factors contributing to non-communicable chronic diseases among global populations (40).

CONCLUSIONS

The main objective of our study is to validate and apply the New Index of Global Food Quality in a population according to sociodemographic variables in the southern region of Chile. It is concluded that values above 52.5 points are considered healthy on the new evaluation scale of the index, supported by statistical reliability tests. Similarly, the components of the adjusted New Index of Global Food Quality, particularly fruits and vegetables in greater proportion, show a beneficial relationship with daily consumption in reducing BMI and mass. Moreover, our findings indicate a greater effect among populations according to their educational level, where individuals with higher education are more likely to have better food quality. We recommend interpreting this information with caution and conducting new studies with populations in person to apply the values of this proposed new index.

IMPLICATIONS FOR RESEARCH AND PRACTICE

In our evaluation, we believe that the New Index of Global Food Quality by Ratner et al. (2017) could benefit from modifications aimed at enhancing its reliability through simpler statistical tests and the introduction of a new scoring scale. Additionally, we emphasize the importance of increasing the consumption of fruits and vegetables, given their positive impact on reducing body mass index, a factor closely linked to non-communicable chronic diseases. Furthermore, we highlight the pressing need to implement nutrition education programs in school environments. These programs would play a key role in reducing nutritional knowledge gaps and preventing the consumption of unhealthy foods. Finally, we underscore the importance of conducting new studies that act as repeatability tools, improving the scores of the scales presented in this work. This approach will contribute to strengthening the validity and applicability of the obtained results.

LIMITATIONS

Our study presents certain limitations related to the use of online surveys that must be considered. While online surveys offer advantages such as rapid data collection and access to large samples, they also pose challenges such as selection bias, non-response bias, and the use of non-validated scales (41,42). Consequently, the information collected is subject to self-report biases, as participants may provide inaccurate data due to selective memory or the desire to present a healthier image of themselves. Additionally, during pandemic lockdowns, these biases can be exacerbated, potentially influencing the results. The inability to capture cultural and social context in online surveys restricts a comprehensive understanding of dietary habits. This lack of contextualization could impact the applicability and relevance of the results. Therefore, it is crucial to consider implementing this instrument in-person in specific populations, complemented by diverse studies evaluating repeatability. This approach will strengthen the validity and reliability of the scales proposed in this work.

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Trabajo Original

Epidemiología y dietética

Hydration profile of the Latin American population and the contribution of total daily pure water. The ELANS study

Perfil de hidratación de la población latinoamericana y el aporte de agua pura total diaria. Estudio ELANS

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Abstract

Introduction: water is a crucial component of human health useful for various bodily functions. Despite its importance, previous research has largely overlooked hydration in Latin America, focusing instead on regions with greater access to a variety of food sources.

Objective: hence, this study provides comprehensive data on water consumption patterns in this region and analyses the hydration profiles of urban Latin American populations, emphasizing the role of pure water in daily intake.

Materials and methods: involving 5977 participants from Argentina, Brazil, Costa Rica, Ecuador, and Peru, the study utilized a cross-sectional approach, examining total water intake (TWI) through two nonconsecutive 24-hour dietary recalls. This study focused on understanding the contribution of pure water to daily hydration and identifying disparities in water consumption patterns across different demographic conditions by measuring the TWI from beverages.

Results: the findings indicated significant variations in hydration profiles based on country, sex, and socioeconomic status. The median TWI was 3245.6 g/day, with a median water intake from beverages of 1982.9 g/d kcal, which represented 61 % of the participants' total water intake. A total of 63.8 % of the overall sample met the TWI recommendations. Our data indicate that 38.4 % of the water intake came from plain water, followed by coffee and tea (16.9 %), commercial sugar-sweetened beverages (13.7 %), and homemade SSB (11.7 %).

Conclusion: these findings contribute to a deeper understanding of nutritional behaviors and may serve as a basis for future studies and health interventions focused on improving hydration habits, with emphasis on pure water consumption, especially in urban areas in developing regions.

Keywords:

Hydration profiles. Latin America. Total water intake (TWI). Nutritional behavior. ELANS.

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Resumen

Introducción: el agua es un componente crucial para la salud humana, necesario para diversas funciones corporales. A pesar de su importancia, investigaciones previas han prestado poca atención a la hidratación en América Latina, enfocándose en cambio en regiones con mayor acceso a una variedad de fuentes alimentarias.

Objetivo: por ello, este estudio ofrece datos exhaustivos sobre los patrones de consumo de agua en esta región y analiza los perfiles de hidratación de poblaciones urbanas latinoamericanas, destacando el papel del agua pura en la ingesta diaria.

Materiales y métodos: con la participación de 5977 personas de Argentina, Brasil, Costa Rica, Ecuador y Perú, el estudio empleó un enfoque transversal para examinar la ingesta total de agua (ITA) a través de dos recordatorios dietéticos de 24 horas no consecutivos. El objetivo fue entender la contribución del agua pura a la hidratación diaria e identificar disparidades en los patrones de consumo de agua según diversas condiciones demográficas, midiendo la ITA proveniente de bebidas.

Resultados: los resultados indicaron variaciones significativas en los perfiles de hidratación en función del país, el sexo y el estatus socioeconómico. La mediana de la ITA fue de 3245,6 g/día, con una ingesta media de agua de bebidas de 1982,9 g/d, lo que representó el 61 % de la ingesta total de agua. El 63,8 % de la muestra total cumplió con las recomendaciones de ITA. Los datos revelaron que el 38,4 % de la ingesta de agua provino de agua pura, seguido de café y té (16,9 %), bebidas comerciales azucaradas (13,7 %) y bebidas azucaradas caseras (11,7 %).

Conclusión: estos hallazgos proporcionan una comprensión más profunda del comportamiento nutricional y pueden servir como base para futuros estudios e intervenciones de salud dirigidas a mejorar los hábitos de hidratación, con un enfoque en el consumo de agua pura, especialmente en áreas urbanas de regiones en desarrollo.

Palabras clave:

Perfil de hidratación.
Latinoamérica. Ingesta total de agua (ITA). Hábitos nutricionales. ELANS.

INTRODUCTION

Water is the main constituent of the human body. Comprising approximately 45 %-75 % of the human body weight depending on age and status, and it is essential for maintaining proper hydration in the body and plays an important role in various bodily functions. Insufficient water intake can cause dehydration and trigger symptoms such as fatigue, dizziness, and impaired cognitive function (1-3). High carelessness during hydration has been observed, even when this behavior may cause several physiological problems such as kidney damage, urinary infection, cardiovascular problems, metabolic diseases, and even other psychological factors (4-6).

On the other hand, adequate hydration can have additional benefits, such as helping to improve cognitive development in children and adolescents, as well as reducing stress, and improving concentration. Moreover, hydration is an important factor in the practice of physical activity, itself key component when predicting their future academic and nutritional status (7,8).

The interest in the quantity and quality of consumed beverages daily has been evaluated at several levels through distinct perspectives. Previous analyses have shown that 22 % of water intake comes from food (9). This value is potentially higher in Latin America because of the accessibility to a great variety of fruits and vegetables. However, data on the assessment of hydration in these countries are limited (10) as little or no importance has been given to water consumption, which may be a result of its low energetic/caloric input. In spite of this, promoting adequate hydration can help to control and prevent metabolic and psychological diseases.

Total water intake (TWI) results from the sum of all types of liquids from foods and beverages. However, the recommendations on water intake established by international organizations are based on different methodologies. Thus, the European Food Safety Authority (EFSA) reference values for TWI base their recommendations for adolescents and adults on the population's median water intake and urinary osmolarity (11) and have been documented to be more conservative than the reference values

set by the USA Institute of Medicine (IOM). In this regard, the IOM's recommendations are the median water intakes observed in the National Health and Nutrition Examination Survey (NHANES) (12), and they are unlikely to overestimate the number of people who do not adhere to the recommendations. Considering that other references for TWI are not available in Latin American countries, it is more appropriate to use the adequate TWI established by the IOM (12) in agreement with the findings of other Latin American studies (13,14).

Given the evidence pointing to the crucial role of water intake and hydration play in human health and body weight, it is necessary to develop new studies that can confirm the population's real hydration status. Therefore, this study sought to analyze TWI and the intake of different beverages, determining the associations with IOM recommendations. Using population-based data from the Latin American Study of Nutrition and Health (Estudio Latinoamericano de Nutrición y Salud ELANS), we conducted an analysis on a sample of male and female individuals aged between 15 and 65 years living in urban areas of Argentina, Brazil, Costa Rica, Ecuador and Peru using two nonconsecutive 24-h dietary recalls. This study aimed to determine trends in ingested beverages and thus promote water intake based on international recommendations. In this way, generating knowledge that allows the introduction of hydration processes in an orderly, planned manner and according to the necessary physiological requirements.

MATERIALS AND METHODS

STUDY DESIGN

The Latin American Study of Nutrition and Health (ELANS) is a household-based, multicenter, cross-sectional study of nutrition and health surveillance (14). This study aimed to evaluate the nutritional intake, physical activity levels, and anthropometric data of the participants. ELANS was simultaneously conducted in eight Latin American countries (Argentina, Brazil, Chile,

Colombia, Costa Rica, Ecuador, Peru, and Venezuela). The fieldwork was conducted from September 2014 to July 2015. The Western Institutional Review Board (#20140605) approved the international ELANS protocol, which was registered in ClinicalTrials.gov (#NCT02226627). In addition, the Institutional Review Boards (IRBs) of each country also approved the protocol, which ensured that the study was performed in accordance with the ethical standards. All participants signed a written informed consent/assent before their participation in the survey. The confidentiality of the participants for the pooled data was maintained using numerical identification codes instead of names. All the data were transferred with secure file-sharing systems. The design and methodology of the ELANS study have been described in Fisberg et al., 2016 (14).

SAMPLE

The sample for this study consisted of 5977 participants aged 15 to 65 years from an urban population living in 5 Latin American countries (Argentina, Brazil, Costa Rica, Ecuador, and Peru). The ELANS used a random complex, multistage process in which the data were stratified by geographical region, sex, age, and socioeconomic level (SEL). The sampling size was calculated with 95 % confidence intervals and a sample error of 3.49 %. Sampling weighting was applied for each country. SEL was assessed using a country-dependent questionnaire considering legislative requirements or established local standards. Details of the study design and protocol can be found in Fisberg et al., 2016 (14).

ANTHROPOMETRIC MEASUREMENTS

The anthropometric measurements considered for the present study were body weight and height and were obtained by trained interviewers according to standardized procedures (14). Body weight was measured using a calibrated electronic scale with an accuracy of 0.1 kg. Height was measured with a portable stadiometer with an accuracy of 0.1 cm. For body mass index (BMI = weight (kg) / height (m²)), among the 15-19-year-old participants, BMI was classified according to age and sex using the cutoff points from the WHO z-score (15) as underweight (BMI for age ≤ 2 z-scores), normal weight (-2 to 1 z-scores), overweight (1 to 2 z-scores), or obese (≥ 2 SD); additionally, the BMI for adults and the elderly (older than 19 years) was categorized as underweight (< 18.5 kg/m²), normal weight (18.5-24.9 kg/m²), overweight (25-29.9 kg/m²), or obese (≥ 30.0 kg/m²) (14).

DIETARY ASSESSMENT

Dietary intake was obtained by trained interviewers from two face-to-face 24-hour dietary recalls (R24H) following the Multiple Pass Method (MSM) (16) on two nonconsecutive days. The R24H provided detailed information on all foods and beverages,

including water and alcoholic beverages, recipes, and supplements consumed. Reported intakes were quantified using a photographic album containing the most common household utensils and size portions adapted to each country. This information was transformed into grams and milliliters of food by trained nutritionists, and the data obtained were converted into energy using the Nutrition Data System for Research software (NDS-R version 2013) (10). Trained dietitians in each country performed a standardization procedure for food matching using the NDS-R software, developed by the Nutrition Coordinating Center of the University of Minnesota.

Usual water intake and energy from foods and beverages was determined using the multiple source method (MSM) (<http://msm.dife.de/>), a web-based tool developed by the European Prospective Investigation into Cancer and Nutrition (EPIC) to estimate the usual intake of nutrients, foods (beverages) and energy consumed by the participants. The MSM technique is used to convert individual intakes from the R24H to usual intake distributions (17).

The beverage consumption records included information on the type of fluid consumed and the volume of the intake. Age and sex recommendations for adequate TWI according to the IOM were taken to assess compliance with the TWI. The reference values were 3.7 L/day for adult men and 2.7 L/day for adult women and 3.3 L/day for boys and 2.3 L for girls (3,12,18). Energy intake included total sugars, comprising both intrinsic and added sugars, as sweetened beverages contribute to this nutrient.

The types of beverages were classified into four groups according to the categories proposed by the USDA and their respective subgroups (19): 1. Milk and dairy; 2. Nonalcoholic beverages (which were separated into commercial and homemade beverages); 3. Alcoholic beverages; 4. Water (Table I). The TWI was defined as the sum of all the categories. The amount of water in the reported fluids was given in grams.

Table I. Beverage classification according to the United States Department of Agriculture (USDA)

Group	Subgroup
Milk and dairy	Milk
	Flavored milk
	Dairy drinks and substitutes
	Yogurt
Nonalcoholic beverages	Commercial diet beverages
	Home-made beverages without sugar
	Sweetened commercial beverages
	Sweetened homemade beverages
	Coffee and tea
Alcoholic beverages	
Water	Plain water
	Flavored or enhanced water

USDA.

STATISTICAL ANALYSIS

The data were analyzed using the Statistical Package for Social Science (SPSS) software (version 22.0). For categorical variables, the data are reported as frequencies (i.e., percentages), and comparisons were made through the chi-square test. For continuous variables, the Kolmogorov-Smirnov test was used to evaluate the normality of the distribution. Given that the TWI was not normally distributed, we performed nonparametric tests (e.g., Mann-Whitney or Kruskal-Wallis tests). The descriptive statistics are presented as the mean, median, standard deviation. A p -value < 0.05 was considered to indicate statistical significance.

RESULTS

The TWI from food and type of beverages consumed were analyzed for 5977 ELANS participants, including 52.7 % female individuals aged 15-65 years and from the urban population of five Latin American countries (Argentina, Brazil; Costa Rica, Ecuador; and Perú). Overall, 89 % of the participants were in the middle- and low-income brackets. More than one-third of the participants (37.1 %) were normal in weight, and 59.5 % were overweight or obese (Table II).

Overall, the mean energy intake from the five countries included in this study was 2045 kcal/day: the average was highest in Ecuador (2213 kcal/day), followed by that in Argentina (2181 kcal/day), that in Peru (2111 kcal/day), and that in Costa Rica (1886 kcal/day); the lowest average was in Brazil (1835 kcal/day). The median TWI in the overall sample was 3245.6 g/day. Residents from Argentina (4018.4 g/d), males (3619.3 g/d), and adults (3262.9 g/d) reported a significantly higher TWI. The median water intake from beverages was 1982.9 g/d, which represented 61 % of the participants' total fluid intake, ranging from 89.3 % in Brazil to 63.8 % in Ecuador. The energy intake from beverages for the overall sample represented 23.4 % of the total energy intake. This percentage varies significantly among countries and between sexes, as shown in Table II. The results for compliance with the TWI recommendations according to the sociodemographic characteristics of the sample are shown in table III. In general, 63.8 % of the overall sample, 68.1 % of the men, and 60.0 % of the women consumed adequate amounts of water, as did 59.1 % of the adolescents and 64.2 % of the adults. Additionally, participants in the middle SEL who were overweight or obese had higher compliance than did those in the other subgroups. Compliance with daily water intake recommendations also varies among countries, ranging from 42.8 % in Brazil to 84.4 % in Argentina.

Differences among sex and age by country are shown in figures 1 and 2. A higher percentage of adolescent females were compliant (71.4 % vs 50.6 %, $p < 0.001$). In contrast, adult males had a higher percentage of compliance (69.9 % vs 59.3 %, $p < 0.001$).

The contribution of water from the different groups of beverages included 38.4 % of the total water intake from plain water, followed by coffee and tea (16.9 %), commercial sugar-sweetened beverages (13.7 %), and homemade SSB (11.7 %) (Table IV). The contribution of plain water to total water intake varies among countries, with

Costa Rica (51.0 %) and Brazil (50.4 %) showing the highest percentage and Peru (22.4 %) the lowest. Other significant differences were observed among commercial sugar-sweetened beverages (SSB), where Argentina (14.9 %) reported the highest consumption and Costa Rica (11.4 %) the lowest, and from homemade SSB, Peru showed the highest percentage (31.7 %) and Brazil the lowest (0.7 %). Brazil had the highest percentage of water intake from alcoholic beverages (13.1 %), and Argentina had the highest intake of coffee and tea (29.3 %). The contribution of plain water to total water intake was higher for women (38.5 % vs 37.5 %) and adolescents (39.4 % vs 38.2 %) in the overall sample and in every country, except in Peru, where the percentage of plain water was higher for adults than for adolescents.

Due to the nutritional composition, each beverage group exhibited a different contribution to total energy intake (TEI). Commercial sugar-sweetened beverages had the highest contribution to TEI in all the countries except for Peru, where homemade sugar-sweetened beverages were the contributors. The highest contributors to energy from beverages were coffee and tea (16.9 %), commercial SSB (13.7 %), homemade SSB (11.7 %), dairy drinks and substitutes (5.7 %), and alcoholic beverages (7.2 %). The contribution of alcoholic beverages to TEI was higher in Brazil than in other regions and, in males and adults, for the overall sample and for every country. Other variations among countries, sexes, and age groups are detailed in table V.

DISCUSSION

In the last decade, there has been a significant increase in the analysis of total water intake (TWI) and the hydration profile within the population. This increase is driven by the recognition of the vital role these factors play in sustaining both physical and mental functions. However, the consumption of sugar-sweetened beverages has been linked to a range of health issues, including obesity and a heightened risk of noncommunicable diseases. Consequently, having access to comprehensive data on fluid intake is invaluable for the formulation of effective public health policies and the development of health programs (13,20,21).

Multiple methods have been employed to assess water intake, including smart bottles and wrist-based sensor systems, but practical limitations have prompted the development of more accurate techniques, such as wireless surface electromyography (sEMG) (22). Nevertheless, the R24H repeated in cross-sectional studies has been considered a valuable approach to collecting data on fluid intake, including tap water (23). However, this method has limitations, as it has been observed that as age increases, the population tends to underreport the consumption of sugary beverages (21). Also, the R24H was primarily designed to assess food intake and does not adequately account for fluid consumption outside of meals. In this context, underestimations of up to 500 ml/day have been previously reported (24). This study revealed an apparent underreporting situation, particularly among individuals with low body weight who had lower fluid consumption and those with normal weight and obesity who had higher TWI values.

Table II. The demographic characteristics included total water intake, water intake from beverages, and percentage of energy intake from beverages relative to total energy intake

Variables	n	%	Total water intake (g/d)			Water intake from beverages (g/d)			Percentage of energy from beverages to total energy intake (%)		
			Mean (DS)	Median (P25-P75)	p-value*	Mean (DS)	Median (P25-P75)	p-value*	Mean (DS)	Median (P25-P75)	p-value*
Total	5977	100	3513.8 (2773.1)	3245.6 (2470.5-4192.3)		2572.6 (2707.8)	1982.9 (1284.1-2888.4)		27.1 (19.4)	23.4 (14.5-35.4)	
Country											
Argentina	1266	21.2	4376.1 (5179.8)	4018.4 (3208.9-5009.2)		3559.3 (5154.7)	3202.7 (2410.7-4135.6)		29.7 (19.0)	26.4 (19.2-38.4)	
Brazil	2000	33.5	2922.9 (1578.4)	2067.5 (1894.1-3491.2)		2162.8 (1478.4)	1847.1 (1214.7-2671.2)		26.3 (22.4)	21.2 (12.3-34.0)	
Costa Rica	798	13.3	3465.3 (1488.7)	3141.2 (2540.5-4043.2)	< 0.001	2497.9 (1307.1)	2192.3 (1677.0-2996.8)	< 0.001	23.4 (17.8)	21.2 (11.4-31.9)	< 0.001
Ecuador	800	13.4	3619.9 (1501.8)	3413.1 (2844.7-4080.3)		2395.8 (1348.4)	2180.3 (1752.7-2760.2)		21.7 (15.8)	19.2 (12.5-27.3)	
Peru	1113	18.6	3556.3 (1275.5)	3312.0 (2700.1-4135.5)		2369.6 (1113.3)	2129.9 (1634.4-2876.6)		31.5 (15.5)	29.1 (20.3-40.2)	
Sex											
Male	28.29	47.3	3955.5 (3735.1)	3619.3 (2793.3-4665.9)	< 0.001	2924.8 (3687.3)	2540.3 (1845.8-3532.1)		29.2 (21.2)	25.3 (15.1-38.0)	< 0.001
Female	31.48	52.7	3117.9 (1316.1)	2937.7 (2232.4-3764.9)		2257.0 (1222.6)	2039.5 (1466.3-2792.9)		25.1 (17.3)	21.9 (14.0-33.1)	
Age group											
15 to 17.9	445	7.5	3224.2 (1185.2)	3095.6 (2392.0-3920.4)	< 0.050	2279.7 (1055.5)	2106.0 (1559.9-2857.4)		26.0 (14.1)	24.1 (15.4-34.5)	0.235
18 to 65	5532	92.5	3537.7 (2861.4)	3262.9 (2478.9-4214.0)		2596.6 (2797.4)	2271.3 (1619.0-3184.0)		27.1 (19.7)	23.4 (14.4-35.4)	
Socioeconomic level											
Low	2726	45.6	3500.6 (3746.2)	3195.3 (2387.1-4133.7)	0.350	2578.7 (3700.8)	2188.0 (1558.0-3168.2)		26.8 (21.0)	22.5 (13.5-35.0)	
Middle	2580	43.2	3507.3 (1572.5)	3265.7 (2500.0-4216.0)		2567.3 (1450.4)	2305.9 (1662.2-3143.3)	0.984	27.0 (18.1)	23.8 (14.8-35.4)	0.165
High	671	11.2	3597.7 (1406.1)	3351.1 (2607.9-4307.9)		2572.5 (1264.7)	2282.0 (1678.9-3141.4)		28.4 (16.7)	25.3 (16.5-36.8)	
Body mass index											
Underweight	203	3.4	3136.9 (1246.3)	3032.1 (2148.9-3919.7)	0.231	2153.6 (1131.0)	2029.3 (1350.3-2725.4)		25.0 (17.3)	21.5 (13.3-33.0)	
Normal weight	2211	37.1	3555.0 (4061.2)	3256.4 (2461.4-4215.4)		2595.2 (4008.2)	2250.5 (1616.0-3122.0)	0.148	27.4 (19.3)	24.0 (15.0-35.6)	0.211
Overweight/Obese	3547	59.5	3510.9 (1606.7)	3252.8 (2485.7-4206.3)		2586.2 (1505.1)	2286.4 (1638.2-3195.7)		26.9 (19.6)	22.9 (14.2-35.2)	

*Mann-Whitney and Kruskal-Wallis tests for comparisons between groups. BMI: body mass index. BMI was classified based on WHO specifications.

Table III. Water intake recommendation compliance by sociodemographic characteristics of the sample (n [%])

Variables	Inadequate consumption	Adequate consumption	p-value*
Overall sample	2161 (36.2)	3817 (63.8)	
<i>Sex</i>			
Male	902 (31.8)	1927 (68.1)	< 0.001
Female	1259 (39.9)	1889 (60.0)	
<i>Age group</i>			
15-17.9 years	182 (40.9)	263 (59.1)	< 0.050
18-65 years	1979 (35.7)	35537 (64.2)	
<i>Country</i>			
Argentina	197 (15.6)	1068 (84.4)	< 0.001
Brazil	1145 (57.2)	855 (42.8)	
Costa Rica	297 (37.2)	501 (62.7)	
Ecuador	199 (24.9)	601 (75.1)	
Peru	323 (29.0)	790 (71.0)	
<i>Socioeconomic level</i>			
Low	1032 (37.9)	1694 (62.1)	< 0.010
Middle	921 (35.7)	1659 (64.3)	
High	208 (31.0)	463 (69.0)	
<i>Body mass index</i>			
Underweight	89 (43.8)	114 (56.2)	< 0.050
Normal weight	814 (36.8)	1397 (63.2)	
Overweight/Obesity	626.5 (35.1)	1149 (64.9)	

BMI: body mass index. BMI was classified based on WHO specifications. *p-values were determined through the χ^2 test. A value of $p < 0.05$ was considered to indicate statistical significance.

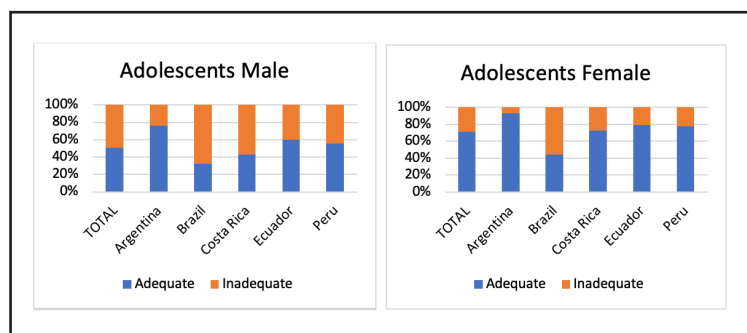


Figure 1. Distribution of those < 18 years old who compliance the water intake.

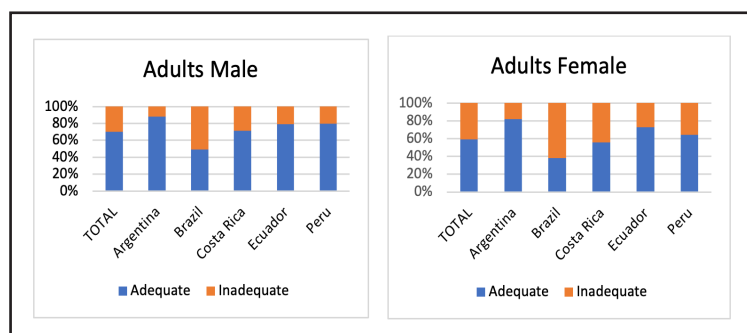


Figure 2. Distribution of those > 18 years old who compliance water intake.

Table IV. Percent contribution (%) of beverage groups to water intake

	Plain water	Flavored or enhanced water	Milk	Flavored milk	Dairy drinks and substitutes	Yogurt	100 % juice	Commercial not SSB	Homemade not SSB	Commercial SSB	Homemade SSB	Coffee and tea	Alcoholic beverages
Overall sample	38.4	2.2	3.0	0.8	1.2	0.7	1.3	0.4	2.5	13.7	11.7	16.9	7.2
Male	37.5	2.4	2.8	0.7	1.1	0.6	1.3	0.4	2.2	14.5	12.1	14.5	10.0
Female	39.8	2.0	3.3	0.9	1.3	0.9	1.2	0.4	3.0	12.1	10.6	19.9	4.5
Adolescents	39.4	1.6	3.4	1.6	1.6	1.1	1.7	0.1	2.5	19.5	13.7	13.1	0.7
Adults	38.2	2.2	3.0	0.7	1.1	0.7	1.2	0.4	2.5	13.2	11.8	17.3	7.6
Argentina	24.8	5.4	1.0	0.9	0.2	0.8	0.4	1.1	3.4	14.9	12.3	29.3	5.4
Male	22.8	5.4	0.7	1.0	0.3	0.7	0.3	1.2	2.4	17.0	16.5	23.5	8.2
Female	28.1	5.1	1.3	0.7	0.1	0.9	0.4	1.0	4.4	12.1	7.4	36.1	2.3
Adolescents	26.1	3.4	1.1	2.7	0.1	1.7	0.3	0.1	3.6	21.7	16.5	21.2	1.5
Adults	25.7	5.3	1.0	0.8	0.2	0.7	0.3	1.1	3.3	14.0	11.7	30.3	5.5
Brazil	50.4	0.3	5.2	0.3	0.3	0.7	1.8	0.1	4.1	14.6	0.7	8.3	13.1
Male	47.9	0.3	4.9	0.2	0.4	0.5	1.9	0.1	3.9	15.6	0.6	7.6	15.8
Female	50.8	0.2	5.8	0.4	0.3	0.9	1.9	0.1	4.5	14.1	0.8	9.4	10.7
Adolescents	51.5	0.1	6.9	0.4	1.1	1.1	3.2	0.2	5.4	22.9	0.7	6.0	0.5
Adults	49.5	0.3	5.2	0.3	0.3	0.7	1.8	0.1	4.1	14.3	0.7	8.5	14.1
Costa Rica	51.0	0.1	3.9	0.3	0.3	0.3	0.3	0.2	0.7	11.4	8.0	18.7	4.7
Male	50.4	0.1	3.8	0.2	0.3	0.2	0.3	0.1	0.5	11.9	8.7	16.5	7.1
Female	53.6	0.1	4.0	0.3	0.3	0.4	0.4	0.3	0.9	10.5	6.8	21.0	1.5
Adolescents	54.8	0.0	4.2	0.6	0.2	0.2	0.1	0.0	0.8	18.6	7.1	13.3	0.2
Adults	51.5	0.1	3.9	0.2	0.3	0.3	0.3	0.2	0.7	10.6	8.0	18.9	5.0
Ecuador	49.8	2.2	4.7	0.2	1.2	0.7	4.1	0.0	0.1	13.3	11.8	6.6	5.1
Male	48.4	2.7	4.2	0.1	1.0	0.7	4.6	0.1	0.1	15.3	10.0	5.5	7.4
Female	51.6	1.5	5.3	0.3	1.5	0.8	3.5	0.0	0.1	10.9	14.0	8.0	2.5
Adolescents	55.1	1.6	4.5	0.0	0.6	1.0	0.0	5.2	0.2	14.2	10.3	6.6	0.7
Adults	49.4	2.3	4.7	0.2	1.3	0.7	4.0	0.1	0.1	13.2	11.9	6.6	5.5
Peru	22.4	1.7	0.8	2.3	4.8	0.9	0.5	0.0	1.7	11.6	31.7	16.1	5.4
Male	22.1	2.3	0.7	1.6	4.3	0.8	0.5	0.0	2.0	12.5	31.1	14.0	8.2
Female	22.8	0.9	1.0	3.1	5.3	1.2	0.5	0.0	1.4	10.6	32.6	18.6	2.0
Adolescents	20.0	2.3	1.0	3.2	6.1	1.1	0.4	0.0	0.6	16.7	33.1	15.3	0.2
Adults	22.6	1.6	0.8	2.2	4.7	0.9	0.5	0.0	1.8	11.2	31.6	16.2	5.8

SSB: sugar-sweetened beverages.

Table V. Percent contribution (%) of beverage groups to total energy intake

	Plain water	Flavored or enhanced water	Milk	Flavored milk	Dairy drinks and substitutes	Yogurt	100 % juice	Commercial not SSB	Homemade not SSB	Commercial SSB	Homemade SSB	Coffee and tea	Alcoholic beverages
<i>Overall sample</i>	0.0	1.4	11.3	4.5	3.8	3.4	2.9	0.0	1.2	29.9	14.3	10.5	16.7
Male	0.0	1.5	9.6	3.7	3.3	2.6	2.8	0.0	1.0	31.1	13.8	8.7	21.9
Female	0.0	1.3	13.1	5.3	4.3	4.3	3.0	0.0	1.5	28.7	14.8	12.4	11.3
Adolescents	0.0	1.2	11.2	7.5	4.3	4.5	3.2	0.0	1.2	38.3	15.9	10.7	2.0
Adults	0.0	1.5	11.3	4.2	3.7	3.3	2.9	0.0	1.2	29.3	14.2	10.5	17.8
<i>Argentina</i>	0.0	4.4	3.8	4.3	1.4	4.5	1.0	0.1	0.5	31.2	5.5	26.8	16.6
Male	0.0	3.9	2.5	4.3	1.6	3.5	0.7	0.1	0.3	33.0	5.7	21.0	23.4
Female	0.0	4.8	5.2	4.3	1.2	5.6	1.4	0.1	0.7	29.4	5.2	33.0	9.3
Adolescents	0.0	2.8	3.5	10.9	0.6	7.7	0.6	0.0	0.4	39.1	7.2	23.7	3.6
Adults	0.0	4.5	3.8	3.8	1.4	4.3	1.0	0.1	0.5	30.7	5.3	27.0	17.5
<i>Brazil</i>	0.0	0.2	19.1	4.9	1.2	3.0	4.3	0.0	2.9	36.3	0.8	0.7	26.6
Male	0.0	0.3	16.4	4.2	1.1	2.0	4.2	0.0	2.5	36.6	0.6	0.7	31.6
Female	0.0	0.1	21.8	5.6	1.2	4.1	4.5	0.0	3.3	36.0	1.0	0.7	21.7
Adolescents	0.0	0.0	21.2	8.6	3.8	3.9	6.0	0.0	3.6	48.4	0.9	0.5	3.1
Adults	0.0	0.2	18.9	4.6	1.0	3.0	4.2	0.0	2.8	35.6	0.8	0.7	28.1
<i>Costa Rica</i>	0.0	0.2	14.4	2.6	1.4	1.4	0.7	0.0	0.9	31.1	27.9	7.7	11.8
Male	0.0	0.2	12.7	2.2	1.1	0.8	0.6	0.0	0.8	29.6	28.8	6.3	17.0
Female	0.0	0.2	16.4	3.0	1.9	2.2	0.9	0.1	0.9	33.0	26.7	9.3	5.4
Adolescents	0.0	0.0	14.6	4.6	0.9	0.9	0.1	0.0	0.4	44.2	22.6	11.3	0.4
Adults	0.0	0.2	14.3	2.4	1.5	1.5	0.8	0.0	0.9	29.9	28.4	7.3	12.8
<i>Ecuador</i>	0.0	0.8	16.2	1.1	4.8	4.0	9.4	0.0	0.1	31.3	20.2	2.6	9.4
Male	0.0	1.2	13.4	0.7	3.3	3.7	10.1	0.0	0.1	35.7	15.6	2.5	13.7
Female	0.0	0.5	19.3	1.6	6.4	4.4	8.6	0.0	0.1	26.5	25.3	2.7	4.6
Adolescents	0.0	1.4	16.1	0.4	2.2	6.0	12.2	0.0	0.4	39.0	18.6	1.9	1.8
Adults	0.0	0.8	16.2	1.2	4.9	3.9	9.2	0.0	0.1	30.8	20.4	2.7	9.9
<i>Peru</i>	0.0	1.1	3.6	6.8	11.0	3.6	0.8	0.0	0.4	17.6	33.7	13.2	8.2
Male	0.0	1.7	3.1	4.9	9.9	2.8	0.7	0.0	0.3	19.1	33.1	11.9	12.6
Female	0.0	0.6	4.2	8.8	12.1	4.4	0.8	0.0	0.4	16.1	34.2	14.5	4.0
Adolescents	0.0	1.5	3.4	8.2	10.8	3.8	0.6	0.0	0.3	23.5	34.3	13.4	0.3
Adults	0.0	1.1	3.7	6.7	11.0	3.6	0.8	0.0	0.4	17.0	33.6	13.2	9.0

SSB: sugar-sweetened beverages.

The evaluation of the population's hydration profile, encompassing both pure water and water from beverages, aligns with findings from other research in different populations (13,15,20,25). The analysis of the TWI in the population belonging to the ELANS Study, revealed a median intake of water from beverages of 1984.4 g/day, with significant variations among countries. Similar medians of approximately 1980 g/day were observed in other cross-sectional surveys conducted in Latin American, European, and Asian countries, with notable disparities between nations. For instance, Japan reported the lowest TWI at 1500 g/day, while Germany had the highest TWI at 2470 g/day. Additionally, it was determined that at least 50% of both women and men did not meet the recommended fluid intake. These variations are often attributed to data collection in different seasons, with countries experiencing hotter summers expected to have higher fluid consumption. In this context, it is essential to consider other factors influencing liquid intake, such as weather, daily physical activity and dietary habits. (24,26) Factors such as age, sex, physical activity, drug consumption in some cases, energy intake, and environmental factors such as temperature and humidity may affect water needs, as mentioned by Laja et al. Therefore, personalized TWI recommendations should be considered if feasible (5).

The median TWI exhibited significant differences between sex and age groups, being significantly lower in women than in men, consistent with findings from various global studies (5,21,24,27,28). This underscores the role of social and academic factors, including education, in fluid consumption, as developed countries tend to exhibit healthier lifestyles, particularly among women (29). In recent years, it has been shown that up to 89.7 % of young people do not meet the daily recommendations for fluid intake (30), which is reflected in the results found the study. In addition, the results obtained can be taken as a pre-pandemic baseline considering that during the pandemic, the interruption in normal academic routines, such as the suspension of face-to-face classes, caused changes in fluid intake behavior, in particular an increase in alcohol consumption among adolescent and young adult students (31).

Pure water accounted for 36 % of the TWI, while the other fluid intake came from nonalcoholic beverages, followed by alcoholic beverages and milk and dairy products. Similar patterns in terms of the contribution of pure water to the TWI and the consumption of other beverages were observed in studies conducted among the adult population, consistent with the present study (13,25,27). Notably, alcoholic beverages contribute energetically but not to hydration, suggesting that they are consumed (5). The patterns found reflect similarities with observations from studies conducted among adult populations, where the contribution of pure water to the TWI was 33 %. Furthermore, the consumption of other beverages closely paralleled the findings obtained in the present study (13,27,32).

When categorizing the sample by BMI, it was observed that subjects with a normal weight and those with overweight or obesity had similar TWIs, unlike the findings of previous research showing that water consumption is greater in adults with higher

BMI, which may be due to the limited amount of data (25). For decades, the sources of TWI and their associations with nutritional status have been researched. Notably, water consumption tends to be relatively low compared to the substantial contributions of other sources, including alcoholic and nonalcoholic beverages, which have been empirically linked to adverse health outcomes. The importance of dairy beverages as valuable sources of essential nutrients is highlighted in the studies conducted by Daniels and Popkin (2010) and O'Connor et al. (2014) (27,33).

A systematic review by Mukelbauer et al. noted that overweight and obese people tend to consume more water than their normal-weight counterparts do; however, it is important to note that Mukelbauer et al.'s review did not explicitly look at TWI (34). The elevated intake of plain water reported among overweight and obese individuals suggests a potential strategy for managing weight through increased fluid intake, as supported by previous research (32). Although Laja et al. also reported inverse associations between water consumption and body weight, body fat mass and waist circumference (5), the analysis of water consumption from pure water and other beverages is important. In our study, the youngest individuals exhibited the lowest level of fluid consumption, and those with a normal weight profile exhibited the highest levels of fluid consumption. Interestingly, the greatest contribution to energy intake from beverages was observed among participants with normal body weights. Furthermore, our study revealed notable disparities in both water and energy consumption patterns across different countries. Specifically, the median energy intake from beverages was calculated at 280.3 kcal/day, particularly in Latin American countries where the consumption of soft-sweetened beverages (SSB) and juices is notably high, representing a significant contribution to TWI (26), and underscoring the fact that the consumption of SSB significantly contributes to overall energy intake, consistent with prior research (21,35).

Fluid intake recommendations should be tailored to an individual's body mass. Typically, individuals with a normal weight tend to better meet their daily fluid needs, particularly women. Various authors have indicated that there is no substantial relationship between body mass index (BMI) and fluid consumption. However, there is evidence to suggest that BMI can influence factors such as body weight, body fat, and waist circumference normalization (5,28). Moreover, research has shown that substituting other beverages with water may promote weight loss in populations dealing with overweight and obesity (36). The meta-analysis by Chen et al. (2024) suggests that while water intake may not significantly affect adiposity in overweight and obese individuals (37). This aligns with our study, where overweight and obese subjects consume more water. However, replacing sugar-sweetened beverages with water could provide modest benefits for weight loss.

Adherence to adequate water intake from beverages, as per the recommendations set by the Institute of Medicine (IOM), exhibits notable variations between countries. Notably, half of the adolescents and less than half of the adult males met the recommendations, whereas half of the adolescent and adult females did. It becomes clear that the TWI shows a decreasing trend with advancing age. Furthermore, in international studies conducted

across diverse regions, comparing fluid intake with recommendations, women consistently exhibit a greater likelihood of meeting adequate intake levels (24,38,39).

Fernández et al. highlighted a higher dairy consumption among children, probably due to constant encouragement from parents, and as people age, dairy consumption tends to decrease, giving way to hot beverages such as tea and coffee, as well as sugar-sweetened beverages. Despite these changes reported, we highlight that a significant percentage of adolescents do not meet the daily requirements of TWI, so we emphasize the importance of promoting proper hydration, given its influence on nutritional status (40).

The insights gleaned from this study underscore the critical need for a balanced and mindful approach to fluid consumption. This emphasizes the crucial importance of promoting increased pure water consumption to potentially mitigate dehydration-associated risks within the population.

CONCLUSIONS

Significant disparities in total fluid intake from beverages and water are readily observed across diverse countries, age cohorts, and nutritional conditions. Remarkably, these disparities do not exhibit any notable correlation with sex or socioeconomic determinants. Substantially, both adult and adolescent populations are susceptible to insufficient water intake related to the recommended water intake levels prescribed by the Institute of Medicine (IOM).

After analyzing the discrepancies based on sex, it becomes apparent that men, regardless of age group, fall shorter than their female counterparts in regard to reaching the recommended water intake. This emphasizes the urgency for further research to explore the potential health implications of inadequate TWI, as it elevates the risk of dehydration.

Recognizing the significance of having comprehensive fluid intake data gathered from population surveys, it becomes apparent that this information is invaluable for the formulation of evidence-based public health policies. In addition, this study provides a basis for the development of specific health programs designed to address these multifaceted concerns. Considering these findings, it is essential to establish region-specific initiatives and strategies within Latin America aimed at promoting water intake through appropriate hydration programs and promoting strong and ongoing hydration education campaigns. In doing so, Latin American nations can effectively address not only the pressing issues of overweightness and obesity and their metabolic consequences but also the prevailing challenges associated with sugary drink consumption and inadequate intake of pure water in the urban population.

STRENGTHS AND LIMITATIONS

This research has both strengths and limitations that warrant consideration when interpreting its outcomes. Among its

strengths, the use of a 24-hour recall method for food intake data collection is notable, as this approach is generally regarded as more precise than the food frequency questionnaires typically employed in studies with similar objectives. Moreover, the study benefits from a substantial sample size, which enables more accurate mean value calculations, the identification of potential outliers that could distort data in smaller samples, and a reduction in the margin of error.

However, certain limitations must be recognized. First, the data were collected before the onset of the SARS-CoV-2 pandemic, which could mean that the study results reflect a different state of total water intake. Along with the post pandemic periods, the pandemic may have further altered water consumption patterns through economic and social factors.

Second, the study's geographical scope was confined to urban areas within five Latin American countries, which excludes rural regions and other nations within the region. Consequently, the findings should not be broadly generalized to encompass all Latin American areas.

In addition, this study focused mainly on analyzing the hydration profile, covering both pure water and water derived from beverages. This approach does not improve the assessment of water intake from other food sources, as has been explored in other related studies.

Moreover, the study did not consider potential climatic variations in the countries under investigation, which could have influenced the results. Furthermore, the assessment of total water and fluid intake, conducted using the 24-hour recall method, may be associated with both insufficient and excessive consumption of various beverage types. Future research should contemplate the utilization of alternative assessment instruments, such as a 7-day fluid record, which is renowned for its heightened sensitivity in capturing fluid intake patterns.

Last, it is worth noting that Bardosono et al. have raised concerns regarding potential errors in calculating water intake based on the R24H method. While this method typically provides adequate estimations of energy and macronutrient intake, it tends to significantly underestimate absolute beverage intake in adolescents and adults when compared to a 7-day dietary record.

AUTHORS' CONTRIBUTION

Conceptualization, M. C. Y. G.; M. V., M. J. M.; R. Y.; formal analysis, G. G., R. Y.; investigation I. K., G. G., M. C. Y. G.; R. G. P.; M. F.; funding acquisition, M. F., I. K.; writing review and editing: M. C. Y. G., M. V., G. G., M. J. M., R. Y., D. A. All the authors have read and agreed to the published version of the manuscript.

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INSTITUTIONAL REVIEW BOARD STATEMENT

Ethical approval was provided by the Western Institutional Review Board (#20140605) and by the ethical review boards of the participating institutions. ELANS is registered at Clinical Trials #NCT02226627.

INFORMED CONSENT STATEMENT

Written informed consent/assent was obtained from all individuals before commencement of the study.

Data availability statement: the datasets generated and/or analyzed during the current study are not publicly available due to the use of consent/assent to which the participants agreed but are available from the corresponding author upon reasonable request. Please contact the corresponding author to discuss the availability of the data and materials.

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Otros

Trabajo Original

Relación entre el consumo de suplementos deportivos y la adicción al deporte en corredores de asfalto y montaña

Relationship between consumption of sports supplements and addiction to sport in road and mountain runners

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Resumen

Introducción: habitualmente, los corredores de asfalto y montaña utilizan la nutrición y suplementación deportiva (SD) para conseguir sus objetivos y mayor rendimiento. No obstante, en ocasiones, la práctica deportiva puede convertirse en una obsesión y/o adicción, aunque la literatura sobre el uso de la SD y la adicción al deporte (AD) es escasa.

Objetivo: describir y analizar la relación entre el consumo de SD y la AD en corredores de asfalto y montaña de Canarias.

Metodología: estudio observacional transversal en una muestra de 613 deportistas adultos mediante un cuestionario *online* autoadministrado que evaluó el consumo de SD y la AD, difundido por las federaciones, clubs deportivos, organizadores de carreras y redes sociales.

Resultados: un 75,7 % de los participantes declaró tomar algún tipo de SD y tener menor edad se relacionó con una mayor probabilidad de tomar SD. En la escala total de AD (SAS-15), la media fue de 9.19 (DT = 3,24), situándose por encima del punto medio del rango teórico (0-15). Entre los participantes que toman y no toman SD existe mayor AD en los que la toman frente a los que no; y entre los que toman SD, la AD es significativamente mayor en los que toman recuperadores y suplementos para el control de peso.

Conclusiones: la muestra presentó indicadores de AD y, en su mayoría, consumían algún tipo de SD. Además, existe una relación significativa entre el uso de SD y la AD en corredores de asfalto y montaña, siendo el nivel de AD un predictor del consumo de SD.

Palabras clave:

Suplementos deportivos.
Adicción al deporte.
Corredores de montaña.
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Abstract

Introduction: sports nutrition and supplementation (SD) are commonly used by road and mountain runners to achieve their goals and increased performance. However, sometimes sports practice can become an obsession and/or addiction, although the literature on the use of DS and sports addiction (SD) is scarce.

Objective: to describe and analyse the relationship between SD use and AD in asphalt and mountain runners in the Canary Islands.

Methodology: a cross-sectional observational study in a sample of 613 adult athletes, using a self-administered online questionnaire that assessed SD use and AD, disseminated by federations, sports clubs, race organisers and social networks.

Results: 75.7 % of participants reported taking some form of SD and being younger was associated with a higher likelihood of taking SD. On the total SD scale (SAS-15) the mean was 9.19 (SD = 3.24), above the midpoint of the theoretical range (0-15). Among participants taking and not taking DS, there is higher AD in those taking versus those not; and among those taking DS, AD is significantly higher in those taking weight management recoverers and supplements.

Conclusions: the sample had indicators of WD and, for the most part, were consuming some form of DS. In addition, there is a significant relationship between the use of DS and WD in road and mountain runners, with the level of WD being a predictor of DS consumption.

Keywords:

Sports supplements.
Sports addiction. Mountain runners. Road runners. Sports. Nutrition.

INTRODUCCIÓN

La práctica deportiva está reconocida como una actividad que beneficia la salud física, psicológica y social de las personas que la realizan (1). En este sentido, la práctica de actividades como las carreras de asfalto y de montaña ha experimentado un auge en popularidad en los últimos años debido a los beneficios que aportan, como el mantenimiento y mejora de la salud, el contacto con la naturaleza y la emoción competitiva que ofrecen (2). La práctica de estos deportes, aunque inicialmente puede ser saludable y beneficiosa, puede volverse perjudicial cuando se convierte en excesiva y adictiva. Aunque las clasificaciones médicas como la Clasificación Internacional de Enfermedades (CIE-11) o el Manual Diagnóstico y Estadístico de los Trastornos Mentales 5 (DSM-5) no incluyen la adicción al ejercicio como un trastorno clínico, puede considerarse una adicción conductual (3). La dependencia del ejercicio se asemeja a otras adicciones, con la aparición de síntomas similares, como cambios en el estado de ánimo, síntomas de abstinencia, conflicto y recaídas. Esta adicción al ejercicio se caracteriza por la incapacidad de los corredores para controlar su dedicación extrema y por la falta de conocimientos necesarios para llevar a cabo estas prácticas de manera saludable (2,4). Muchas personas que experimentan esta adicción al ejercicio buscan la satisfacción que les proporciona la actividad física, sin tener en cuenta las posibles consecuencias negativas. Dado que el ejercicio es ampliamente aceptado socialmente como una actividad saludable, puede ser difícil para quienes están en riesgo de desarrollar esta adicción reconocer y aceptar que la práctica excesiva de correr en asfalto y montaña puede convertirse en una adicción (5).

Los deportes de resistencia, como las carreras de asfalto y montaña, son especialmente propensos a desencadenar esta adicción. Un factor influyente es lo que se conoce como el "subidón del corredor", que se refiere a las intensas emociones y sensaciones que experimentan los corredores antes, durante y después de una carrera. Estas emociones pueden ser similares a los efectos que las personas adictas a sustancias experimentan con sus consumos (6,7).

Habitualmente, los deportistas hacen uso de la nutrición y de la suplementación deportiva (SD) con el fin alcanzar sus objetivos y obtener un mayor rendimiento deportivo (8). Un SD se podría definir como un alimento, componente, nutriente o compuesto no

alimenticio que se ingiere de manera intencionada en la dieta habitual con el objetivo de lograr un beneficio específico de salud y/o rendimiento; es un producto que tiene un cierto aporte nutricional y que los deportistas consumen como complemento a la dieta habitual (9,10). Por tanto, está considerado como una ayuda ergogénica, definida como aquella sustancia que mejora el rendimiento, permitiendo a quien las consume realizar mejor un trabajo físico del que sería capaz de realizar sin ellas (9). En la actualidad, tanto los atletas profesionales como los recreativos toman la decisión de hacer uso de este tipo de ayudas. La toma de SD que antes se limitaba a los atletas de élite, ahora también se extiende a los atletas amateur y a los deportistas aficionados de todas las edades, convirtiéndose en ocasiones en un problema de salud pública (11). En los últimos años, se ha registrado un aumento de la prevalencia del consumo de la SD entre quienes realizan actividades físicas y, de modo específico, carreras de asfalto y de montaña (12). No obstante, los corredores y, en ocasiones, los propios entrenadores no siempre tienen el conocimiento necesario sobre cómo implementar estas pautas nutricionales saludables y equilibradas, así como los principios básicos del uso y consumo de la SD (13). Para ello el Instituto Australiano del deporte ha desarrollado el sistema de clasificación de alimentos y de SD, dividido en cuatro grupos (ABCD), basado en la evidencia científica, con el fin de servir de base para que los profesionales de la salud y los propios deportistas se puedan asesorar en este sentido (14,15).

La investigación sobre adicción al deporte y toma de suplementos deportivos es muy escasa a nivel internacional, por lo que este estudio plantea un primer acercamiento en nuestro país, con el objetivo de conocer los niveles de adicción al deporte y la toma de SD en una muestra de corredores de asfalto/montaña, así como la relación entre ambos fenómenos y sus correlatos sociodemográficos y relacionados con la práctica deportiva.

MATERIAL Y MÉTODOS

TIPO DE ESTUDIO

Se trata de un estudio observacional transversal en el que se evaluó la AD y el consumo de SD en corredores de asfalto y/o montaña de las Islas Canarias, España.

PARTICIPANTES

Se incluyeron personas adultas que durante los últimos 5 años hayan participado en carreras de asfalto y/o montaña de al menos 5 km (federados o no), y no se hayan retirado de dicha práctica deportiva.

INSTRUMENTOS

Las variables se recogieron en un cuestionario autoadministrado online, que incluye: 1) datos sociodemográficos e histórico-deportivos; 2) Escala de Adicción al Deporte SAS-15 (Sport Addiction Scale-15): cuestionario de 15 ítems con respuesta sí/no, que se distribuyen en 5 subescalas (i.e., dependencia, falta de control, pérdida de interés, continuidad y preocupación) (1); 3) Consumo de SD: uso de SD (estimulantes, potenciadores del rendimiento, control de peso, recuperadores); lleva control por parte de un especialista (sí/no); se asegura de que los productos que consumen certifiquen que no incluyen sustancias prohibidas (sí/no).

PROCEDIMIENTO

Para seleccionar la muestra del estudio, se contactó vía correo electrónico con las distintas federaciones provinciales (Santa Cruz de Tenerife y Las Palmas de Gran Canaria) y organizadores de la carreras (es decir, Maratón del Meridiano en El Hierro, Trial de Guía de Isora en Tenerife, Transgrancanaria en Las Palmas de Gran Canaria, otras) para informarles de las características del estudio y solicitar su colaboración. Tras aceptar participar, las federaciones y organizadores enviaron un correo electrónico con el enlace al cuestionario a todos los participantes para que los deportistas pudieran completarlo de forma voluntaria, anónima y cuando les resultase más conveniente. Además se facilitó este enlace mediante las redes sociales y conseguir así un efecto bola de nieve. El protocolo cumplió con la Declaración de Helsinki para la investigación en humanos y fue aprobado por el Comité Ético de la Universidad Isabel I (Expediente 1413-22).

ANÁLISIS ESTADÍSTICO

Se utilizó el programa estadístico IBM SPSS Statistics (Statistical Package for the Social Sciences) versión 27.0. Se calcularon los estadísticos descriptivos (medias, desviaciones típicas, porcentajes) para todas las variables. Las diferencias entre sujetos con valores perdidos en el SAS-15 y los casos válidos se analizaron mediante el test t de Student para muestras independientes (variables continuas) y el test chi cuadrado para las variables categóricas. Para posteriores análisis, las siguientes variables fueron dicotomizadas: nivel educativo (primaria/secundaria vs. estudios superiores), estado civil (casado/en pareja vs. soltero/divorciado/viudo) e isla de residencia (provincia de Tenerife vs. Las Palmas).

La consistencia interna de la escala se calculó con el índice alfa de Cronbach. Para el análisis de correlatos de la escala SAS-15 y la toma de suplementos se usaron modelos de regresión múltiple lineal (SAS-15 y número de suplementos), y regresión logística para las variables sobre supervisión por parte de un especialista y certificación de ausencia de sustancias prohibidas.

RESULTADOS

Cumplimentaron el cuestionario un total de 613 participantes (75,5 % hombres), con una edad media de 42 años (DT = 9) (Tabla I). Una mayoría tiene estudios superiores (66,5 %), están casados o en pareja (63,7 %) y con hijos (55,6 %). La mayor parte de los corredores realiza carreras en montaña (53,3 %), en distancias iguales o superiores a 21 km (67,2 %). Un 16 % corre exclusivamente en asfalto. Por último, la mayor parte de la muestra no se realizaba analíticas de control, ni pruebas de esfuerzo, así como desconocían la aplicación NoDopApp.

NIVEL DE ADICCIÓN AL DEPORTE Y SUS PREDICTORES

El número de sujetos perdidos en la SAS-15 estuvo entre 97-100 (15,8-16,3 %) para las subescalas y 103 (16,8 %) para la escala total. En esta última, no hubo diferencias significativas entre perdidos y no perdidos en ninguna variable sociodemográfica o relacionada con la actividad física. En el caso del nivel de estudios recodificado en dos valores la diferencia quedó en el límite de la significación estadística ($p = 0,05$); hubo un mayor porcentaje de pérdidas en los participantes con educación secundaria o primaria (21,0 %) frente a los que poseían educación superior (14,7 %).

La escala total mostró una consistencia interna (alfa de Cronbach) de 0,75. La tabla II muestra las medias y desviaciones típicas. En la escala total la media fue de 9,19 (DT = 3,24). En todas las subescalas las medias se sitúan por encima del punto medio del rango teórico, excepto en preocupación (1,46 en un rango de 0-3).

La tabla III muestra los resultados de los modelos de regresión sobre la escala SAS-15. En la puntuación total, se asociaron significativamente con una mayor puntuación ser soltero/separado/viudo frente a casado o en pareja ($B = -0,67$, $p = 0,033$), competir en asfalto frente a trail/montaña ($B = 1,43$, $p = 0,002$), una mayor distancia de competición (B 's = 1,53-2,95, valores p entre 0,003 y $< 0,001$) y realizar pruebas de esfuerzo ($B = 0,86$, $p = 0,003$). En las subescalas, el estado civil solo fue significativo en dependencia, la especialidad solo en dependencia y pérdida de interés, y la prueba de esfuerzo solo en falta de control y preocupación. En el caso de la distancia de competición, en general los coeficientes siguieron una tendencia creciente cuanto mayor la distancia (salvo para dependencia y falta de control), aunque varias comparaciones no fueron significativas. La única variable significativa en las subescalas que no lo fue en la escala total fue la edad, que se relacionó inversamente con la falta de control ($B = -0,01$, $p = 0,024$).

Tabla I. Características sociodemográficas de los participantes

	n = 613		n = 613
Edad, <i>media (DT)</i>	41,5 (9,06)	<i>Especialidad</i>	
<i>Sexo (n = 613)</i>		Asfalto	100 (16,3 %)
Hombre	463 (75,5 %)	Trail/montaña	327 (53,3 %)
Mujer	150 (24,5 %)	Ambas	186 (30,3 %)
<i>Nivel educativo</i>		<i>Distancia</i>	
Básicos	41 (6,7 %)	5 k	67 (10,9 %)
Medios	164 (26,8 %)	10 k	133 (21,7 %)
Superiores	408 (66,5 %)	21 k	207 (33,8 %)
<i>Estado civil</i>		42 k	103 (16,8 %)
Casado	226 (36,9 %)	+ 42 k	103 (16,8 %)
Conviviente	164 (26,8 %)	<i>Análíticas (c/ 3 meses)</i>	
Divorciado(a)/separados	44 (7,2 %)	No	518 (84,5 %)
Soltero(a)	178 (29,0 %)	Sí	95 (15 %)
Viudo(a)	1 (1,1 %)	<i>NoDop_APP</i>	
<i>Tiene hijos</i>		No	591 (96,4 %)
No	272 (44,4 %)	Sí	22 (3,6 %)
Sí	341 (55,6 %)	<i>Pruebas de esfuerzo</i>	
<i>Provincia</i>		No	327 (53,3 %)
Santa Cruz de Tenerife	472 (76,9 %)	Sí	286 (46,7 %)
Las Palmas de Gran Canaria	141 (23,0 %)		

Fuente: elaboración propia.

Tabla II. Estadísticos descriptivos de la escala SAS-15

Escala (rango teórico)	n	Media (Dt)
<i>Total (0-15)</i>	510	9,19 (3,24)
Dependencia (0-3)	514	1,60 (1,06)
Falta de control (0-2)	515	1,60 (0,56)
Pérdida de interés (0-5)	515	2,97 (1,44)
Continuidad (0-2)	516	1,55 (0,71)
Preocupación (0-3)	513	1,46 (1,11)

Tabla III. Modelos de regresión sobre la escala SAS-15

	Total (n = 510)	Dependencia (n = 514)	Falta de control (n = 515)	Pérdida de interés (n = 515)	Continuidad (n = 516)	Preocupación (n = 513)
Edad	-0,02 (0,257)	-0,00 (0,885)	-0,01 (0,024)*	-0,01 (0,217)	-0,00 (0,246)	0,00 (0,915)
Mujer	-0,18 (0,595)	0,12 (0,395)	-0,06 (0,337)	0,10 (0,508)	-0,07 (0,317)	0,06 (0,614)
Estudios superiores	-0,38 (0,223)	0,17 (0,091)	0,03 (0,638)	0,25 (0,072)	0,04 (0,615)	0,01 (0,891)
Casado o en pareja	-0,67 (0,033)*	-0,25 (0,019)*	0,00 (0,983)	0,20 (0,145)	0,03 (0,676)	-0,20 (0,063)
Tiene hijos	0,18 (0,619)	0,08 (0,492)	0,04 (0,563)	0,28 (0,073)	0,05 (0,499)	0,07 (0,579)
Provincia Tenerife	-0,17 (0,632)	0,01 (0,910)	-0,07 (0,212)	0,04 (0,780)	-0,09(0,264)	0,06 (0,667)

(Continúa en página siguiente)

Tabla III (cont.). Modelos de regresión sobre la escala SAS-15

	Total (n = 510)	Dependencia (n = 514)	Falta de control (n = 515)	Pérdida de interés (n = 515)	Continuidad (n = 516)	Preocupación (n = 513)
<i>Especialidad</i>	-	-	-	-	-	-
Trail/montaña	1,43 (0,002)*	0,38 (0,014)*	0,09 (0,278)	0,62 (0,003)*	0,00 (0,991)	0,30 (0,064)
Asfalto	0,52 (0,126)	0,20 (0,069)	0,00 (0,983)	0,09 (0,553)	0,07 (0,384)	0,14 (0,213)
Ambas						
<i>Distancia</i>						
5 km	-	-	-	-	-	-
10 km	1,53 (0,005)*	0,38 (0,038)*	0,23 (0,015)*	0,40 (0,099)	0,10 (0,399)	0,33 (0,078)
21 km	1,81 (0,001)*	0,29 (0,113)	0,37 (< 0,001)*	0,60 (0,015)*	0,14 (0,259)	0,36 (0,054)
42 km	2,47 (< 0,001)*	0,33 (0,110)	0,29 (0,006)*	0,91 (0,001)*	0,18 (0,201)	0,65 (0,002)*
> 42 km	2,95 (< 0,001)*	0,40 (0,058)	0,45 (< 0,001)*	0,94 (0,001)*	0,33 (0,022)*	0,76 (0,001)*
Analítica cada 3 meses	0,13 (0,746)	0,21 (0,109)	0,03 (0,659)	0,00 (0,964)	-0,03 (0,790)	-0,29 (0,527)
Pruebas de esfuerzo	0,86 (0,003)*	0,14 (0,146)	0,16 (0,001)*	0,17 (0,085)	0,01 (0,882)	0,33 (0,001)*

Los valores son coeficientes beta no estandarizados (valor p) obtenidos en los modelos de regresión lineal múltiple. Fuente: elaboración propia.

USO DE SUPLEMENTOS Y SUS PREDICTORES

Un 75,7 % de los participantes declaró tomar algún suplemento (Tabla IV). Los suplementos más frecuentemente usados fueron los recuperadores (47,1 % sobre el total válido y 63,7 % de los que toman suplementos) y los estimulantes (43,7 % y 58,2 % respectivamente). Los potenciadores del rendimiento fueron consumidos por un tercio de la muestra, y solo un 4,8 % tomaron suplementos para el control de peso. Entre los participantes que tomaron suplementos con datos válidos sobre el número de estos (446, 96,1 %), la media fue de 3,01 (DT = 1,74) y la mediana de 3.

La tabla V muestra los predictores de la toma de suplementos. Una menor edad se relacionó con una mayor probabilidad de tomar suplementos en general (OR = 0,96, $p = 0,001$), así como, de modo específico, estimulantes (OR = 0,97, $p = 0,016$) y potenciadores (OR = 0,97, $p = 0,008$). En cuanto a la distancia, correr 42 km (frente a correr 5 km) se asociaba a la toma de suplementos en general y, en el caso de los potenciadores, los resultados fueron significativos para todas las distancias en comparación a los 5 km. Por último, realizar pruebas de esfuerzo se relacionaba significativamente con tomar suplementos en general (OR = 1,94, $p = 0,002$) y recuperadores (OR = 1,99, $p < 0,001$). No hubo otras relaciones significativas. Entre los que toman suplementos, los predictores significativos del número de estos fueron no tener hijos ($B = -0,45$, $p = 0,024$) y correr más de 42 km frente a correr 5 km ($B = 1,29$, $p = 0,001$).

Al incluir la escala SAS-15 en los modelos de regresión, no cambian los predictores significativos. La puntuación en el SAS-15 se relacionó con mayor probabilidad de tomar suplementos (OR = 1,11, $p = 0,002$), estimulantes (OR = 1,10, $p = 0,003$), potenciadores (OR = 1,09, $p = 0,008$), suplementos

para el control del peso (OR = 1,26, $p = 0,004$) y recuperadores (OR = 1,15, $p < 0,001$). En el caso del número de suplementos, al incluir la escala SAS-15 en el modelo de regresión ($n = 366$), esta se relacionó significativamente con el número de suplementos ($B = 0,12$, $p < 0,001$).

Casi dos tercios (63,1 %) de los participantes que tomaban suplementos ($n = 455$) no lo hacían bajo control de un especialista. Los predictores significativos de tomar la suplementación sin control por un especialista fueron una mayor edad (OR = 1,04, $p = 0,004$), ser hombre (OR = 0,42, $p < 0,001$), correr 5 km frente a 42 km (OR = 0,38, $p = 0,043$) y no hacerse analíticas cada tres meses (OR = 0,35, $p < 0,001$). Al incluir el SAS-15 en el modelo ($n = 373$) no se obtuvo un resultado significativo.

El 80 % de los participantes que tomaron suplementos seleccionaron solo aquellos en los que se certifica que están libres de sustancias prohibidas. Los predictores significativos de esta conducta fueron un menor nivel educativo (OR = 0,54, $p = 0,033$) y realizarse analíticas cada 3 meses (OR = 2,55, $p = 0,027$). Al incluir en el modelo el SAS-15 ($n = 373$), ninguna variable resultó significativa.

DISCUSIÓN

El estudio de investigación se enfocó en analizar la relación entre el consumo de SD y la AD en corredores de asfalto y montaña en Canarias. Se encontró que la mayoría de los participantes consumían algún tipo de SD y se observó una relación significativa entre el uso de SD (como estimulantes, potenciadores, recuperadores y suplementos de control de peso) y la AD. El nivel de AD se identificó como un predictor del consumo de SD en general y de sus subtipos.

Tabla IV. Porcentaje de participantes que toman suplementos

Tipo suplemento	Casos perdidos sobre la muestra total	n válido	n (% sobre el total válido)	% sobre los que toman suplementos
Suplementos	0 (0 %)	613	464 (75,7 %)	-
Estimulantes	14 (2,3 %)	599	262 (43,7 %)	58,2 %
Potenciadores	24 (3,9 %)	589	174 (29,5 %)	39,5 %
Recuperadores	40 (6,5 %)	573	270 (47,1 %)	63,7 %
Control del peso	33 (5,4 %)	580	28 (4,8 %)	6,5 %

Tabla V. Predictores de la toma de suplementos

	Suplementos (n = 613)	Estimulantes (n = 599)	Potenciadores (n = 589)	Recuperadores (n = 573)	Control de peso (n = 580)	N.º de suplementos (n = 443)
Edad	0,96 (0,001)*	0,97 (0,016)*	0,97 (0,008)*	0,98 (0,114)	1,01 (0,820)	-0,01 (0,604)
Mujer	0,98 (0,921)	1,07 (0,732)	0,75 (0,204)	0,95 (0,799)	0,30 (0,056)	-0,01 (0,967)
Estudios superiores	1,10 (0,655)	0,84 (0,358)	1,48 (0,063)	0,95 (0,787)	1,77 (0,219)	-0,17 (0,345)
Casado o en pareja	1,28 (0,2,63)	0,88 (0,494)	0,85 (0,428)	1,17 (0,420)	0,66 (0,355)	-0,08 (0,678)
Tiene hijos	0,98 (0,925)	0,98 (0,934)	0,85 (0,488)	0,91 (0,648)	1,34 (0,563)	-0,45 (0,024)*
Provincia Tenerife	1,15 (0,553)	0,99 (0,958)	1,12 (0,638)	1,11 (0,628)	3,57 (0,090)	-0,37 (0,068)
<i>Especialidad</i>						
Trail/montaña	-	-	-	-	-	-
Asfalto	0,76 (0,376)	0,68 (0,186)	1,68 (0,100)	1,18 (0,570)	1,20 (0,770)	0,30 (0,318)
Ambas	0,89 (0,635)	0,70 (0,085)	1,48 (0,078)	1,14 (0,512)	1,20 (0,697)	0,07 (0,710)
<i>Distancia</i>						
5 km	-	-	-	-	-	-
10 km	1,14 (0,700)	1,42 (0,301)	3,10 (0,006)*	1,55 (0,191)	1,61 (0,513)	0,57 (0,103)
21 km	1,49 (0,264)	1,21 (0,579)	2,78 (0,015)*	1,26 (0,501)	1,01 (0,988)	0,56 (0,111)
42 km	1,44 (0,006)*	2,07 (0,056)	4,32 (0,001)*	1,43 (0,648)	0,58 (0,567)	0,45 (0,238)
> 42 km	1,97 (0,120)	1,74 (0,162)	4,07 (0,003)*	1,64 (0,218)	0,91 (0,923)	1,29 (0,001)*
Analítica cada 3 meses	0,83 (0,496)	1,04 (0,881)	0,67 (0,144)	0,78 (0,304)	0,87 (0,804)	-0,18 (0,421)
Pruebas de esfuerzo	1,94 (0,002)*	1,34 (0,093)	1,20 (0,336)	1,99 (< 0,001)*	0,99 (0,989)	0,26 (0,126)

Los valores son odd ratios (OR) (valor p) obtenidos en los modelos de regresión logística múltiple excepto en N.º de suplementos (beta no estandarizados (valor p) obtenidos en los modelos de regresión lineal múltiple).

En cuanto al uso de suplementos, se observó que el 76 % de los participantes consumían algún tipo de SD, lo que se asemeja a investigaciones previas (16). En esta misma línea, se encontraron similitudes con estudios de Estados Unidos, donde un alto porcentaje de adultos reportaron consumir suplementos para obtener energía, datos que están en concordancia con los del presente estudio y otros de características similares (17,18). Además, el estudio mostró que cerca de la mitad de los deportistas consumían SD con efecto estimulante, como la cafeína, con el propósito de mejorar su rendimiento deportivo (19,20). El uso de suplementos recuperadores también era común, tanto en entrenamientos como en competiciones (21).

El consumo de suplementos potenciadores del rendimiento es más probable cuanto mayor es la distancia de la carrera (16). En

relación con el sexo, no se observaron diferencias significativas en el consumo de SD en general, aunque las mujeres tenían una mayor probabilidad de consumir suplementos para el control del peso (22).

Respecto a la edad, se observó que las personas más jóvenes tenían una mayor probabilidad de consumir SD en general, así como estimulantes y potenciadores en particular (23). No se encontró una relación significativa entre el nivel educativo y el estado civil de los participantes con el consumo de SD. Además, el estudio no encontró una relación entre el consumo de SD y la realización de analíticas cada 3 meses, aunque sí se relacionó significativamente la realización de pruebas de esfuerzo con el consumo de SD en general y de recuperadores en particular, pero no para otros tipos de suplementación, como estimulantes, potenciadores y suplementos para el control de peso (22).

En relación a la toma o no de suplementos, el presente estudio abordó varios aspectos relacionados con la toma de SD entre los participantes. Los resultados mostraron que el 88 % de los participantes consumieron suplementos recuperadores con el propósito de acelerar la recuperación después de entrenamientos y competiciones. Este hallazgo se alinea con investigaciones anteriores que resaltan la importancia de una ingesta adecuada de recuperadores para mejorar la recuperación muscular y preservar la masa muscular tras el ejercicio (24). Asimismo, el 43 % de los deportistas utilizaron suplementos estimulantes con la expectativa de mejorar su rendimiento. Entre estos, los geles deportivos, con o sin cafeína, fueron los más consumidos como ayuda ergogénica, a pesar de reportarse posibles molestias gastrointestinales debido a su composición (25). Mientras que los suplementos con efecto potenciador se consumieron con diversos objetivos, como mejorar el rendimiento y facilitar la recuperación durante y después de entrenamientos y competiciones (19). Más del 50 % de los participantes recurrieron a suplementos para el control de peso, posiblemente motivados por el deseo de alcanzar una mejor composición corporal o fortalecer el sistema inmunológico. Esto coincide con investigaciones que indican que los probióticos son suplementos populares entre los deportistas para fortalecer su sistema inmunológico (26).

Sin embargo, es relevante destacar que los atletas no siempre tienen un conocimiento completo de la composición y los efectos de los SD que consumen. Un porcentaje significativo (23 %) de los participantes utilizó suplementos sin conocer su composición ni sus efectos positivos o negativos. Esto es una preocupación importante, ya que el uso de SD no siempre es beneficioso, y algunos suplementos pueden ser perjudiciales y tener interacciones con otras sustancias, lo que puede dar lugar a reacciones adversas para la salud. Además, es común que los deportistas excedan las dosis recomendadas, a pesar de que la evidencia sugiere que "más no es necesariamente mejor" (27,28).

En términos de orientación, la toma de SD suele estar acompañada de asesoramiento nutricional proporcionado por entrenadores, nutricionistas, médicos y otras personas influyentes, como familiares y amigos. En este estudio se observó que un 63 % de los participantes tomaba los SD sin supervisión profesional. Este modelo de asesoramiento guarda similitud con lo observado en otros estudios, donde con frecuencia se hacen referencia a entrenadores y amigos como fuentes de orientación (29).

La mayoría de los participantes presentaba indicadores de AD, aunque no superaban el punto de corte que sugeriría la necesidad de evaluación profesional. Esto concuerda con investigaciones previas que también identificaron una proporción significativa de deportistas en riesgo de AD (1). Además, las personas más jóvenes mostraban una mayor falta de control en su actividad física, similar a hallazgos en otros estudios (30,31). No obstante, la edad y la distancia en las carreras parecen estar relacionadas con la AD, pero de forma independiente: cuánto más joven más AD, cuanto más distancia más AD (32).

Las personas que no estaban en una relación (solteros, separados y viudos) tenían una mayor AD en comparación con aquellas en pareja. Este hallazgo coincide con otros estudios que

muestran que las personas solteras muestran una mayor disposición a realizar actividades intensas o vigorosas (33).

La especialidad deportiva también influyó en la AD, con los corredores de asfalto mostrando una AD mayor en comparación con los corredores de montaña, posiblemente debido a las diferencias en el terreno y el riesgo de lesiones (34).

Aunque no se encontraron resultados significativos relacionados con la realización de análisis cada tres meses, se observó una relación significativa entre la AD y la realización de pruebas de esfuerzo, posiblemente debido a la percepción de que estas revisiones están vinculadas a la mejora del rendimiento deportivo (35).

En este estudio, se encontró una relación significativa entre el uso de SD y la AD. Estos resultados concuerdan con investigaciones previas que también han explorado la conexión entre la AD y las actitudes hacia el consumo de SD (36). Un estudio con universitarios concluyó que la AD predice una actitud favorable hacia el consumo de SD de manera positiva y significativa. Además, investigaciones similares han demostrado que la ortorexia nerviosa (obsesión patológica por comer sano) está relacionada con el consumo de SD (37).

Este estudio de corredores de Canarias es uno de los primeros en España que investiga la relación entre el consumo de SD y la AD. Se analizaron 613 participantes, garantizando una muestra representativa. Se encontró una relación significativa entre el uso de SD y la AD, respaldando investigaciones previas. Sin embargo, el estudio tiene limitaciones, como la disparidad de participación entre provincias, un desequilibrio de género en la muestra y la falta de muestreo aleatorio.

Las conclusiones principales destacan que la mayoría de los corredores en Canarias muestra indicios de AD y consume SD. Se encontró una relación significativa entre el uso de SD (estimulantes, potenciadores, recuperadores y suplementos para el control de peso) y la AD en ambos sexos. Además, los participantes más jóvenes tienen más probabilidades de consumir SD, especialmente estimulantes y potenciadores, y muestran menos autocontrol en su actividad física. El género, el nivel educativo y el estado civil no se relacionan significativamente con el consumo de SD, pero las mujeres tienen una mayor probabilidad de consumir suplementos para el control de peso. También se observa que la falta de pareja y el tipo de terreno de carrera se asocian con una mayor AD. Los suplementos potenciadores del rendimiento son consumidos en mayor medida en todas las distancias de carrera. Aunque no se encontraron resultados significativos en las analíticas cada tres meses, se observa una relación entre la AD y la realización de pruebas de esfuerzo, que también se relaciona con el consumo de SD en general y recuperadores en particular.

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Trabajo Original

Otros

Adaptation and validation of the Brief Questionnaire for Measuring Disordered Eating Behaviors in Mexican children

Adaptación y validación del Cuestionario Breve para Medir Conductas Alimentarias de Riesgo en niñas y niños mexicanos

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Abstract

Introduction: disordered eating behaviors (DEBs) and eating disorders (Eds) mainly occur in adolescence, but they currently already occur at an early age between the ages of five and twelve. Although there are instruments for EDs, it is necessary to have a self-applicable instrument for evaluating DEBs in children.

Objective: to determine the reliability and exploratory and confirmatory factorial validity of the Brief Questionnaire for Measuring Disordered Eating Behaviors (BQDEB) in children ages eight to twelve years.

Material and methods: the sample comprised 386 Mexican children with an average age of 10.2 years. The BQDEB was adapted for this population, with questions being reduced from ten to seven and answer choices from four to three. Frequency and percentage, reliability, and exploratory and confirmatory validity analyses were undertaken.

Results: concern over gaining weight was the most frequent DEB. The exploratory factorial analysis yielded seven items grouped into two factors: 1) compensatory/restrictive behaviors; and 2) binge eating, with a total ordinal alpha reliability of 0.95. Confirmatory factor analysis showed that the model fits the data well.

Conclusions: since the psychometric properties of the BQDEB for children were adequate, it constitutes a useful instrument for identifying DEBs in children.

Keywords:

Children. Disordered eating behaviors. Measurement. Validity. Reliability.

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Resumen

Introducción: las conductas alimentarias de riesgo (CAR) y los trastornos de la conducta alimentaria (TCA) se presentan principalmente en la adolescencia, pero actualmente ya se presentan en edades tempranas, entre los cinco y los doce años. Si bien existen instrumentos para medir los TCA, es necesario contar con un instrumento autoaplicable para evaluar las CAR en niños.

Objetivo: determinar la confiabilidad y validez factorial exploratoria y confirmatoria del Cuestionario Breve para Medir Conductas Alimentarias de Riesgo (CBCAR) en niñas y niños de ocho a doce años.

Material y métodos: la muestra estuvo compuesta por 386 niñas y niños mexicanos con una edad promedio de 10.2 años. El CBCAR se adaptó para esta población, reduciendo las preguntas de diez a siete y las opciones de respuesta de cuatro a tres. Se realizaron análisis de frecuencias y porcentajes, confiabilidad y validez exploratoria y confirmatoria.

Resultados: la preocupación por el aumento de peso fue la CAR más frecuente. El análisis factorial exploratorio arrojó siete ítems agrupados en dos factores: 1) conductas compensatorias/restrictivas; y 2) atracones, con una confiabilidad alfa ordinal total de 0,95. El análisis factorial confirmatorio mostró que el modelo se ajusta bien a los datos.

Conclusiones: al ser las propiedades psicométricas del CBCAR en niñas y niños adecuadas, constituye un instrumento útil para identificar los CAR en niñas y niños.

Palabras clave:

Niñas. Niños. Conductas alimentarias de riesgo. Medición. Validez. Confiabilidad.

INTRODUCTION

While similar to eating disorders (EDs), disordered eating behaviors (DEBs) do not meet the criteria established in diagnostic manuals (1). They occur less frequently and intensely and have a shorter duration than the latter yet cause significant health problems and poor quality of life, in addition to being associated with the presence of other psychopathologies (2). Examples of DEBs include restrictive diets, binge eating, and the use of compensatory methods such as laxatives, diuretics, overexercising, anorexigenics, and self-induced vomiting.

Accordingly, instruments, questionnaires, and interviews have been designed and validated to obtain information on the prevalence of DEBs in Latin American children, adolescents, and youth. For example, Urzúa et al. (3) assessed disordered eating behaviors in Chilean students ages eight to eighteen through the Eating Attitudes Test-EAT-26 comprising twenty-six items. Encina et al. (4) used the Children's Eating Behavior Questionnaire-CEBQ, consisting of thirty-five questions, in a sample of both Chilean children and their mothers/guardians, to determine whether they had positive or negative attitudes towards food intake. For their part, Cofré et al. (5) used the Three-Factor Eating Questionnaire (TFEQ-P19), adapted from the original version (6) to measure eating behaviors in a hundred Colombian children ages six to nine.

With regard to other instruments used to measure DEBs in children, in Mexico, Ponce de León et al. (7) validated the ChEAT (Children's Eating Attitudes Test) in a sample of children and early adolescents with a mean age of eleven. However, this is an instrument developed in another culture, with twenty-six questions and six answer choices, which can prove hard for younger children to answer. Likewise, Platas and Gómez Peresmitré (8) designed and validated the Scale of Risk Factors Associated with Eating Disorders (EFRATA-II) in preadolescents aged nine to twelve, obtaining robust psychometric characteristics. However, this is an instrument with sixty-one questions with five answer choices, whose length makes it impossible to use in population studies.

The Brief Questionnaire for Measuring Disordered Eating Behaviors (BQDEB) was designed in 1997 to obtain information on the student population through the Survey on the Prevalence of

Drug and Alcohol Use in the Student Population of the Federal District. It has been validated in adolescent girls (10), patients with eating disorders (9,11), adolescent boys and young men (12). It has been used to assess DEBs in six measurements of the Survey on Drug Use in Students, conducted in Mexico City (13-16), three editions of the National Health and Nutrition Survey (ENSANUT) (17-19) and one of the ENSANUT-continua (20). The need to measure DEBs in children ages eight to twelve led to the adaptation of the BQDEB, in which the number of questions was reduced, and answer choices simplified to make it easier to understand and answer.

The purpose of this study was therefore to obtain the reliability and exploratory and confirmatory factorial validity of the BQDEB in the version for children ages eight to twelve, 4th to 6th grade students at public elementary schools in the states of Campeche and Mexico. An additional objective was to report the percentage distribution of each of the questions in the questionnaire by sex.

MATERIALS AND METHODS

SAMPLE

The total sample comprised 386 children, eight of whom were eliminated, because they did not agree to participate, leaving a total of 378 (193 girls = 51.1 % and 185 boys = 48.9 %), elementary school students in the morning shift, at six schools in the federal school system of the Ministry of Public Education in the States of Campeche (249 girls = 51 %) and Mexico (129 girls = 51.2 %) in the period May-July 2022 through an Internet link. The mean age was 10.2 years (SD = 0.94), with no differences by sex.

INSTRUMENT

The BQDEB is a ten-item scale designed to assess disordered eating behaviors such as restrictive diets, binge eating, and the use of compensatory methods such as laxatives, diuretics, excessive physical exercise, anorexigenics, and self-induced vomiting (9,21).

For the present study, the questionnaire was adapted through cognitive laboratories with fifteen children ages eight to twelve to check the understanding of the terms included in the questions, the meaning of the latter, and the answer choices. This evaluation resulted in a seven-item instrument with three ordinal response options (No = 0, Sometimes = 1, Yes = 2) that evaluate behaviors in the last three months: 1) Have you been worried about gaining weight? 2) Have you sometimes overeaten or binged? 3) Have you lost control over what you eat (do you have the feeling of being unable to stop eating)? 4) Have you vomited after eating to try to lose weight? 5) Have you skipped breakfast, lunch, or dinner to try to lose weight? 6) Have you stopped eating certain types of food to try to lose weight? 7) Have you exercised to try to lose weight? A pilot study was subsequently conducted with the proposed version in which understanding of the items was tested in a group of ten children within the age range.

PROCEDURE

The researchers contacted local school authorities, who, after agreeing to participate in the study, liaised between the former and school principals. Questionnaires were administered by sending Internet links via WhatsApp, initially to the school principals, and subsequently to 4th to 6th grade elementary school teachers, who then forwarded them to parents. Teachers sent the internet link to parents, explaining that before answering the questions, they should read the informed consent form and decide whether they wished their children to participate. If they chose not to, that would indicate the end of their participation. Given that the children were asked to provide their informed consent, parents were asked to help them if they had problems understanding and answering the consent form, although the questionnaires were answered exclusively by the children.

DATA ANALYSIS

Frequency and percentage analyses were conducted, together with measures of central tendency of demographic variables and of each of the scale items. Reliability and exploratory and confirmatory factor analyses were also conducted.

Item-total correlations were obtained, considering that items with a value of less than .20 should be eliminated. An exploratory factor analysis was conducted based on Yela's criteria; also a confirmatory factor analysis was conducted. The sample was randomly divided into two parts, yielding an initial sample of 197 subjects (ninety-six girls and one hundred and one boys) and a second sample with 181 subjects (ninety-seven girls and eighty-four boys), so that the exploratory analysis could be undertaken with one and the confirmatory analysis with the other, in both cases, the quota of five to twenty participants per item was achieved, and the minimum requirement of 150 subjects was met to conduct the confirmatory factor analysis. Reliability was obtained with ordinal alpha with the total sample ($n = 378$). The

SPSS program version 21, the statistical program Factor, and the JASP program version 13 were used for the data analysis.

The protocol was approved by the Research Ethics Committee of the National Institute of Public Health on April 13, 2021, approval number 1542. Parents' or guardians' informed consent and children's assent were included in the links to the questionnaires sent to parents.

RESULTS

DISORDERED EATING BEHAVIORS

The analysis by sex of DEBs in the "yes" answers showed that 3.1 % of girls and 11.9 % of boys are worried about gaining weight, 1 % of girls and 2 % of boys had binged, 2.1 % of girls and 5 % of boys had felt a loss of control when eating, 2 % of girls and 0 % of boys had avoided meal times to lose weight, 2.1 % of girls and 2 % of boys had stopped eating certain foods and 12.5 % of girls and 5.9 % of boys had exercised to lose weight. In the "sometimes" category, the answers were 40.6 % and 39.6 % in girls and boys, respectively, for concern over gaining weight; 44.8 % and 55.4 % in girls and boys, respectively, for binge eating; 24 % and 25.7 % in girls and boys, respectively, for feeling a lack of control when eating; 8.3 % in girls and 5 % in boys for avoiding meal times; 18.8 % in girls and 12.9 % in boys for refraining from eating certain foods; and 40.6 % in girls and boys for doing exercise. No statistically significant differences were found by sex.

FACTOR ANALYSIS

An exploratory factor analysis was performed with the seven items from the complete scale. The item-total correlations of the scale were obtained using ordinal alpha, showing that all the questions obtained loads higher than 0.20, except for question four: "Have you vomited after eating to try to lose weight?", which would indicate the need to eliminate this item from a strictly psychometric perspective. However, due to its theoretical importance and mainly because it is a worrying behavior from a diagnostic point of view, it was decided to keep it for the confirmatory factor analysis without considering the psychometric values obtained in the item-total correlations.

With the remaining six items, exploratory factor analysis was conducted using unweighted least squares (ULS) type with Promin rotation. A configuration in two factors that explained 63.7 % of the variance, with a significant Bartlett's test of sphericity ($B = 176.60$, $df = 21$; $p < 0.001$) and a value of 0.60 in the Kaiser-Meyer-Olkin (KMO) test. Factor 1, containing questions on compensatory behaviors or food restriction, obtained an ordinal alpha of 0.90, while Factor 2 contained questions on binge eating and feeling a lack of control while eating with an ordinal alpha of 0.90, and a total ordinal alpha reliability of the scale of 0.91 (Table I).

Confirmatory factor analysis was conducted with the JASP program, estimating discrepancies using the diagonally weighted least squares method (suitable for ordinal measurement levels). To conduct this analysis, item 4 was re-examined, to assess its fit with the final model. First, it was observed that discrepancies were not statistically significant. In addition, goodness of fit proved adequate, with values of RMSEA \leq 0.08, CFI \geq 0.95, TLI \geq 0.90, GFI \geq 0.90 and SRMR \leq 0.08 being obtained.

Confirmatory factor analysis (Fig. 1) generally showed adequate goodness-of-fit indices (RMSEA = 0.000, 90 % CI [$<$ 0.034]; CFI = 1.00; TLI = 1.02; GFI = 0.99; SRMR = 0.07; Chi² ($\chi^2 = 7.16$, df = 13, $p = 0.89$). Factor covariances are statistically significant (estimate = 0.85, $Z = 8.5$, $p < 0.001$) and there were no modification or residual covariance indices.

DISCUSSION

Although DEBs and EDs mainly occur in adolescence, they currently already occur at an early age between the ages of five and twelve (22). In addition, DEBs are extremely common in overweight and obese people, which increases the risk of developing EDs (23). Although there are instruments for EDs, it is necessary to have a self-applicable instrument for evaluating DEBs in children that is brief, easy to administer, and specifically designed for the Mexican population. This instrument was adapted from the version for the adolescent and adult population, which has been widely administered and validated in Mexico (13-20).

When DEBs were evaluated, the most frequent behavior that emerged was concern over gaining weight, with 3.1 % of girls

Table I. Factor weightings for the exploratory factor analysis of the Brief Questionnaire to Measure Disordered Eating Behaviors in Children

	Item	Factor 1	Factor 2
1	In the past three months, have you been worried about gaining weight? (En los últimos tres meses, ¿te ha preocupado engordar?)	0.378	
2	In the past three months, have you sometimes overeaten or binged? (En los últimos tres meses, ¿en ocasiones has comido demasiado, te has atascado de comida?)	0.440	
3	In the past three months, have you lost control over what you eat (do you have the feeling of being unable to stop eating)? (En los últimos tres meses, ¿has perdido el control sobre lo que comes (tienes la sensación de no poder parar de comer?)	0.889	
4	In the past three months, have you vomited after eating to try to lose weight? (En los últimos tres meses, ¿has vomitado después de comer para tratar de bajar de peso?)		0.648
5	In the past three months, have you skipped breakfast, lunch, or dinner to try to lose weight? (En los últimos tres meses, ¿has dejado de desayunar, comer o cenar para tratar de bajar de peso?)		0.647
6	In the past three months, have you stopped eating certain types of food to try to lose weight? (En los últimos tres meses, ¿has dejado de comer algunos alimentos para tratar de bajar de peso?)		0.761
7	In the past three months, have you exercised to try to lose weight? (En los últimos tres meses, ¿has hecho ejercicio para tratar de bajar de peso?)		0.634
	Factor ordinal alpha reliability	0.90	0.90
	Total ordinal alpha reliability	0.91	

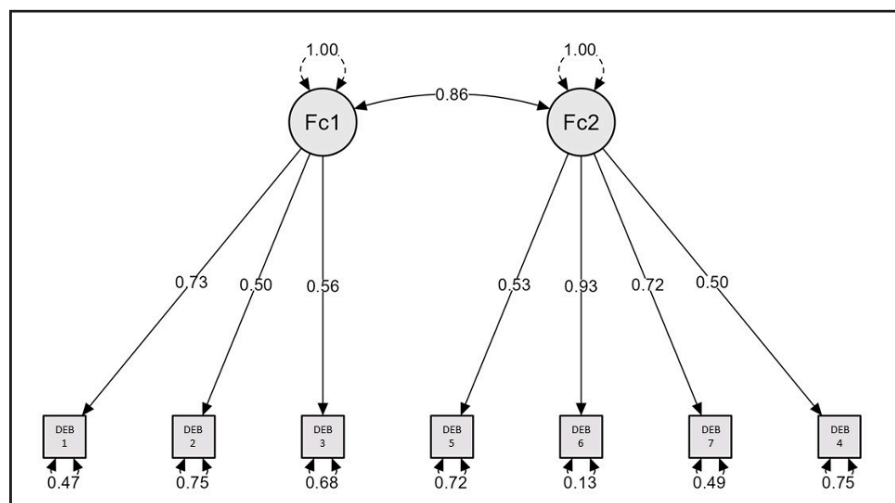


Figure 1. Confirmatory factor analysis of the Brief Questionnaire to Measure Disordered Eating Behaviors in Children.

answering “yes” and 40.6 % “sometimes,” 11.9 % of boys answering “yes” and 39.6 % “sometimes.” This concern has been reported in other studies. In ENSANUT 2012, in the group ages ten to thirteen, it occurs in 11.4 % of boys and 11.3 % of girls (17). In another study of children ages eight to twelve with obesity in the United States, 31.7 % of subjects, including 25 % of boys and 37.7 % of girls have this characteristic (24). In regard to binge eating, 1 % of girls answered “yes” and 44.8 % “sometimes”; 2 % of boys answered “yes” and 55.4 % “sometimes” In ENSANUT 2012 (17), 10 % of boys and 9.9 % of girls reported binge eating. In regard to loss of control when eating, 2.1 % of girls answered “yes” and 24 % “sometimes”; 5 % of boys answered “yes” and 25.7 % “sometimes;” in the ENSANUT 2012 (17), 5.8 % of girls and 7 % of boys did so. The ENSANUT 2018 found that 3.9 % and 0.4 % of the group ages ten to eleven showed a moderate or high risk of eating disorders respectively (25). In Jalisco, Mexico, in a study with non-probabilistic, intentional sampling (26), the set of abnormal behaviors and attitudes as regards eating in children with an average age of 10.9 years was present in 13.8 % of subjects, being higher in those with overweight, 22.9 %, and obesity, 15.9 %. Other behaviors and attitudes found in studies of children ages eight to twelve show the presence of the thin ideal in 42 % of boys and 53 % of girls. Thirty-two per cent would prefer to be thinner, even those with normal weight, and 18.5 % were attempting to lose weight (27). Eating food without being hungry, having a high BMI, weight-related cognitions, and negative affect in childhood predict the presence of binge eating disorders in adolescence (28). The presence of DEBs reported in several studies varies partly as a result of the questionnaire administered and the age of the subjects. A number of studies have confirmed that the older the subjects and the higher their BMI, the greater the presence of DEBs (26-29).

Our reliability analysis was satisfactory for all the questions with the exception of question four, “Have you vomited after eating to try to lose weight?” However, the item was retained because of its theoretical importance. The seven questions were grouped into two factors unlike the version for adolescents and adults, comprising three factors. Factor one (compensatory behaviors-restriction) contains questions on compensatory behaviors or food restriction, whereas factor two (binge eating) comprises questions on binge eating and feeling a lack of control when eating, and concern over gaining weight. Results are consistent with DEBs that occur more frequently in the nine-to-twelve-year age group, since those under thirteen engage less in compensatory behaviors, binge eating, and the use of pills and laxatives than those over thirteen (30). The confirmatory factorial analysis performed yielded adequate goodness-of-fit indices and all items presented statistically significant loads in their factors.

Early cases of eating disorders or psychological risk factors probably go undetected in the child population, meaning that cases fail to receive medical attention until they are severe (31). Moreover, various screening studies for EDs in the child population have found the lack of validated instruments for this specific population group to be a major limitation (32-33). It is therefore

essential to have instruments that can be used in epidemiological studies to detect DEBs at an early age, since research has found both avoidant and restrictive food intake disorder (ARFID) and other EDs among the pediatric population (32,33). These instruments should also be able to significantly decrease the presence of serious problems in adolescence.

Limitations of the study included the fact that the sample was neither random nor representative of the child population ages eight to twelve in Mexico, and the questionnaire is not sufficient to establish a diagnosis, validations of the scale should be undertaken on its self-reported version in other contexts, which would shed more light on the risk of DEBs in the child population, as well as convergent, divergent, predictive, test-retest validation and a comparison with clinical samples. Nevertheless, the version of the BQDEB for children constitutes a useful instrument for determining the extent of DEBs in children. One of the greatest advantages of the BQDEB for children in relation to other instruments used to detect DEBs is that it is a brief, specific, ideal for epidemiological studies and designed for the Mexican population, enabling one to determine prevalence, attend cases in a timely manner, and undertake preventive actions with better results.

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Artículo Especial

Dietista-nutricionista interno residente (D-NIR): una necesidad a años luz de producirse en España

Dietitian-nutritionist intern resident (D-NIR) – A need light years away from occurring in Spain

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Resumen

El dietista-nutricionista (D-N) es un profesional sanitario con título universitario en nutrición humana y dietética encargado de la correcta alimentación según las necesidades fisiológicas y patológicas de las personas, tal y como recoge la Ley de Ordenación de las Profesiones Sanitarias desde el año 2003.

Diversas sociedades nacionales e internacionales, apoyadas en numerosos estudios, apuntan a la necesidad de incorporar al D-N en el Sistema Nacional de Salud (SNS) para mejorar la atención sanitaria en el contexto de equipos multidisciplinares.

No obstante, a pesar de la importancia de las funciones del D-N dentro de la cartera del SNS, y a diferencia del resto de profesiones sanitarias, son múltiples las comunidades autónomas de España que aún no cuentan con la figura de este profesional. Así mismo, no existe un sistema de Formación Sanitaria Especializada (FSE) específico para este, siendo esta una necesidad que impide su propia formación y especialización oficial.

Por tanto, se propone la creación de una FSE para el dietista-nutricionista interno residente (D-NIR) con el objetivo de mejorar su formación integral, sus competencias y responsabilidades, mejorando así la calidad asistencial del SNS en el contexto de equipos multidisciplinares.

Palabras clave:

Dietista-nutricionista.
Dietista. Nutricionista.
Sistema Nacional de Salud.
Recursos humanos. Cartera de servicios.

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Abstract

The dietitian-nutritionist (D-N) is a health professional with a university degree in human nutrition and dietetics in charge of the correct nutrition according to the physiological and pathological needs of people, as stated in the Law on the Regulation of Healthcare Professions since 2003.

Various national and international societies, supported by numerous studies, point to the need to incorporate the D-N in the National Health System (NHS) to improve healthcare in the context of multidisciplinary teams.

Keywords:

Dietitian-nutritionist.
Dietitian. Nutritionist.
National Health System.
Human resources.
Specialised health training.

However, despite the importance of the functions of the D-N within the NHS portfolio, and unlike the rest of the health professions, there are many regions in Spain that still do not have the figure of this professional. Likewise, there is no specific system of Specialized Health Care Training (SHCT) for this professional, which is a need that impedes his or her own official training and specialization.

Therefore, the creation of an SHCT for the dietitian-nutritionist intern resident (D-NIR) is proposed with the aim of improving their comprehensive training, competencies and responsibilities, thus improving the quality of care in the NHS in the context of multidisciplinary teams.

INTRODUCCIÓN

Desde el año 2003, en España se encuentra regulado el ejercicio de las profesiones sanitarias a través de la Ley 44/2003, de 21 de noviembre, bajo la denominada Ley de Ordenación de las Profesiones Sanitarias (LOPS) (1). Dicho marco legal considera profesionales sanitarios a los licenciados y licenciadas en medicina, farmacia, veterinaria y odontología, así como a aquellos licenciados y aquellas licenciadas en física, química, biología, bioquímica o psicología, que posean un título de especialista en ciencias de la salud. Además, se consideran también profesionales sanitarios a diplomados y diplomadas en enfermería, fisioterapia, terapia ocupacional, podología, óptica y optometría, logopedia y, finalmente, a diplomados y diplomadas en nutrición humana y dietética. Según el artículo 7.2.g de la citada Ley (1), el dietista-nutricionista (D-N) es un profesional sanitario con título universitario en nutrición humana y dietética que desarrolla actividades orientadas a la alimentación de las personas, adecuadas a las necesidades fisiológicas y patológicas de las mismas, y de acuerdo con los principios de prevención y salud pública.

En general, la Ley regula los aspectos básicos de las profesiones sanitarias tituladas en lo que se refiere a su ejercicio por cuenta propia o ajena, a la estructura general de la formación, al desarrollo profesional y a su participación en la planificación y ordenación de las propias profesiones. Además, el artículo 16 de la citada Ley (1), otorga al Gobierno de España la competencia para el establecimiento de los títulos de especialista en ciencias de la salud y los diplomas de área de capacitación específica, así como su supresión o cambio de denominación.

Actualmente, todas las profesiones sanitarias descritas están instauradas en el Sistema Nacional de Salud (SNS) como desprende el Real Decreto 184/2015, de 13 de marzo, por el que se regula el catálogo homogéneo de equivalencias de categorías profesionales de personal estatutario de los servicios de salud (2). No obstante, a pesar de que esta instauración se encuentra realizada dentro del SNS, la Formación Sanitaria Especializada (FSE) no es igual para todas las profesiones sanitarias.

Se entiende por FSE al sistema de formación con residencia de determinadas especialidades de ciencias de la salud (licenciaturas o grados universitarios de medicina, enfermería, farmacia, psicología, biología, bioquímica, física y química). Mediante esta formación, los profesionales y las profesionales obtienen un aprendizaje a través de la práctica clínica que es supervisada

y retribuida por los distintos servicios de salud autonómico. Cada formación depende de la especialidad a la que se opte desde la licenciatura o grado cursado, y atiende a una duración variable en función de los programas de cada especialidad.

Esta formación se regula a través del Ministerio de Sanidad y de los departamentos de salud de las distintas comunidades autónomas. A través de un contrato laboral, el personal residente tiene la obligación de prestar personalmente los servicios asistenciales que establezca el correspondiente programa de formación nacional para adquirir la competencia profesional relativa a la especialidad y, además, para contribuir a los fines propios de la institución sanitaria.

La FSE se consolidó en España como única vía legal de especialización en el año 1984, aunque varias normativas españolas posteriores han logrado que esta especialización se adapte a las nuevas necesidades de la sociedad y del sistema europeo. Concretamente, el Real Decreto 183/2008 de FSE en ciencias de la salud viene a actualizar dicho sistema favoreciendo una formación más adaptada con una visión multidisciplinar (3). En la tabla I se representan las especialidades en ciencias de la salud que pueden optar dentro del sistema de residencia para obtener el correspondiente título oficial de especialista.

Posteriormente al año 2008, el Real Decreto 639/2014, de 25 de julio (4), y el Real Decreto 589/2022, de 19 de julio (5), continúan regulando la FSE, estableciendo una formación transversal de las especialidades en ciencias de la salud pero, también, estableciendo el procedimiento y los criterios para la propuesta de nuevos títulos de especialista en ciencias de la salud y los diplomas de área de capacitación específica.

Ante tanta normativa, conviene reflejar que son varias las profesiones sanitarias que no cuentan con una FSE dentro del sistema sanitario. Los grados en veterinaria, odontología, fisioterapia, terapia ocupacional, podología, óptica y optometría, logopedia y nutrición humana y dietética no cuentan con esta posibilidad de formación especializada. Sin embargo, todas estas profesiones sanitarias sí están instauradas de forma prácticamente homogénea en el SNS, salvo los profesionales y las profesionales de la nutrición humana y dietética.

En la actualidad, la presencia de D-N (Grado Universitario o Diplomado Universitario en Nutrición Humana y Dietética) continúa siendo prácticamente nula en el SNS español. Si bien se requiere mayor investigación, los estudios existentes hasta la fecha sugieren estos hechos (Tabla II). Prácticamente la totalidad

de las profesiones sanitarias están establecidas dentro del SNS con su respectiva categoría profesional en cada comunidad autónoma. Sin embargo, la categoría profesional del D-N aún no se ha instaurado en seis comunidades autónomas como se observa en la tabla II.

El hecho de esta carencia dentro del SNS hace poco probable a corto plazo la creación de la FSE para el dietista-nutricionista interno residente (D-NIR). Evidentemente, antes de dicha especialización es necesaria la consolidación de la categoría profesional de D-N en todos los sistemas de salud autonómicos. No obstante, este paradigma no es nuevo, y son varias las instituciones europeas (6,7) y nacionales (8,9) que destacan la escasa presencia de D-N en los sistemas de salud de España.

En el año 2010, se presentó el Informe de la Ponencia de Estudio de las necesidades de recursos humanos en el SNS, constituido en el seno de la Comisión de Sanidad, Política Social y Consumo. En este documento se declararon una serie de necesidades sobre recursos humanos en todo el SNS, destacando las carencias en el ámbito de la nutrición humana y la dietética. En concreto, en el apartado III, punto 2.7, se define claramente que la situación del profesional D-N es irregular dentro del SNS, y en su informe final de conclusiones establecen que “existe una ausencia de previsión de puestos para D-N en el SNS en España, a diferencia de lo que ocurre en otros países de la Unión Europea” (10).

La recomendación que se estableció en ese entonces recoge que, la prestación de los servicios propios de D-N precisa de una intervención por parte de las autoridades sanitarias para modernizar el SNS, a través de la incorporación de estos profesionales sanitarios. Sin embargo, únicamente once comunidades autónomas han realizado tal incorporación desde esa fecha, y aún quedan seis comunidades por establecerla (Tabla II).

En este sentido, resulta paradójico que el SNS español no incorpore la figura profesional del D-N en todo el territorio nacional en vista de asegurar una atención asistencial de calidad (9,11,12), en el contexto de equipos multidisciplinares, teniendo más si cabe presente que el principal factor de riesgo de pérdida de años de vida de la población se atribuye a patrones de consumo de alimentos poco saludables. La necesidad de una prescripción dietoterápica idónea en cada situación de enfermedad es crucial en el tratamiento de la enfermedad, siendo precisamente los universitarios en nutrición humana y dietética los profesionales capacitados para guiar en este proceso de manera efectiva. Su incorporación no sólo se justifica por la estrecha relación que hay entre la nutrición y la enfermedad, sino también por el ahorro económico que supondría para el sistema. Numerosos estudios ponen de manifiesto el impacto económico que podría suponer la actividad de este profesional siendo beneficiosa en términos de coste-eficacia (13,14).

A pesar de estos datos, actualmente no se cumplen los ratios que han propuesto diversas sociedades científicas nacionales e internacionales para fijar dicha inclusión dentro del SNS, repercutiendo esta cuestión no sólo en la población, sino también en la formación del profesional (9,14). Teniendo en cuenta que la FSE está ausente en esta profesión, la mayor parte de profesionales deben buscar otras vías para poder especializarse, formarse, e incluso, reciclarse.

La inexistencia de una FSE en modalidad de D-NIR hace que dichos profesionales busquen formación a través de otros formatos, pero, también, hace que no puedan especializarse mediante una vía oficial acreditada por el ministerio correspondiente. En la actualidad, debido a esta situación, la mayoría de profesionales cursan másteres universitarios oficiales o no oficiales en vistas de obtener una especialización. Sin embargo, esta “especialización” carece de oficialidad, tal y como se desprende de la legislación vigente según el Real Decreto 183/2008 (3). La formación de un máster en sí tiene la finalidad de adquirir una formación más avanzada por el alumnado en una materia en cuestión (buscando cierta especialización), pero no puede aplicarse el concepto de “especialista en” de una manera oficial y reglada. Igualmente, ningún curso, experto o programa de doctorado que se haya cursado y superado puede equivaler a ningún título de especialista.

En general, los másteres universitarios oficiales en España (relacionados con la salud) requieren como único requisito haber cursado un grado en ciencias de la salud para poder cursarlo. Este hecho refleja que, para la mayoría de másteres, solo se requiere poseer una titulación universitaria sanitaria según la LOPS del año 2003 (1) y, por ende, el propio máster no tiene capacidad para reconocer una especialidad en una determinada profesión. Actualmente, los únicos másteres que se ofrecen para una determinada carrera universitaria se denominan “habilitantes” y son necesarios para poder ejercer dicha profesión.

El sistema de formación de Especialistas Internos Residentes en España cuenta con varios objetivos comunes para todas las especialidades que se describen en la tabla I. La adquisición de competencias permite asegurar que los residentes adquieran las aptitudes profesionales necesarias para ejercer de manera autónoma y competente en su especialidad, incluyendo conocimientos teóricos, habilidades prácticas y destrezas profesionales. Asimismo, la formación proporciona una enseñanza integral que combine la práctica clínica supervisada con la formación teórica, permitiendo a los residentes desarrollar tanto habilidades clínicas como capacidades de investigación y gestión sanitaria.

Se persigue, a su vez, la progresión de responsabilidades en busca de facilitar la adquisición progresiva de competencias en el cuidado del paciente, garantizando que los residentes puedan asumir tareas de mayor complejidad y responsabilidad a medida que avanzan en su formación. Además, se promueve la calidad asistencial y la seguridad del paciente mediante la formación en buenas prácticas clínicas, ética profesional y uso seguro de medicamentos y tecnologías sanitarias.

El desarrollo profesional fomenta la educación continua, preparando a los residentes para el aprendizaje a lo largo de toda su carrera profesional y para adaptarse a los avances científicos y tecnológicos. Esto se complementa con la promoción de la cooperación y el trabajo en equipos multidisciplinares, reflejando la realidad del entorno asistencial y mejorando la coordinación y efectividad de la atención sanitaria, además de facilitar la movilidad de los residentes a través de rotaciones en diferentes unidades y centros, tanto nacionales como internacionales, para ampliar su experiencia y conocimiento.

Tabla I. Relación de especialidades de ciencias de la salud por el sistema de residencia

Especialidad	Denominación	Título de especialista
Medicina	Especialidades médicas para cuyo acceso se exige estar en posesión de un título universitario oficial que habilite para el ejercicio en España de la profesión de médico o médica	Alergología Anatomía Patológica Anestesiología y Reanimación Angiología y Cirugía Vascul ar Aparato Digestivo Cardiología Cirugía Cardiovascular Cirugía General y del Aparato Digestivo Cirugía Oral y Maxilofacial Cirugía Ortopédica yTraumatología Cirugía Pediátrica Cirugía Plástica, Estética y Reparadora Cirugía Torácica Dermatología Médico-Quirúrgica y Venereología Endocrinología y Nutrición Farmacología Clínica Geriatría Hematología y Hemoterapia Hidrología Médica Inmunología Medicina de la Educación Física y el Deporte Medicina del Trabajo Medicina Familiar y Comunitaria Medicina Física y Rehabilitación Medicina Intensiva Medicina Interna Medicina Legal y Forense Medicina Nuclear Medicina Preventiva y Salud Pública Nefrología Neumología Neurocirugía Neurofisiología Clínica Neurología Obstetricia y Ginecología Oftalmología Oncología Médica Oncología Radioterápica Otorrinolaringología Pediatria y sus Áreas Específicas Psiquiatría Psiquiatría Infantil y de la Adolescencia Radiodiagnóstico Reumatología Urología
Farmacia	Especialidades farmacéuticas para cuyo acceso se exige estar en posesión de un título universitario oficial que habilite para el ejercicio en España de la profesión de farmacéutico o farmacéutica	Farmacia Hospitalaria

(Continúa en página siguiente)

Tabla I (cont.). Relación de especialidades de ciencias de la salud por el sistema de residencia

Especialidad	Denominación	Título de especialista
Psicología	Especialidades de Psicología para cuyo acceso se exige estar en posesión del título universitario oficial de Grado en el ámbito de la Psicología o de Licenciado o Licenciada en Psicología	Psicología Clínica
Enfermería	Especialidades de Enfermería para cuyo acceso se exige estar en posesión de un título universitario oficial que habilite para el ejercicio en España de la profesión de enfermera.	Enfermería de Salud Mental Enfermería de Cuidados Médico-Quirúrgicos Enfermería del Trabajo Enfermería Familiar y Comunitaria Enfermería Geriátrica Enfermería Obstétrico-Ginecológica (Matrona) Enfermería Pediátrica
Física	Especialidades de Física para cuyo acceso se exige estar en posesión de un título universitario oficial que habilite para el ejercicio en España de la profesión de físico o física	Radiofísica Hospitalaria
Especialidades multidisciplinares	Especialidades multidisciplinares para cuyo acceso se exige estar en posesión de los títulos universitarios oficiales de Grado, o en su caso de Licenciado o Licenciada, en cada uno de los ámbitos que a continuación se especifican	Análisis Clínicos: Biología, Bioquímica, Farmacia, Medicina o Química Bioquímica Clínica: Biología, Bioquímica, Farmacia, Medicina o Química Inmunología: Biología, Bioquímica, Farmacia o Medicina Microbiología y Parasitología: Biología, Bioquímica, Farmacia, Medicina o Química. Radiofarmacia: Biología, Bioquímica, Farmacia o Química

Tabla II. Relación de comunidades autónomas que cuentan con la categoría profesional de dietista-nutricionista dentro del Sistema Nacional de Salud español

Comunidad autónoma	Decreto	Fecha	Categoría profesional
Murcia	Decreto 119/2002, de 4 de octubre, por el que se configuran las opciones correspondientes a las categorías del personal estatutario del Servicio Murciano de Salud	2002	B
Comunidad Autónoma del País Vasco	Decreto 186/2005, de 19 de julio, por el que se regulan los puestos funcionales del Ente Público de Derecho Privado Osakidetza-Servicio Vasco de Salud	2005	B1
Cataluña	Ley 8/2007, de 30 de julio, del Instituto Catalán de la Salud. Categoría recogida en la relación de categorías, especialidades y titulaciones que requiere el Instituto Catalán de Salud para acceder a la bolsa de trabajo público	2007	B
Castilla y León	LEY 2/2007, de 7 de marzo, del Estatuto Jurídico del Personal Estatutario del Servicio de Salud de Castilla y León	2007	B
Comunidad Foral de Navarra	Decreto Foral 234/2011, de 2 de noviembre, por el que se actualiza el Anexo de estamentos y especialidades de la Ley Foral 11/1992, de 20 de octubre, reguladora del régimen específico del personal adscrito al Servicio Navarro de Salud Osasunbidea	2011	A3
Comunidad Valenciana	Decreto 70/2013, de 7 de junio, del Consell, por el que se ordenan diversas categorías de personal estatutario de la Agència Valenciana de Salut	2013	A2
Comunidad de Madrid	LEY 9/2015, de 28 de diciembre, de Medidas Fiscales y Administrativas de la Comunidad de Madrid. Artículo 22. Creación de categorías estatutarias del Servicio Madrileño de Salud	2015	A2

(Continúa en página siguiente)

Tabla II (cont.). Relación de comunidades autónomas que cuentan con la categoría profesional de dietista-nutricionista dentro del Sistema Nacional de Salud español

Comunidad autónoma	Decreto	Fecha	Categoría profesional
Illes Balears	Decreto 64/2016 de 28 d'octubre de 2016, pel qual es creen categories noves de personal estatutari en l'àmbit del Servei de Salut de les Illes Balears i es canvia la denominació de tres categories ja existents	2016	A2
La Rioja	Decreto 2/2018 de 19 de enero, por el que se crean las categorías estatutarias de Dietista-Nutricionista, Técnico/a Especialista en Documentación Sanitaria y se integra la categoría de Psicólogo Clínico en la de Facultativo Especialista de Área, en el ámbito del Servicio Riojano de Salud	2018	A2
Aragón	ORDEN SAN/973/2018, de 5 de junio, por la que se crea la categoría estatutaria de Titulado/a Superior en Nutrición y Control de Alimentos en el ámbito de los Centros Sanitarios del Servicio Aragonés de Salud	2018	A1
Galicia	DECRETO 221/2022, de 22 de diciembre, por el que se crea la categoría estatutaria de dietista-nutricionista del Servicio Gallego de Salud	2024	A2
Andalucía	Sin consolidar	2024	Pendiente
Canarias	Sin consolidar	2024	Pendiente
Cantabria	Sin consolidar	2024	Pendiente
Castilla-La Mancha	Sin consolidar	2024	Pendiente
Extremadura	Sin consolidar	2024	Pendiente
Principado de Asturias	Sin consolidar	2024	Pendiente

Todos estos objetivos son fundamentales para garantizar que los especialistas en formación puedan ofrecer una atención sanitaria de alta calidad y estén preparados para responder a las necesidades cambiantes del sistema de salud. La creación del D-NIR facilitaría la consecución de estos objetivos tanto para el profesional D-N como para el SNS.

CONCLUSIONES

La FSE bajo la denominación D-NIR en el SNS español se hace necesaria en las próximas décadas. Evidentemente, es indispensable, previo a su instauración, el reconocimiento homogéneo de D-N en todos los sistemas autonómicos de salud de España. Para una adecuada implantación del D-NIR, deben estar reconocidos los profesionales y las profesionales D-N en todo el ámbito sanitario.

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Grupo de Trabajo SENPE

Revisión y actualización del documento de consenso SENPE-SEDOM-SEEN sobre la codificación de la desnutrición hospitalaria

Review and update of the SENPE-SEDOM-SEEN consensus document on the coding of hospital malnutrition

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Resumen

El concepto de "desnutrición relacionada con la enfermedad" (DRE) dista mucho del concepto de la malnutrición diagnosticada clásicamente en salud pública, que se encuentra determinada por factores sociodemográficos. En el año 2008, la Sociedad Española de Nutrición Clínica y Metabolismo (SENPE) y la Sociedad Española de Documentación Médica (SEDOM) publicaron un consenso definiendo de una forma más precisa los tipos de desnutrición atendidas en los hospitales y su correspondiente codificación. Los cambios de la Clasificación Internacional de Enfermedades (CIE) y la evolución de la información clínica, pone de manifiesto la necesidad de revisar y actualizar dicho consenso para establecer nuevos criterios que sirvan de guía en el registro y codificación de los diagnósticos de desnutrición en el ámbito de la atención hospitalaria. Este consenso puede facilitar el trabajo tanto de clínicos como de codificadores y mejorar la visibilidad de la DRE, mediante una adaptación de los diagnósticos clínicos de desnutrición basados en los criterios GLIM (*Global Leadership Initiative on Malnutrition*) propuestos por las sociedades científicas a los códigos actuales propuestos por la CIE-10-ES.

El presente documento refleja el nuevo consenso de las sociedades SENPE, SEEN y SEDOM, y se refiere a la codificación de la DRE, otros diagnósticos nutricionales y procedimientos del tratamiento médico nutricional, expone los criterios de codificación y propone sugerencias para mejorar la codificación a nivel hospitalario.

Palabras clave:

Desnutrición. Hospital.
Codificación clínica.
Clasificación Internacional de Enfermedades.
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Abstract

The concept of "disease related malnutrition" (DRM) is far from the concept of malnutrition classically diagnosed in public health, which is determined by socio-demographic factors. In 2008, the Spanish Society of Clinical Nutrition and Metabolism (SENPE) and the Spanish Society of Medical Documentation (SEDOM) published a consensus defining more precisely the types of malnutrition seen in hospitals and their corresponding coding. Changes in the International Classification of Diseases (ICD) and the evolution of clinical information have made it necessary to revise and update this consensus in order to establish new criteria to guide the recording and coding of diagnoses of malnutrition in the field of hospital care, thus facilitating the work of both clinicians and coders and improving the visibility of DRE, by adapting from the clinical diagnoses of undernutrition based on the GLIM criteria (*Global Leadership Initiative on Malnutrition*) proposed by the scientific societies to the current codes proposed by ICD-10-ES.

This document reflects the new consensus of the SENPE, SEEN and SEDOM societies, and refers to the coding of DRE, other nutritional diagnoses and medical nutritional treatment procedures, sets out the coding criteria and proposes suggestions to improve coding at the hospital level.

Keywords:

Malnutrition. Hospitals. Clinical coding. International Classification of Diseases. Scientific societies.

INTRODUCCIÓN Y JUSTIFICACIÓN

El concepto de desnutrición relacionada con la enfermedad (DRE) dista mucho del concepto de la malnutrición diagnosticada clásicamente en la salud pública, que se encuentra determinada, en gran parte, por factores sociodemográficos. En el ámbito hospitalario, el déficit nutricional es consecuencia de diferentes circunstancias relacionadas con la patología del paciente y con la respuesta inflamatoria, que pueden alterar el consumo y los requerimientos de nutrientes. Este déficit nutricional constituye una entidad clínica que se debe discriminar por sí sola, independientemente de la patología o del cuadro nosológico relacionado que la originó y que debe constar en la documentación del episodio asistencial por su repercusión en la atención del paciente.

La codificación clínica es el proceso mediante el cual la información clínica recogida en la documentación clínica o la historia clínica con lenguaje natural se convierte en un lenguaje estandarizado y normalizado, generalmente basado en la asignación de códigos. De esta forma, la codificación clínica permite unificar y homogeneizar el lenguaje médico, los diagnósticos y los procedimientos diagnósticos y terapéuticos, haciendo posible su tratamiento y comparación para diversos fines. Se trata pues de una transformación a un lenguaje universal.

Las áreas de Documentación y de Sistemas de Información y Control de Gestión de los hospitales trabajan con bases de datos médicas que requieren el uso de nomenclaturas o terminologías en la que se identifiquen los diagnósticos que motivan la hospitalización, las comorbilidades presentes en el momento del ingreso, las complicaciones que pudieran presentarse y los procedimientos médicos/quirúrgicos realizados durante la estancia.

En el año 2004, la Sociedad Española de Nutrición Enteral y Parenteral (SENPE) y la Sociedad Española de Documentación Médica (SEDOM) adquirieron el compromiso de llegar a acuerdos para poder definir de una forma más precisa y acertada los tipos de desnutrición y su correspondiente codificación. Dicho acuerdo se materializó en un consenso publicado en 2008, cuyo principal objetivo fue sensibilizar a los médicos responsables para que incluyeran el diagnóstico de desnutrición y los procedimientos con ella relacionados en los informes de alta, y establecer criterios comunes de codificación en la Clasificación Internacional de Enfermedades vigente en ese momento, la CIE-9-MC (1).

Este consenso dio un impulso importante que se vio reflejado en las estadísticas de morbilidad. Al revisar la serie histórica del Con-

junto Mínimo Básico de Datos (CMBD) desde 1997, se observa a partir del año 2008 el aumento progresivo del número de altas hospitalarias que incluyen diagnósticos principales o secundarios de la categoría de "Carencias nutricionales", sobre todo en los hospitales de entre 100 y 200 camas. Con relación a los procedimientos, por el contrario, se observó una estabilización del registro en las altas hospitalarias.

En España, a partir de año 2016, se debe comenzar a utilizar para la codificación clínica, tanto de los diagnósticos como de los procedimientos, una nueva Clasificación Internacional de Enfermedades, la CIE-10 ES (2). El cambio de la CIE-9-MC a la CIE-10-ES coincide con un menor número de altas codificadas bajo esta categoría, probablemente justificado por la curva de aprendizaje y la adaptación de las unidades de codificación al nuevo sistema, mucho más complejo que el anterior, especialmente en los hospitales de más de 1000 camas. Sin embargo, el Registro de Actividad Sanitaria Especializada (RAE-CMBD), según establece el Real Decreto 69/2015, de 6 de febrero, antes CMBD, refleja la recuperación constante de los datos hasta el año 2020, incluso en el contexto de la pandemia de COVID-19 (Fig. 1).

Además de los cambios de la CIE, la evolución de la información clínica pone de manifiesto la necesidad de revisar y actualizar el consenso de 2008 para establecer nuevos criterios que sirvan de guía en el registro y codificación de los diagnósticos de desnutrición en el ámbito de la atención hospitalaria. Aunque en el momento actual se está evolucionando hacia la CIE-11 y existen propuestas de sociedades científicas como la ESPEN para adecuar el diagnóstico de malnutrición (3,4), se requiere una adaptación desde los diagnósticos clínicos de desnutrición basados en los criterios GLIM propuestos por las sociedades científicas (5,6) a los códigos actuales propuestos por la CIE-10-ES para facilitar el trabajo tanto de los clínicos como de los codificadores y mejorar la visibilidad de la DRE.

OBJETIVOS

OBJETIVO GENERAL

Revisar el acuerdo realizado por la Sociedad Española de Nutrición Clínica y Metabolismo y la Sociedad Española de Documentación Médica en 2008 sobre la definición de la desnutrición relacionada con la enfermedad (DRE) y su codificación en el contexto de la actualización de la práctica clínica y el uso de la CIE-10-ES como clasificación de diagnósticos y procedimientos.

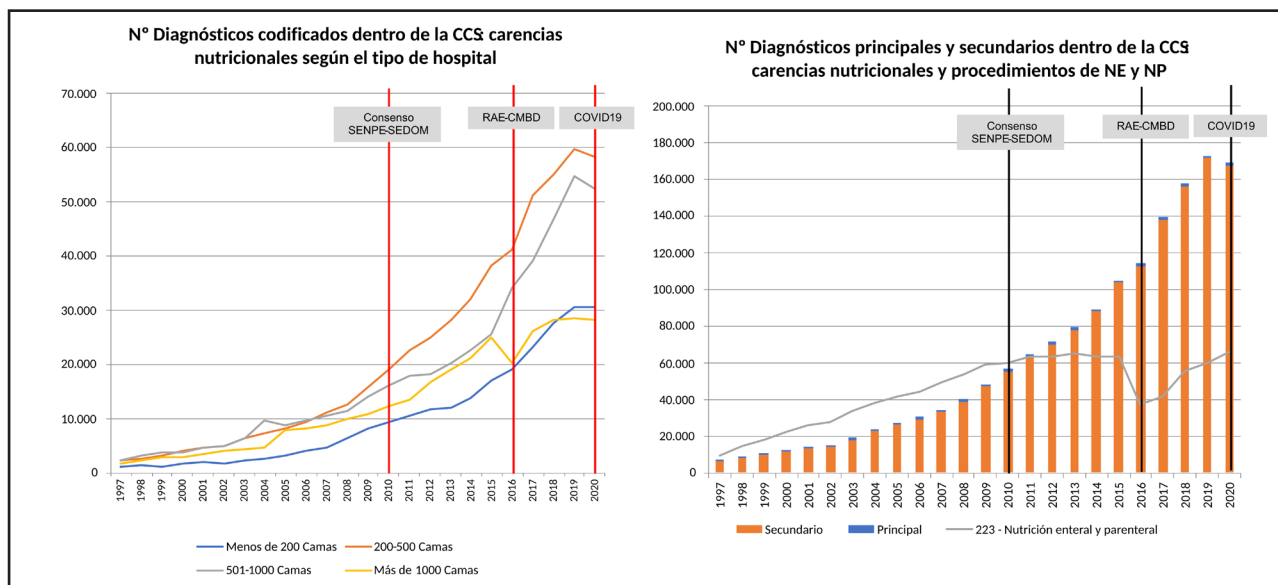


Figura 1.

Serie histórica de los diagnósticos codificados dentro de la categoría de Carencias nutricionales y los procedimientos de soporte nutricional en el CMBD de 1997 al 2020. Fuente: <https://pestadistico.inteligenciadegestion.mscls.es>

OBJETIVOS ESPECÍFICOS

Acordar los criterios de clasificación para el diagnóstico clínico de desnutrición relacionada con la enfermedad, otros diagnósticos relacionados y los procedimientos de tratamiento nutricional, así como su correcta correlación con los códigos de la CIE-10-ES.

- Sensibilizar a los facultativos responsables de los pacientes hospitalizados con DRE sobre la importancia de trasladar el diagnóstico a los informes de alta.
- Realizar una propuesta de mejora del proceso de documentación y codificación de los registros clínicos de los pacientes atendidos por las Unidades de Nutrición Clínica y Dietética.

CRITERIOS CLÍNICOS DE CLASIFICACIÓN

DESNUTRICIÓN RELACIONADA CON LA ENFERMEDAD (DRE)

Riesgo nutricional o fenotipo de desnutrición

Situación que viene definida por la presencia de un resultado positivo en una prueba validada de cribado nutricional (p. ej., MUST, NRS-2002, NST, CIPA, CONUT) o por el cumplimiento de uno o más criterios fenotípicos de DRE según la GLIM (4), en cualquier grado, en ausencia de criterios etiológicos (Tabla I). La existencia de DRE en grado moderado o grave excluye la inclusión en esta categoría.

DRE leve

Este diagnóstico no está incluido en los criterios GLIM que hemos adoptado como patrón de referencia, por lo que proponemos no utilizar este código.

DRE moderada

Presencia de uno o más criterios fenotípicos de DRE, de grado moderado, en presencia de uno o más criterios etiológicos. Ante la ausencia de criterios para distinguir entre la reducción de masa muscular moderada y la grave, cuando el criterio definitorio de DRE sea este, el grado que constará será el moderado (4).

DRE grave

Presencia de algún criterio fenotípico de DRE de grado grave (pérdida de peso o IMC bajo) junto con al menos un criterio etiológico.

DRE no especificada

Presencia de datos indirectos de desnutrición como circunferencia braquial ($\leq 23,5$ cm) o circunferencia de pantorrilla < 33 cm, o alteración analítica o sospecha de desnutrición (7). Esta medida se debe ajustar en las personas con sobrepeso-obesidad. Así, para un IMC entre 25 y 29,9 kg/m² se deben restar

3 cm a la medida efectuada. En las personas con IMC entre 30 y 39,9 kg/m² se deben restar 7 cm, y en las personas con obesidad mórbida (IMC > 40 kg/m²) se deben restar 12 cm (8).

OTROS DIAGNÓSTICOS NUTRICIONALES

Entidades relacionadas con el estado nutricional que suponen un diagnóstico de DRE en sí mismos, coexisten y determinan el consumo alimentario o son factores de riesgo cuando no se puede establecer el diagnóstico clínico de desnutrición.

Malabsorción

Alteración en el proceso de digestión o absorción de los alimentos. En realidad, cuando está alterada la fase luminal de la digestión se debe hablar de maldigestión, pero en la práctica se utiliza el término malabsorción para las alteraciones de todo el proceso. El síntoma habitual es la diarrea crónica acompañada de pérdida de peso.

Sarcopenia

Enfermedad progresiva del músculo esquelético que se caracteriza por una pérdida de masa y función muscular. Para establecer el diagnóstico de masa muscular reducida, las técnicas validadas más usadas, por su accesibilidad y por disponer de puntos de corte establecidos, son la bioimpedanciometría y la circunferencia de la pantorrilla (Tabla II). Otras técnicas diagnósticas también tienen puntos de corte establecidos pero son menos accesibles (TAC, resonancia magnética).

Obesidad

Enfermedad multifactorial crónica y compleja definida como una acumulación excesiva de tejido adiposo que puede deteriorar el estado de salud; se define según la Organización Mundial de la Salud por un índice de masa corporal (peso en kg dividido entre el cuadrado de la talla en metros) superior a 30. La demostración, mediante técnicas de composición corporal, de un porcentaje de tejido adiposo superior al percentil 95 para la edad y el sexo del paciente también puede servir para establecer el diagnóstico de obesidad (Tabla III).

Tabla I. Criterios de desnutrición según la *Global Leadership Initiative on Malnutrition (GLIM)* (3,5)

Criterios fenotípicos		
Pérdida de peso	IMC bajo	Reducción de la masa muscular (4)
> 5 % en < 6 meses o > 10 % en > 6 meses	< 20 si < 70 años < 22 si > 70 años	Con métodos de medida de composición corporal validados
Criterios etiológicos		
Ingesta o absorción de nutrientes reducida	Inflamación	
≤ 50 % de los requerimientos energéticos > 1 semana o cualquier reducción > 2 semanas	Enfermedad o daño agudo	
Presencia de enfermedad GI crónica que afecte a la absorción	Relacionada con enfermedad crónica	
Gravedad de la malnutrición en función del criterio fenotípico		
	% pérdida de peso	IMC (kg/m ²)
Estadio 1 (moderada)	5-10 % en < 6 meses	< 20 si < 70 años
	10-20 % en > 6 meses	< 22 si ≥ 70 años
Estadio 2 (severa)	> 10 % en < 6 meses	< 18,5 si < 70 años
	> 20 % en > 6 meses	< 20 si ≥ 70 años

1. Se requiere al menos un criterio fenotípico y un criterio etiológico para el diagnóstico de malnutrición.
2. Puede basarse en el uso de técnicas como la bioimpedanciometría, la ecografía, la absorciometría de rayos X o la tomografía axial computarizada, o en métodos clínicos como la medición de la circunferencia de la pantorrilla o del brazo, o el examen físico realizado por personal entrenado.
3. Considerar los síntomas gastrointestinales como marcadores que dificultan la ingesta o la absorción (disfagia, náuseas, vómitos, diarrea o dolor abdominal). Valorar su severidad, intensidad, frecuencia y duración.
4. La reducción de la asimilación de comida o nutrientes se asocia a enfermedades malabsorptivas como el síndrome de intestino corto, insuficiencia pancreática o la cirugía bariátrica. También con trastornos como la estenosis esofágica, la gastroparesia y la pseudoostrucción intestinal. La malabsorción es un diagnóstico clínico que se manifiesta como diarrea crónica, esteatorrea o alto débito por ostomías. Usar el juicio clínico o estudios adicionales para valorar la severidad en base a la frecuencia, duración o cuantificación de la grasa fecal y/o volumen de las pérdidas.
5. La inflamación aguda grave generalmente aparece en pacientes con infección grave, quemaduras, trauma o traumatismo craneoencefálico. El resto de las situaciones de daño / enfermedad aguda deben considerarse moderadas o leves.
6. La inflamación grave generalmente no aparece en situaciones de cronicidad. La inflamación crónica o recurrente, de intensidad leve a moderada, generalmente ocurre en pacientes con enfermedad maligna, enfermedad pulmonar obstructiva crónica, insuficiencia cardíaca congestiva, enfermedad renal crónica o en cualquier enfermedad con inflamación crónica o recurrente. Nótese que la inflamación transitoria de intensidad leve no sobrepasa el umbral de este criterio etiológico.
7. La proteína C reactiva puede usarse como medida de laboratorio de apoyo.
8. La gravedad de la DRE se establece en base a los criterios fenotípicos (los criterios etiológicos sirven para contextualizar el caso, guiar la intervención nutricional y anticipar los resultados).

Tabla II. Límites recomendados para el diagnóstico de masa muscular reducida o sus marcadores alternativos (6-8)

	Hombres	Mujeres
Índice de masa magra apendicular (ALMI) o índice de músculo esquelético apendicular (ASMI), kg/m ² (BIA)	< 7	< 5,7
Índice de masa magra (FFMI), kg/m ² (BIA)	< 17	< 15
Circunferencia de pantorrilla, cm (1)	< 34	< 33

(1) Se debe ajustar el valor obtenido en función del IMC, sumando 4 cm (IMC < 18,5) o restando 3 cm (IMC: 25-30), 7 cm (IMC: 30-40) o 12 cm (IMC > 40).

Tabla III. Puntos de corte (percentil 95) de porcentaje de tejido adiposo (bioimpedanciometría, 50 kHz) en individuos sanos (9)

Edad (años)	Hombres	Mujeres
15-24	24,4	34,9
25-34	26,8	35,4
35-44	28,1	35,9
45-54	28,7	36,5
55-64	30,6	40,5
65-74	32,6	44,4
75-84	31,2	45,2
≥ 85	33,4	46,9

Disfagia orofaríngea

Dificultad para que pase el alimento desde la boca y la faringe hasta el esófago. Aunque su presencia puede ser muy evidente en las situaciones de mayor gravedad (ictus extenso, enfermedad neurodegenerativa avanzada, etc.), en otros casos se necesita un alto índice de sospecha clínica o el uso sistemático de técnicas de cribado (EAT-10) en las poblaciones de riesgo, cuyos resultados deben confirmarse con técnicas como el método de exploración clínica volumen-viscosidad (MECVV), la fibroendoscopia de la deglución o la videofluoroscopia.

PROCEDIMIENTOS DEL TRATAMIENTO MÉDICO NUTRICIONAL (TMN)

- *Nutrición parenteral por vía central*: método de alimentación diferente de la vía digestiva mediante el que se administran por vía endovenosa la mayoría de los nutrientes y el agua que precisa el paciente. El extremo del catéter endovenoso se localiza en la vena cava superior o la aurícula derecha.

- *Nutrición parenteral por vía periférica*: método de alimentación diferente de la vía digestiva mediante el que se administran por vía endovenosa periférica la mayoría de los nutrientes que precisa el paciente.
- *Suplementos orales/nutrición enteral oral*: uso de *alimentos para usos médicos especiales* (o fórmula enteral) como complemento de una alimentación convencional insuficiente para las necesidades del paciente. Se denomina nutrición enteral oral a aquella situación en que la fórmula administrada por vía oral aporta más de 1000 kcal diarias o más del 50 % de las necesidades calóricas del paciente.
- *Nutrición enteral por sonda nasogástrica (SNG) o gastrostomía*: administración de una fórmula enteral mediante una sonda cuyo extremo distal se encuentra localizado en el estómago.
- *Nutrición enteral por sonda nasoyeyunal (SNY) o yeyunostomía*: administración de una fórmula enteral mediante una sonda cuyo extremo distal se encuentra localizado en el yeyuno.

Igualmente, se deben tener en cuenta los procedimientos relacionados con la colocación de los diferentes dispositivos de nutrición.

- *Catéter central*: catéter percutáneo, de inserción central o periférica y de corta, media o larga duración, que permite la infusión de nutrientes directamente en la vena cava superior o la aurícula derecha.
- *Sonda nasogástrica*: catéter colocado a través de la nariz, con el extremo distal ubicado en la cámara gástrica, que permite la administración de nutrientes por esta vía. El procedimiento de sondaje puede realizarse a ciegas o bajo visión directa con técnicas de imagen endoscópica o radiológica.
- *Gastrostomía*: catéter colocado a través de la pared abdominal, con el extremo distal ubicado en la cámara gástrica, que permite la administración de nutrientes por esta vía. Puede ser endoscópica, radiológica o quirúrgica.
- *Yeyunostomía*: catéter colocado a través de la pared abdominal, con el extremo distal ubicado en el yeyuno, que permite la administración de nutrientes por esta vía. Puede ser radiológica o quirúrgica.

CRITERIOS DE CODIFICACIÓN

CONSTATACIÓN Y FUENTES DOCUMENTALES

Para la asignación de un código será necesario que cualesquiera de las entidades nosológicas se refleje como diagnóstico (principal y/o secundario) y que las actuaciones de tratamiento nutricional se reflejen como procedimientos en la historia clínica del paciente, cualquiera que sea su formato.

La fuente documental fundamental es el informe de alta del episodio asistencial. Sin embargo, para la correcta codificación del episodio también pueden consultarse otros documentos complementarios. Por tal motivo, es válida la consignación, por

el médico responsable o por el equipo de Tratamiento Médico Nutricional, del diagnóstico de desnutrición en otros documentos o informes clínicos del episodio.

PAUTAS Y NORMATIVA DE CODIFICACIÓN

- Se seguirán las pautas del proceso de codificación clínica según las normas y convenciones de la CIE vigente, es decir, la CIE-10-ES.
- De forma general, y en el ámbito de la hospitalización, siempre que se refleje un diagnóstico como “sospecha de” se considerará como si estuviera confirmado o presente, tal y como lo establece la normativa CIE-10 para estas situaciones (2).

CODIFICACIÓN DEL DIAGNÓSTICO DE DESNUTRICIÓN RELACIONADA CON LA ENFERMEDAD (DRE)

Como se indica en el *Manual de codificación (2)*, estando actualmente vigente la 5.ª edición, en la CIE-10-ES no se considera específicamente la desnutrición relacionada con la enfermedad en el paciente adulto. Se definen los distintos tipos de desnutrición y su clasificación como se muestra a continuación:

- E40 Kwashiorkor, o desnutrición proteica.
 - E41 Marasmo nutricional, o desnutrición calórica (marasmo).
 - E42 Kwashiorkor marasmático, o desnutrición mixta calórico-proteica (Kwashiorkor marasmático).
- La desnutrición mixta se clasifica según su severidad en:
- Leve o de primer grado, código E44.1: Malnutrición calórico-proteica leve.
 - Moderada o de segundo grado, código E44.0: Malnutrición calórico-proteica moderada.
 - Grave o de tercer grado, código E43: Malnutrición calórico-proteica grave no especificada.
 - La desnutrición en la edad pediátrica se codifica con el código E45: Retraso del desarrollo secundario a malnutrición calórico-proteica.
 - Desnutrición no especificada, código E46.

La tabla IV muestra la adaptación de los criterios GLIM a estos códigos.

La codificación de los términos incluidos en el apartado de *Otros diagnósticos nutricionales* se deberá regir siguiendo la normativa habitual. Se deben tomar en cuenta algunos diagnósticos específicos que quedan excluidos del diagnóstico principal, recogido como “*Excluye*” para los códigos de malabsorción (K90-K91). Los códigos de *Estado* incluidos en esta sección tienen el objetivo de aportar información adicional y facilitar su registro en la historia clínica.

En cuanto a la codificación de dispositivos, si se coloca el dispositivo durante el ingreso, se debe codificar el procedimiento de colocación del dispositivo y, si el paciente es portador del dispositivo, se debe codificar con un código diagnóstico de portador: códigos Z de la tabla V.

CODIFICACIÓN DE LOS PROCEDIMIENTOS DE TRATAMIENTO MÉDICO NUTRICIONAL

- En la nutrición parenteral se deberá codificar la colocación del catéter correspondiente siempre que se realice durante el ingreso o el mismo episodio asistencial.
- La nutrición enteral por sonda se codificará como tal, pero es importante recalcar que, cuando se coloca un dispositivo durante el episodio, se debe codificar como procedimiento. Sin embargo, la presencia del dispositivo no presupone la prescripción de un tratamiento nutricional, que debe estar documentado a mayores, es decir, que se debe documentar como nutrición enteral sea a la dosis que sea, incluso si se trata de una nutrición enteral trófica o complementaria.
- Si la suplementación oral es mayor de 1000 kcal día, se codificará como nutrición enteral, debiendo quedar reflejada en la documentación del episodio asistencial por parte del profesional responsable o correspondiente.
- La realización de un procedimiento nutricional no conlleva la presunción del diagnóstico de desnutrición.
- Ante la presencia de un tratamiento nutricional sin diagnóstico de desnutrición se deberá constatar la existencia de este y, si no existe, se registrarán solo los códigos del procedimiento correspondiente.

La tabla VI incluye la relación de los códigos de los distintos procedimientos de tratamiento médico nutricional.

Tabla IV. Codificación de la desnutrición según la gravedad y la etiología

Diagnóstico	Código	Definición
Riesgo nutricional (cribado positivo o solo un criterio GLIM que no permite diagnóstico)	E46	Cribado de riesgo nutricional empleando cualquier herramienta validada (MUST, MNA-SF, NRS 2002, MST, SNAQ, otros) Presencia solo un criterio GLIM fenotípico que no permite diagnóstico
DRE moderada	E44.0	Diagnóstico de DRE moderada según criterios GLIM* (al menos un criterio etiológico y un criterio fenotípico)
DRE grave	E43	Diagnóstico de DRE grave según criterios GLIM* (al menos un criterio etiológico y un criterio fenotípico)

Tabla V. Codificación de otros diagnósticos nutricionales

Diagnóstico	Código
Malabsorción intestinal (según etiología)	K90.0-K90.9 (codificar según la causa de la malabsorción)
Malabsorción intestinal después de cirugía gastrointestinal	K91.2
Sarcopenia	M62.84
Sobrepeso y obesidad (diversos tipos y etiología) Con todos los códigos de la categoría E66 tenemos la instrucción: Utilice código adicional para identificar índice de masa corporal (IMC), si se conoce (códigos Z68.-)	E66.01-E66.9
Disfagia, no especificada	R13.10
Disfagia neurógena	R13.19
Estado de portador de dispositivos de alimentación: Portador de SNG Estado de gastrostomía Estado de ileostomía Estado de otras estomas artificiales del tracto gastrointestinal	Z97.8 Z93.1 Z93.2 Z93.4
Estados posprocedimiento que pueden comprometer el aporte nutricional: Estado de derivación intestinal y anastomosis Estado de cirugía bariátrica	Z98.0 Z98.84

Tabla VI. Codificación de procedimientos de tratamiento médico nutricional

Procedimiento	Código
Nutrición parenteral por vía central	3E0436Z
Nutrición parenteral por vía periférica	3E0336Z
Suplementos orales/nutrición enteral oral/nutrición por SNG	3E0G76Z
Nutrición enteral por SNY	3E0H76Z
Nutrición enteral por SNG/gastrostomía	3E0G36Z
Nutrición enteral por SNY/yeyunostomía	3E0H36Z
Inserción de catéter central (VCS)	02HV33Z
Inserción de sonda nasogástrica	0DH67UZ
Inserción de gastrostomía percutánea (+ añadir método de guiado: p. ej., ENDOSCOPIA → PEG)	0DH63UZ + 0DJ68ZZ
Inserción de yeyunostomía percutánea (añadir método de guiado como en el caso de PEG)	0DHA3UZ
Inserción de gastrostomía quirúrgica	0DH60UZ
Inserción de yeyunostomía quirúrgica	0DHA0UZ

CÓMO MEJORAR LA CODIFICACIÓN A NIVEL HOSPITALARIO

Diversas razones justifican la necesidad de optimizar la *calidad* de la estructura de nuestros registros clínicos:

- *Formación*: es importante tener una formación básica sobre el proceso de codificación. Debería incluirse formación sobre estos aspectos, en el marco de la gestión de la calidad, en el período de formación como médico interno residente (MIR). Es importante que la información se recoja con la máxima fiabilidad y exactitud, por lo que es necesario estar al día de las actualizaciones periódicas no solo de la CIE-10-ES sino también de las publicaciones periódicas en forma de Cuadernos de Codificación que realiza el Ministerio de Sanidad.
- *Comunicación*: es fundamental que se implique a los profesionales de Documentación y Sistemas de Información y Control de Gestión de nuestros hospitales que vayan a codificar nuestra actividad. Para ello, debemos tener claro de qué estamos hablando y transmitir con buenos argumentos la importancia de una codificación lo más correcta posible. Es esencial un esfuerzo conjunto entre clínicos y codificadores para lograr una documentación, codificación y recuperación de la información completa y precisa. La labor de los clínicos es dejar reflejado en los informes, de forma correcta y teniendo en cuenta lo que se quiere codificar, la mejor descripción del diagnóstico principal y de los secundarios, así como de los procedimientos.
- *Simplicidad*: las fichas que se utilicen en la historia clínica electrónica (HCE) deben facilitar el registro de la información clínica de forma sencilla e intuitiva pero estructurada, con la posibilidad de identificar términos y conceptos que puedan codificarse y sean explotables.
- *Economía*: la utilización del sistema de codificación representa una mejora en la gestión de las unidades, favoreciendo los estudios clínicos, epidemiológicos y de investigación, y la financiación por procesos.

- *Gestión de la calidad*: en los tiempos actuales, la gestión se impone y tenemos la posibilidad de “humanizarla”. No se trata solo de registrar códigos, se trata de que esos números describan lo más fehacientemente posible nuestro trabajo diario y que eso repercuta en un mejor cuidado de nuestros pacientes.

PROPUESTAS DE MEJORA EN EL PROCESO DE DOCUMENTACIÓN Y CODIFICACIÓN

Por todo lo anteriormente expuesto, y con el fin de mejorar los registros clínicos de los pacientes con desnutrición relacionada con la enfermedad (DRE) y de las Unidades de Nutrición y Dietética (UNCyD), proponemos las siguientes mejoras en el proceso de documentación y codificación, que deberían incorporarse obligatoriamente en todos los centros.

- *Diseñar un modelo de registro en la HCE para las UNCyD que facilite la documentación y estandarización de la evaluación, el diagnóstico, el seguimiento y el tratamiento de los pacientes con DRE*. La información clínica debe cumplimentarse de forma estructurada, con campos definidos como variables, con índices y diagnósticos basados en las guías y consensos clínicos y de codificación. Se recomienda incluir ayudas al registro (desplegables, calculadoras, etc. Anexo 1: <https://www.nutricionhospitalaria.org/anexos/05419-01.pdf>) que garanticen la calidad de la información en la historia clínica electrónica. El campo de diagnóstico debe ser de registro obligatorio y en formato codificado.
- *Consensuar la realización de un informe complementario al informe de alta* (ejemplo en el Anexo 2: <https://www.nutricionhospitalaria.org/anexos/05419-02.pdf>). Cuando lo anterior no es posible, y dada la dificultad de que los informes de alta reflejen las intervenciones de las UNCyD, en algunos centros se realizan informes complementarios y/o de interconsulta por parte de las UNCyD en los que quedan reflejados los diagnósticos y procedimientos realizados.
- *Pactos de gestión*: dada la importancia y relevancia de una adecuada codificación, desde las gerencias y direcciones de los centros se deberían incluir en los pactos de gestión los indicadores relacionados. En el caso de los códigos relacionados con la DRE y expuestos anteriormente en este documento, si tenemos datos que puedan llegar a afectar a 1 de cada 3 pacientes al ingreso, se podría considerar incluso —como se ha hecho con los códigos vinculados a la infección por SARS-CoV-2— que figuren por defecto en el listado de “diagnósticos favoritos” de todos los servicios y secciones.
- *Flujo de información*: se debe garantizar siempre el flujo correcto y en todas direcciones de la información entre los diferentes departamentos del centro asistencial.
- *Equipos*: hay que analizar las necesidades de cada departamento y estructurar la información clínica según las necesidades de cada servicio. Se deben buscar métodos de optimización y resolución de problemas ante cualquier problema que pueda surgir durante la gestión de la información. Es necesario que todos los miembros del equipo que usen y traten la información clínica se impliquen para solucionar cualquier problema que surja en la gestión de la información y para mejorar el proceso de gestión de dicha información.

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LA IMPORTANCIA DE LOS DETERMINANTES SOCIALES EN LA DETECCIÓN DE SÍNTOMAS DEPRESIVOS Y SU RELACIÓN CON EL CONSUMO DE AGUA DEL GRIFO

Sr. Director:

Tenemos algunas consideraciones acerca del estudio de Pérez-Fernández y cols. (1). En primer lugar, queremos señalar que el artículo no considera los determinantes sociales que podrían influir en la relación entre el origen del agua consumida y los síntomas de depresión y ansiedad. En la propia bibliografía citada, el origen étnico y el nivel educativo son covariables importantes (2). En este contexto, la Organización de Consumidores y Usuarios recoge que el agua del grifo es 150 veces más barata que el agua embotellada (3), situando a Ourense como una de las ciudades donde es más asequible (4), lo cual podría introducir un sesgo en la muestra.

Los autores indican un aumento importante de la prevalencia de la depresión a nivel mundial citando un estudio del inicio de la pandemia de COVID-19 (5). Si bien la evidencia disponible no permite asegurar que exista un aumento claro de las enfermedades mentales en los adultos (6), sí hay numerosos estudios en los que se describe un aumento puntual de problemas de salud mental durante y tras el confinamiento por la pandemia de COVID-19. Esta situación tuvo consecuencias negativas directas e indirectas en las relaciones sociales y en el desarrollo habitual de la mayoría de los empleos que requerían contacto directo con otras personas. Una revisión sistemática (7) sobre esta cuestión en una población europea mostró que factores como la sensación de soledad y el miedo a la infección o al desempleo se relacionaban con un incremento del riesgo de desarrollar o de que empeorasen los síntomas relacionados con

la ansiedad, la depresión, el estrés postraumático o la ideación suicida. Además, este riesgo era significativamente mayor entre las clases socioeconómicas bajas y entre las mujeres. En el caso de las mujeres, el riesgo de mantener estos síntomas en los años posteriores, a pesar de la disminución de las restricciones, era significativamente mayor.

Existen numerosas sustancias en el agua del grifo que podrían relacionarse con la depresión y que el artículo obvia al analizar los efectos observados. En un estudio de cohortes reciente (8) se describieron varias sustancias asociadas con la depresión y la ansiedad, como el manganeso, el selenio, el cadmio, el cobre y el hierro.

Tampoco se valora en el análisis el consumo de suplementos de biotina. En un boletín de 2023, la Agencia Española de Medicamentos y Productos Sanitarios expuso que la biotina interfiere con la estreptavidina en los inmunoanálisis tiroideos, provocando resultados de función tiroidea falsamente elevados o reducidos (9). En este boletín se recomienda informar al profesional de laboratorio sobre el consumo de biotina antes de solicitar las pruebas.

Nos gustaría preguntar a los autores si realmente coincide el *odds ratio* del IMC con el límite superior (ambos 0,76) y si consideran que el tipo de agua consumida de manera habitual es una variable robusta, ya que puede variar a lo largo de la vida.

De cara a futuras investigaciones, recomendamos aumentar el tamaño de la muestra para aumentar la precisión y poder considerar factores adicionales, especialmente los determinantes sociales, para reforzar la validez de las conclusiones.

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OMEGA-3 Y PARTO PRETÉRMINO: DESCIFRANDO LAS PIEZAS DEL ROMPECABEZAS PARA SU PREVENCIÓN

Sr. Editor:

Cada año nacen aproximadamente 15 millones de recién nacidos prematuros. El parto pretérmino es la causa principal de mortalidad neonatal a nivel mundial. Aunque la mayoría de los nacimientos pretérmino ocurren en la atapa tardía, aquellos que nacen más tempranamente experimentan desproporcionadamente más tasas altas de complicaciones relacionadas con la prematuridad (1).

Después de más de tres décadas de estudio se han definido con más claridad los beneficios de la ingesta de los AGPI omega-3 en la gestación, principalmente la del ácido docosahexanoico (DHA) y el ácido eicosapentanoico (EPA), incluidas la reducción del parto pretérmino (< 37 semanas) y del parto pretérmino temprano (< 34 semanas) (2,3), y una positiva influencia sobre el desarrollo del cerebro fetal (4) y la composición corporal (5,6).

Derivado de la última revisión Cochrane sobre la acción de los omega-3 en el embarazo, que se publicó en el 2018, incluyó más de 70 estudios controlados y fue realizada por Middleton y cols. (7), se encontró una evidencia fuerte en los estudios cualitativos entre las mujeres gestantes asignadas al grupo con ingesta de pescado, aceite de pescado, DHA o EPA, o a las que se recomendó que ingiriesen alimentos con omega-3; estas tuvieron una reducción del riesgo de parto pretérmino a < 37 semanas del 11 % y una reducción del riesgo de parto pretérmino temprano a < de 34 semanas del 42 %. El posible mecanismo de acción es que los AGPI omega-3 compiten con el ácido araquidónico inhibiendo la producción de eicosanoides

proinflamatorios e incrementando los leukotrienos antiinflamatorios como el B5 y la prostaglandina F3, en lugar del leukotrieno B4 y la PGE2 (8).

Para los tomadores de decisiones de la salud pública nacional surgen necesidades urgentes por resolver en nuestro país sobre este tema: aumentar la información sobre los beneficios de los AGPI omega-3 en los pacientes en edad reproductiva, incrementar los recursos para obtener los niveles óptimos de AGPI omega-3 en sangre en población gestante, financiar la suplementación de las mujeres embarazadas con deficiente ingesta de omega-3 y promover el desarrollo de estudios donde se puedan validar cuestionarios para estimar la ingesta de AGPI omega-3 en la población gestante mexicana sobre la base de un registro diario de alimentos, como ya se ha comprobado en otros países, lo cual ahorraría recursos a nuestro sistema de salud, con el propósito de ofrecer la prevención primaria para disminuir el parto pretérmino (9,10). Los ginecólogos debemos estar comprometidos en nuestra práctica diaria para recomendar la ingesta de AGPI omega-3 a través de la nutrición y/o suplementación en la etapa preconcepcional y en el embarazo, y con ello disminuir el alto costo de los nacimientos pretérmino y sus secuelas en la población infantil de nuestro país.

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Conflicto de intereses: los autores declaran no tener conflicto de interés.

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Nutrición Hospitalaria

DOI: <http://dx.doi.org/10.20960/nh.05430>

LA NECESARIA Y COMPLEJA MIRADA BIOPSIOSOCIAL A LA ALIMENTACIÓN

Sr. Editor:

En el número 3 de la revista *Nutrición Hospitalaria* de este año se publicó una interesante réplica realizada por Zúñiga (1) que, entre otros aspectos de la malnutrición por exceso en Chile, expresa la necesidad de que cada persona deba presentar concienciación sobre la alimentación que realiza, considerando el grado de voluntad que el comer en sí implica en la presentación de enfermedades crónicas. Estando de acuerdo con este paradigma, ¿qué otros factores condicionan la alimentación?

Desde la teoría, el acto voluntario de comer conjuga a la vez factores intraindividuales biológicos y psicológicos, y extra individuales, donde se pueden mencionar la cultura o la situación económica de la persona, diferenciado, además, la existencia de una diversidad en la alimentación según el sexo, el género y las conductas alimentarias (2). Este entrelazado complejiza a la alimentación y la enmarca en la necesidad de revalorar las condicionantes que facultan a una persona a comer, teniendo en cuenta situaciones que son direccionadas, entre otros aspectos, por los entornos y patrones alimentarios, así como por la disponibilidad de algunos alimentos.

Entonces, ¿las personas comen lo que pueden o eligen comer lo que quieren? Si existiera una respuesta adecuada a esta interrogante, las políticas públicas, las actividades y las acciones destinadas a lograr una alimentación saludable estarían más resueltas. Pero, esta enmarañada situación vuelve a contextualizar a la alimentación en la complejidad biopsicosocial que representa. Motivaciones emocionales, culturales, sociales o sanitarias, entre otras, son reconocidas al momento del comer (3).

¿Se puede elegir qué comer? Entre las atribuciones propias del ser humano y sus derechos está la autonomía en el co-

mer; pero ¿siempre elijo lo que como? Vuelve esta compleja situación biopsicosocial que acompaña a la alimentación: la presentación de alguna enfermedad, la afectación del estado anímico, el nivel educacional o la situación económica, entre otras condicionantes, retoman el levantamiento de una barrera que limita la elección de alimentos o preparaciones culinarias para el consumo.

Entonces, ¿las personas comen lo que pueden? Esta pregunta se alinea inevitablemente al reconocer una influencia de los aspectos económicos que dirigen la alimentación que, a veces o en momentos de crisis, lleva a recibir ayuda social para cubrir estas necesidades básicas o, en otros casos, obliga al endeudamiento individual y familiar con tarjetas de crédito en la adquisición de alimentos (4).

Otro aspecto relevante en el “comer lo que se puede” está direccionado por las normas socioculturales de la comunidad de origen de una persona (5), las que a la vez se ven potenciadas por los entornos alimentarios saludables... o no saludables. En estos últimos, ambientes alimentarios donde exista, por ejemplo, una mayor oferta del comercio minorista de frutas y verduras, se relaciona con un mayor consumo de estos alimentos saludables, acción que suele acompañarse de un limitado marketing alimentario y, por lo mismo, presenta una baja adherencia comunitaria o individual (6).

Como reflexión final, la alimentación debe estar acompañada de una mirada más holística que entretela aspectos biológicos, psicológicos, sociales y también, por qué no mencionarlo, espirituales. La individualidad se expresa de manera latente en la alimentación, ya que los miembros de una misma cultura o los grupos familiares presentan diversos patrones alimentarios. Es complejo pero necesario recordar por quienes practicamos la dietética en sujetos que están viviendo diversas trayectorias vitales.

Conflictos de interés: la autora declara no presentar conflictos de interés en relación con el artículo.

Uso de inteligencia artificial (IA): para su redacción, no se ha hecho uso de la IA ni de otras tecnologías que usen IA en el proceso de elaboración del artículo.

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RELATIONSHIP BETWEEN FERMENTED DAIRY CONSUMPTION, GUT MICROBIOTA AND TYPE 2 DIABETES

Dear Editor,

The article by Baraquet et al. (1), published in *Nutrición Hospitalaria*, analyzed the relationship between consumption of dairy products and type 2 diabetes (T2D) in an Argentine population. Clinical and anthropometric variables were evaluated. The results showed that the consumption of fermented dairy products was inversely associated with blood glucose levels and glycated hemoglobin. Additionally, higher total dairy intake was related to a lower probability of developing T2D. Here, we wish to contribute with a reflection on this research, considering the role of the microbiota.

The relationship between gut microbiota and type 2 diabetes (T2D) is an emerging field of study that promises to offer new perspectives on the pathogenesis and treatment of this disease (2). The gut microbiome participates in complex metabolic networks, influencing diseases such as T2D, Alzheimer's, and Parkinson's (3).

It has been demonstrated that treatment with the plant *Astragalus* improves intestinal barrier function and immunity, acting on the microbiome to treat T2D (4). Furthermore, bidirectional interactions between hypoglycemic medications and the gut microbiome have been identified in patients with T2D, suggesting that the microbiome may influence the effectiveness of these treatments (2). In Latin America, genetic and epigenetic variability, along with microbiome composition due to historical factors, could have a particular impact on the association between the microbiome and T2D, factors that we believe would be valuable to consider (5).

Finally, the study by Perazza et al. (6) found that fermented dairy protein intake modulates gut microbiota composition and improves insulin sensitivity in diet-induced obese mouse models. These findings are consistent with the results observed in the article commented on here. These associations point the way for future research integrating dairy product consumption, microbiota, and T2D to develop effective preventive strategies.

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Artificial intelligence: the authors declare not to have used artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.



Nutrición Hospitalaria

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SOBRE LA OBESIDAD EN NIÑOS DE MÉXICO

Sr. Editor:

Nos dirigimos a usted para comentar sobre el artículo titulado “Sobrepeso y obesidad en niños de 5 a 11 años en México en el periodo 1999-2021: ¿Por qué es necesario un abordaje interdisciplinario?” de García Alvarado, recientemente publicado en *Nutrición Hospitalaria*. Agradecemos cómo los autores resaltan la gravedad de la obesidad infantil y su evolución en el país.

Coincidimos plenamente con la necesidad de un abordaje interdisciplinario para enfrentar este problema que es multifactorial (Fig. 1). Sin embargo, queremos llamar la atención sobre un aspecto crucial: el actual sistema de etiquetado de alimentos en México. Consideramos que esta medida, aunque bien intencionada, no ha logrado reducir significativamente el consumo de productos procesados (1). Al contrario, puede incrementar la sensación de culpa en los consumidores y, en los individuos con predisposición genética, favorecer el desarrollo de trastornos de la conducta alimentaria (TCA), como los atracones y la bulimia, especialmente prevalentes entre los adolescentes (1).

Además, queremos abordar la eficacia del índice de masa corporal (IMC) como herramienta de evaluación como lo hace la encuesta nacional de nutrición. Este método no considera variables importantes como el desarrollo muscular, el edema o la talla baja (2), características frecuentes en la población mexicana. Otras mediciones, como el porcentaje de grasa corporal, pueden ser más precisas, especialmente al evaluar el riesgo de desarrollar enfermedades metabólicas (3). Un enfoque más adecuado debería integrar las dimensiones genéticas, metabólicas, psicológicas, pediátricas y psiquiátricas, involucrando a las familias en su totalidad.

Otro tema a considerar es que, en México, muchos padres no tienen una percepción adecuada del estado nutricional de sus

hijos, buscando ayuda nutricional para pacientes “delgados” y no para niños con sobrepeso (4).

Proponemos un cambio hacia políticas y propuestas educativas que promuevan la actividad física y la convivencia familiar durante las comidas. Es fundamental crear espacios que reduzcan el sedentarismo y fomentar hábitos saludables desde una perspectiva integral y holística tal y como lo sugieren los autores.

Según las predicciones de este artículo (6), es probable que veamos un aumento de la obesidad, especialmente entre mujeres y niños. Por lo tanto, debemos enfocarnos en los pacientes que actualmente se encuentran en percentiles adecuados pero que están en situaciones de riesgo, como el sedentarismo o las dietas inapropiadas, antes de que desarrollen sobrepeso u obesidad. Esto subraya que la prevención es nuestra mejor herramienta, idealmente a través de metabolitos que nos permitan identificar qué pacientes están en riesgo de desarrollar enfermedades metabólicas de forma temprana.

Adicionalmente, estamos explorando otros metabolitos como el mio-inositol, ya utilizado en pacientes con síndrome de ovarios poliquísticos, que podrían mejorar condiciones metabólicas como la resistencia a la insulina (5). Creemos que la inclusión de estos enfoques innovadores podría ofrecer nuevas perspectivas en el tratamiento de la obesidad infantil y contribuir a una mejora significativa en la salud de los niños mexicanos.

Agradecemos la oportunidad de compartir nuestras observaciones y esperamos que estas contribuyan a una discusión más amplia sobre cómo abordar eficazmente la obesidad infantil en México.

Norma Cipatli Ayuzo del Valle, Perla Pérez Treviño,
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Conflicto de intereses: los autores declaran no tener conflicto de interés.

Inteligencia artificial: los autores declaran no haber usado inteligencia artificial (IA) ni ninguna herramienta que use IA para la redacción del artículo.

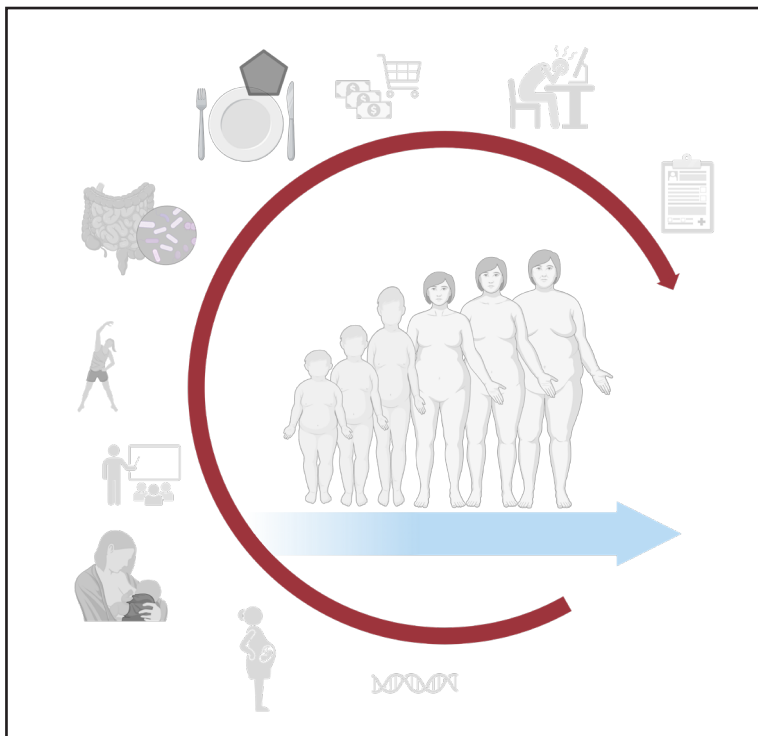


Figura 1.

Factores que afectan al desarrollo de la obesidad: dieta y nutrición, ambiente socioeconómico, estilo de vida sedentario, atención médica y políticas de salud, microbioma, actividad física, salud mental, factores genéticos y prenatales. La flecha azul en la parte inferior representa el tiempo, mostrando que estos factores influyen a lo largo de la vida de una persona desde la infancia.

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Crítica de Libros

TRATADO DE NUTRICIÓN (4.ª EDICIÓN)

Director: Ángel Gil Hernández
Editorial: Editorial Médica Panamericana

Recientemente se ha presentado la 4.ª edición del *Tratado de Nutrición*, dirigido por el Profesor Ángel Gil Hernández, Profesor Emérito y Catedrático del Departamento de Bioquímica y Biología de la Universidad de Granada, y editado por Editorial Médica Panamericana. Esta nueva obra consta de 193 capítulos, 20 más que en la edición anterior, agrupados en 5 tomos, que aúnan las bases fisiológicas, bioquímicas y moleculares de la nutrición, junto con los conocimientos relativos a la composición y el valor nutritivo de los alimentos, la nutrición en el estado de salud y la nutrición clínica. En el *Tratado de Nutrición* han participado más de 350 autores especialistas en diversas áreas de las Ciencias de la Nutrición.

Se trata de un libro didáctico y moderno auspiciado por la Sociedad Española de Nutrición Clínica y Metabolismo (SENPE) y la Fundación Iberoamericana de Nutrición (FINUT). La obra es, sin duda, la más completa e importante escrita en español hasta la fecha sobre nutrición. Su principal objetivo es servir de apoyo a la docencia de estudiantes de grado y posgrado en los ámbitos de Nutrición y Dietética, Ciencias de la Salud, Farmacia, Medicina, Biología, Bioquímica y Biología Molecular, y Enfermería. Asimismo, se trata de un libro de consulta de gran utilidad para los profesionales relacionados con las Ciencias de la Nutrición. La estructura de todos los capítulos sigue el criterio de "libro útil para la enseñanza", centrándose en los objetivos docentes y apoyándose en imágenes y tablas que facilitan la comprensión de la materia.

Durante los últimos 7 años se han producido avances notables en las Ciencias de la Nutrición que justifican esta nueva 4.ª edición, muy especialmente en todo lo que se refiere a las



interacciones de los nutrientes y de otros compuestos de los alimentos con diferentes tejidos órganos y sistemas; a las ciencias ómicas y a sus aplicaciones en el diagnóstico, prevención y tratamiento de la enfermedad; a los efectos de la dieta sobre el microbioma intestinal; a los compuestos bioactivos de los alimentos y sus efectos nutricionales; a los probióticos, prebióticos, simbióticos y posbióticos; a los usos y abusos de los alimentos denominados "ultraprocesados"; a la generación de evidencia de determinados patrones alimentarios como la dieta mediterránea en la prevención de las enfermedades; a los usos de la inteligencia artificial en nutrición y a la publicación de las nuevas guías de tratamiento nutricional de diversas patologías, promovidas y

publicadas por diversas sociedades internacionales, en particular por la European Society of Clinical Nutrition and Metabolism (ESPEN). A continuación se describen brevemente los contenidos de los tomos de esta 4.^a edición y las novedades más importantes respecto a la anterior.

El tomo I está dedicado a las bases fisiológicas y bioquímicas de la nutrición, siendo esencial para la correcta comprensión de los conceptos modernos de la nutrición y el resto de los volúmenes de la obra. En esta nueva edición se han incorporado varios temas sobre la fisiología y el metabolismo de tejidos, órganos y sistemas.

El tomo II contiene información completa para el estudio de la Nutrición Molecular y los últimos avances en las áreas de señalización celular mediada por nutrientes y otros compuestos bioactivos de los alimentos. En este volumen se abordan aspectos fundamentales de la nutrición moderna como son la Nutrigenética, la Nutrigenómica, la Nutriepigenética, así como la Metabolómica, la Metagenómica y la Cronobiología y sus relaciones con la nutrición humana y la nutrición personalizada.

El tomo III aborda la composición y el valor nutritivo de los principales grupos de alimentos e ingredientes alimentarios, describe diferentes tratamientos tecnológicos, su influencia sobre la calidad nutritiva y estudia la estructura de las tablas de composición de alimentos y las bases de datos nutricionales. Además, analiza aspectos relacionados con la producción genética de alimentos, los efectos de los alimentos ultraprocesados sobre la salud y la seguridad e higiene alimentaria, y la información alimentaria que se transmite al consumidor.

El tomo IV estudia los requerimientos nutricionales del ser humano y las guías dietéticas y de vida saludable en las diferentes etapas de vida. Considera aspectos relativos a la nutrición y salud pública, sistemas de información y documentación en nutri-

ción, y la importancia de la inteligencia artificial en la aplicación de la nutrición personalizada y de precisión.

El tomo V se centra en la nutrición en situaciones de enfermedad cuando esta tiene una causa relacionada con la nutrición, su diagnóstico y tratamiento nutricional (desde las recomendaciones dietéticas hasta el tratamiento médico enteral o parenteral). Analiza también la nutrición en diferentes procesos patológicos agudos y crónicos (en niños y adultos), en diferentes ámbitos asistenciales. En ese sentido, se han incorporado los nuevos consensos de las sociedades internacionales de nutrición como ESPEN (European Society for Clinical Nutrition and Metabolism) y ASPEN (American Society for Parenteral and Enteral Nutrition) para el tratamiento nutricional de diversas enfermedades.

La calidad de un buen libro destinado fundamentalmente a la docencia no es algo que se improvisa; es siempre el resultado del deseo continuado de mejorar lo hecho con anterioridad. Por ello, deseo agradecer a todos y cada uno de los autores del *Tratado de Nutrición* su compromiso, dedicación y esmero en la redacción y posterior revisión de cada uno de los capítulos en los que han participado. Asimismo, agradezco a todos los coordinadores de los tomos su participación y trabajo continuado para hacer que esta nueva edición del *Tratado de Nutrición* sea mejor que la anterior.

Ángel Gil Hernández
Profesor Emérito de la Universidad de Granada. Catedrático
del Departamento de Bioquímica y Biología Molecular II.
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En el siguiente artículo publicado en el número 2 de la revista *Nutrición Hospitalaria* los autores han comunicado que hubo un error en los datos de la tabla II:

Pérez-Fernández MR, Martínez Lede I, Fernández Varela MM, Fariñas Valiña N, Calvo Ayuso N, Rodríguez Garrido JI. Síntomas depresivos en una muestra de mujeres con hipotiroidismo subclínico y su relación con los cloratos del agua del grifo. *Nutr Hosp* 2024;41(2):439-46. DOI: <http://dx.doi.org/10.20960/nh.04919>

A continuación se reproduce la tabla con los datos correctos (fondo gris):

Tabla II. Análisis de regresión logística de las variables relacionadas con el estado depresivo en mujeres con hipotiroidismo subclínico

Variable	Estimador	Error Estándar	OR	IC 95%		p valor
				Límite inferior	Límite superior	
Consumo agua grifo	3,325	1,217	27,799	2,557	302,193	0,006
Síntoma frío	-1,375	1,308	0,253	0,019	3,280	0,293
Síntoma cansancio	-0,058	0,969	0,944	0,141	6,302	0,952
Síntoma tristeza	4,675	1,714	107,187	3,728	3082,081	0,006
Síntoma mialgias	3,120	1,286	22,641	1,822	281,282	0,015
Síntoma pérdidas memoria	4,783	1,470	119,410	6,694	2129,963	0,001
Síntoma aumento peso	1,627	1,127	5,089	0,559	46,318	0,149
Trastornos sueño	4,598	1,706	99,288	3,503	2814,505	0,007
Edad	0,042	0,070	1,043	0,910	1,195	0,545
IMC	- 0,274	0,130	0,760	0,589	0,981	0,035

OR: Odds Ratio, IC 95%: intervalo de confianza al 95%, IMC: índice de masa corporal.