Tesis Doctoral Internacional/International Doctoral Thesis

NIVEL DE ADHESIÓN E INFLUENCIA DE LA DIETA MEDITERRÁNEA SOBRE LA SALUD MENTAL EN FIBROMIALGIA Y EL RIESGO CARDIOMETABÓLICO Y DENSIDAD MINERAL ÓSEA EN MUJERES PERIMENOPÁUSICAS

DEGREE OF ADHERENCE TO THE MEDITERRANEAN DIET AND ITS INFLUENCE ON MENTAL HEALTH IN FIBROMYALGIA PATIENTS AND CARDIOMETABOLIC RISK AND BONE MINERAL DENSITY IN PERIMENOPAUSAL WOMEN.

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PROYECTOS DE INVESTIGACIÓN RELACIONADOS CON LA PRESENTE TESIS [RESEARCH PROJECTS RELATED WITH THE PRESENT THESIS]

El trabajo desarrollado y los artículos que componen la presente memoria de Tesis Doctoral están basados en los siguientes proyectos de investigación:

- **PROYECTO:** Evaluación de los Hábitos de Salud y Calidad de Vida de Mujeres Peri y Menopáusicas tras un Programa de Intervención Educativa Multidisciplinar.PI-0339. Entidad Financiadora: Consejería de Salud de la Junta de Andalucía. Convocatoria: Orden 19 de julio de 2007 (BOJA Nº 149, 30 de julio de 2007).Fecha y Duración: Del 26/12/2008 al 25/12/2011. Financiación: 32.500 euros. Investigador principal: Dra. Pilar Aranda Ramírez. [Este proyecto condujo al Estudio I de la presente tesis doctoral].
- **PROYECTO:** Coste-Efectividad de un Programa de Ejercicio Físico en Mujeres Perimenopáusicas.PI-0667-2013.Entidad Financiadora: Consejería de Salud de la Junta de Andalucía. Fecha y Duración: Del 01/01/2014 al 31/12/2015 (24 meses). Financiación: 38.500 euros. Investigadora principal: Virginia A. Aparicio. [Este proyecto condujo a los Estudios II y III de la presente tesis doctoral].
- **PROYECTO:** Physical Activity in Women with Fibromyalgia: Effects on Pain, Health and Quality of Life (Actividad Física en Mujeres con Fibromialgia: Efectos sobre el Grado de Dolor, Salud y Calidad de Vida). DEP2010-15639 (subprograma DEPO). Entidad Financiadora: Plan Nacional I+D+i 2008-2011, Ministerio de Ciencia e Innovación. Fecha y Duración: Del 01/07/2010 al 30/06/2013. Financiación: 120.000 euros. Investigador principal: Manuel Delgado Fernández.[Este proyecto condujo al Estudio IV de la presente tesis doctoral].

LISTA DE PUBLICACIONES [LIST OF PUBLICATIONS]

La presente memoria de Tesis Doctoral está compuesta por los siguientes artículos científicos:

I. **Ruiz-Cabello P**, Aparicio VA, Fernández-Martínez MM, Moratalla N, Gregorio E, Aranda P. *Mediterranean countries facing the Mediterranean diet, are we still on track? The example of southern Spain midlife women*. Nutrición Hospitalaria, 2015, 31(6), 2523–32. JCR-Science área: Nutrition and Dietetics. Impact factor: 1.5, Q3.

II. **Ruiz-Cabello P**, Coll-Risco I, Acosta-Manzano P, Borges-Cósic M, Gallo-Vallejo F, Aranda Ramírez P, López-Jurado M, Aparicio VA. *Influence of the degree of adherence to the Mediterranean diet on the cardiometabolic risk in peri and menopausal women. The Flamenco project*. Nutrition, Metabolism & Cardiovascular Diseases, 2016. In press. http://dx.doi.org/10.1016/j.numecd.2016.10.008. JCR-Science área: Nutrition and Dietetics. Impact factor: 3.4, Q2.

III. Aparicio VA, **Ruiz-Cabello P**, Borges-Cósic M, Andrade A, Coll-Risco I, Acosta-Manzano P, Soriano-Maldonado A. *Association of physical fitness, body composition, cardiometabolic markers and adherence to the Mediterranean diet with bone mineral density in perimenopausal women. The Flamenco project.* Journal of Sports Sciences. 2016. Jun 16; 414:1–8. JCR-Science área: Sport Sciences. Impact factor: 2.1, Q2.

IV. **Ruiz-Cabello P**, Soriano-Maldonado A, Delgado-Fernández, M, Álvarez-Gallardo I.C, Segura-Jiménez V, Estévez-López F, Camiletti-Moirón D, Aparicio VA. *Association of dietary habits with psychosocial outcomes in women with fibromyalgia: The al-Ándalus project.* Journal of the Academy of Nutrition and Dietetics, 2016. *In press.* http://dx.doi.org/10.1016/j.jand.2016.09.023. JCR-Science área: Nutrition and Dietetics. Impact factor: 3.6, Q1.

RESUMEN

Actualmente, la Dieta Mediterránea es el patrón dietético más estudiado hasta la fecha, con una fuerte evidencia científica que la certifica como la dieta más adecuada para la prevención de enfermedades crónicas y la promoción de la salud.

El objetivo general de esta Tesis Doctoral ha sido analizar el patrón nutricional y de Dieta Mediterránea en un grupo de mujeres perimenopáusicas del sur de España, y determinar su influencia sobre determinantes de salud asociados a la perimenopausia (riesgo cardiovascular y osteoporosis), así como su relación con el estado de salud mental de un subgrupo de mujeres perimenopáusicas enfermas de fibromialgia. Los principales resultados de la Tesis sugieren que i) Existe un progresivo distanciamiento del patrón de Dieta Mediterránea entre las mujeres perimenopáusicas del sur de España, cuya adhesión es mayoritariamente moderada y donde sólo un tercio presenta alta adhesión. ii) El consumo de cereales no refinados y legumbres por debajo de las recomendaciones, así como el excesivo consumo de proteína animal, resultan en una dieta hipoglucídica, hiperproteica e hiperlipídica. iii) Una alta adhesión al patrón de Dieta Mediterránea podría favorecer un perfil cardiometabólico más saludable en mujeres perimenopáusicas, caracterizado por una menor frecuencia cardíaca basal, menores concentraciones plasmáticas de colesterol total, lipoproteínas de baja densidad (LDL-C), ratio colesterol total/lipoproteínas de alta densidad (HDL-C), triglicéridos y proteína C-reactiva, independientemente de la edad, índice de masa corporal (IMC), menstruación regular, hábito tabáquico, uso de terapia hormonal sustitutiva y niveles de actividad física. iv) Una alta adhesión al patrón de Dieta Mediterránea podría reducir el riesgo cardiometabólico global, mientras que dicho efecto no se observa cuando la adhesión es moderada o baja. Aunque algunos de los componentes de la Dieta Mediterránea muestran una asociación inversa con el riesgo cardiometabólico global,

estas asociaciones individuales no son tan fuertes como la observada con la Dieta Mediterránea estudiada en su conjunto. v) La fuerza muscular, el peso, el IMC y la masa magra se asocian positivamente con la densidad mineral ósea (DMO) en mujeres perimenopaúsicas, no presentando asociación la adhesión a la Dieta Mediterránea, la masa grasa, ni ninguno de los marcadores cardiometabólicos estudiados.vi) La masa magra muestra una asociación fuerte e independiente con la DMO, explicando el 14% de su variabilidad y mostrando una diferencia clínicamente relevante entre las mujeres perimenopaúsicas en el primer y cuarto cuartil de masa magra. vii) El estudio de los hábitos dietéticos en una muestra representativa de mujeres perimenopáusicas del sur de España con fibromialgia muestra que un consumo diario de fruta y verdura, así como un consumo moderado (2-5 raciones/semana) de pescado, se asocia con mejor salud mental y optimismo y menor depresión. Por otro lado, un consumo diario o casi diario de embutidos y bebidas azucaradas se asocian a menor optimismo y mayor depresión. viii) La Dieta Mediterránea asegura una ingesta adecuada de estos grupos de alimentos, al mismo tiempo que presenta una amplia evidencia científica de su correlación directa con los componentes mentales de la calidad de vida e inversa con la depresión.

Los resultados de la presente memoria de Tesis ponen de manifiesto la importancia, en esta población, de mantener una alta adhesión al patrón de Dieta Mediterránea para reducir el riesgo cardiometabólico, así como una adecuada fuerza y masa muscular que preserve la densidad mineral ósea. Asimismo, en la mujer perimenopáusica con fibromialgia, la ingesta diaria de fruta y verdura y el consumo semanal, pero moderado (2-5 raciones/semana), de pescado pueden mejorar su salud mental.

SUMMARY

Nowadays, the Mediterranean diet is the most evidenced-based and well-studied dietary pattern for disease prevention and health promotion.

The overall objective of this Thesis has been to assess the dietary habits, particularly the Mediterranean dietary pattern, in a group of perimenopausal women from Southern Spain, to analyze their association with potentially modifiable health markers related with menopause (such as cardiovascular risk factors and osteoporosis), as well as the relationship with mental health in a subgroup of perimenopausal women with fibromyalgia. The main findings from this Thesis suggest that i) There is a progressive distancing from the Mediterranean dietary pattern among the perimenopausal women studied, whose adherence is mostly moderate, with less than one third of the study population showing a high adherence. ii) The lack of cereals, mainly whole grain cereals, and pulses in the diet in favor of a higher consumption of animal proteins determine a hypoglycemic, hyperproteic and hyperlipidemic diet. iii) A high adherence to the Mediterranean Dietary pattern promote a better cardiometabolic profile among perimenopausal women, characterized by lower resting heart rate, plasma total cholesterol, LDL-cholesterol, total cholesterol/HDL-cholesterol ratio, triglycerides and C-reactive protein than those with a low adherence regardless of potential confounders such as age, BMI, regular menstruation, smoking habit, use of substitutive hormone therapy and physical activity levels. iv) Women with a high adherence to the Mediterranean Dietary pattern showed a lower clustered cardiometabolic risk, a protection that was not afforded when adherence was low or medium. Although some of the components of the Mediterranean Diet, such as whole grains, legumes and red wine showed an inverse association with the clustered cardiometabolic risk, these individual associations are not as strong as those observed when the Mediterranean Diet is studied as a whole. v) Muscle strength, body weight, BMI and lean mass are significantly

associated with bone mineral density in perimenopausal women. By contrast, neither cardiorespiratory fitness, flexibility, motor agility, cardiometabolic markers (blood pressure, plasma lipids, fasting glucose or C-reactive protein), nor the Mediterranean Diet are associated with bone mineral density in this population. vi) Lean mass is the only factor independently associated with bone mineral density, explaining 14% of its variability. The difference in bone mineral density between the groups with the highest and the lowest quartile of lean mass is clinically meaningful. vii) The study of the dietary habits in a representative sample of perimenopausal women from Southern Spain with fibromyalgia indicate that a daily consumption of fruit and vegetables as well as a moderate but weekly (2-5 servings/week) consumption of fish is positively associated with better mental health, optimism and a lower risk of severe depression. In contrast, a daily or almost-daily consumption of cured meats and sweetened beverages are associated with less favorable psychosocial outcomes. viii) The Mediterranean diet ensures an adequate intake of several nutrients which negatively correlate with depression and mental disorders, and has an extensive scientific evidence for its role in general health, showing a direct relationship with quality of life mental components.

These findings of the present Thesis highlight that, among the perimenopausal women studied, the Mediterranean Diet adherence is mainly low-moderate, with an overconsumption of animal protein and refined carbohydrates and an intake below recommendations of non-refined cereals and pulses. These results also show the importance of maintaining a high adherence to the Mediterranean Diet in order to reduce the cardiometabolic risk, as well as an adequate lean mass to preserve bone mineral density. Likewise, in perimenopausal women with fibromyalgia, a daily intake of fruit and vegetables and a weekly, but moderate (2 -5 servings/week), consumption of fish can improve the patient's mental health.

INTRODUCCIÓN

1. Dieta Mediterránea

1.1. Introducción

La Dieta Mediterránea es, desde el 2010, Patrimonio Cultural Inmaterial de la Humanidad por la UNESCO. Dicha candidatura se otorgó para salvaguardar, no sólo la forma de conservar, transformar, cocinar, compartir y consumir los alimentos propios de los países mediterráneos, sino el patrón antropológico que lo rodea, ya que la Dieta Mediterránea se caracteriza por "un conjunto de habilidades, conocimientos, prácticas y tradiciones que van desde el paisaje hasta la mesa[1].

Ahora bien, la Dieta Mediterránea emergió como un régimen de comida saludable mucho antes de que se conocieran qué componentes de ésta eran responsables de los beneficios observados[2]. El mar Mediterráneo (del latín, *medius-terra,*), al que esta dieta debe su nombre, es un mar "entre tierras" al que se abren tres continentes: Europa, Asia y África. En él se han gestado las civilizaciones más antiguas, los mundos egipcio, griego y romano, las civilizaciones cristiana y musulmana, las vías de comunicación con el lejano Oriente, la ruta de la seda, el África de los animales exóticos y la India de las especias. Fruto de este mestizaje se configuró uno de los modelos alimentarios más saludables del mundo[3], que ha perdurado hasta nuestros días, que ha ido evolucionando, acogiendo e incorporando nuevos alimentos y técnicas fruto de la posición geográfica estratégica y de la capacidad de mestizaje e intercambio de los pueblos mediterráneos[3].

No fue hasta la segunda mitad del siglo XX cuando el carácter excepcional del estilo de vida mediterráneo y su influencia sobre la salud fueron puestos de manifiesto. Estos beneficios fueron inicialmente descritos en los años 1950-60 a través del "Estudio de los 7 países"[4], un gran estudio ecológico en el que participaron 16 cohortes de países mediterráneos y no mediterráneos. En él, los hábitos alimentarios del área mediterránea

llamaron la atención como consecuencia de la constatación de que, en los países mediterráneos, la incidencia de enfermedades coronarias era significativamente menor que en otros países del norte de Europa. Los beneficios de la Dieta Mediterránea sobre la salud y su papel en la prevención de muchas enfermedades crónicas son, a día de hoy, una evidencia científica, como demuestran numerosos estudios recogidos en revisiones sistemáticas de gran impacto científico[5,6].

1.2 ¿Qué es la Dieta Mediterránea?

Se podría hablar de Dieta Mediterránea como la representante del patrón de consumo dietético de los países que bordean el mar Mediterráneo. Sin embargo, las diferencias sociales, políticas, religiosas y económicas introducen variaciones en este patrón, tanto dentro de cada país, como entre países[7], lo que hace difícil encontrar un modelo único. No obstante, sí que persisten diversos aspectos comunes: alta ingesta de verduras, hortalizas, frutas frescas, leguminosas y cereales; una cantidad abundante, según la zona, de aceite de oliva, que es la principal grasa culinaria; un consumo moderado de alcohol, principalmente en forma de vino tinto durante las comidas; algo de pescado, moderada ingesta de lácteos y baja ingesta de carnes y derivados[8].

La Pirámide Mediterránea

La Pirámide Mediterránea indica, de una forma gráfica, las proporciones y la frecuencia de consumo de los diferentes alimentos y grupos de alimentos que conforman este modelo dietético. Además, incorpora elementos cualitativos relativos a las características sociales y culturales del estilo de vida mediterráneo: la convivencia, la moderación, las técnicas culinarias, la estacionalidad, biodiversidad, respeto al medio ambiente y uso de productos tradicionales así como la importancia de la actividad física realizada regularmente[9]. En el 2010 se presentó la última versión de la Pirámide de la

Dieta Mediterránea, dirigida a la población adulta española y adaptada a la idiosincrasia del país (figura 1).

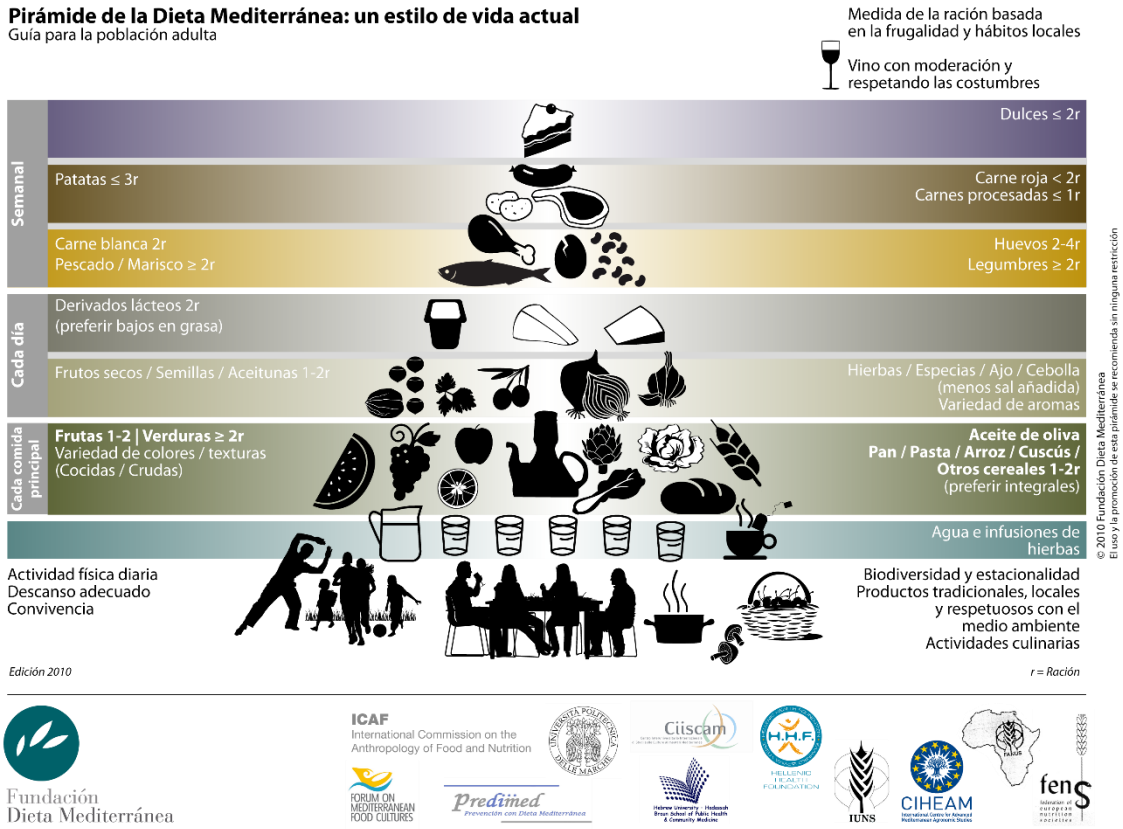

Figura 1. Pirámide de la Dieta Mediterránea actual.

La base del patrón dietético mediterráneo es el consumo de una amplia variedad de productos mínimamente procesados como granos enteros, frutas, verduras, legumbres y frutos secos. Una dieta basada en estos alimentos proporciona una fuente natural de fibra, vitaminas esenciales y minerales, además de ser naturalmente ricos en antioxidantes y bajos en grasas saturadas[10]. El aceite de oliva es el componente central de la Pirámide Mediterránea, principal grasa de adición en esta región[11]. Está compuesto por una fracción mayoritaria de tipo oleoso, del que el ácido oleico es su principal representante, y una fracción minoritaria no oleosa, representada por la oleuropeína y su subproducto, el hidroxitirosol, de propiedades antioxidantes[5]. El aceite de oliva virgen, producido mediante prensado mecánico de aceitunas maduras, es el que contiene estos compuestos bioactivos y antioxidantes. Los procesos químicos, térmicos y físico-

químicos a los que se someten otros aceites de oliva de menor calidad son responsables de dicha pérdida.

El patrón dietético mediterráneo también incluye pequeñas cantidades de productos lácteos de una variedad de animales, principalmente en forma de queso o yogur. También contempla el consumo de proteína animal, principalmente pescado, fuente abundante de ácidos grasos poliinsaturados, especialmente omega-3, minerales y vitaminas[5]. El consumo de carnes rojas y procesadas es ocasional[10]. La pirámide actualizada incorpora la adición de hierbas y especias, que mejoran el sabor y palatabilidad de los alimentos, reduciendo la necesidad de agregar sal o grasa al cocinar. Además, las hierbas son una fuente natural de fitoquímicos, de propiedades antioxidantes[5]. Finalmente, el vino tinto, rico en flavonoides, se considera una parte opcional del patrón dietético mediterráneo, y su consumo debe basarse en circunstancias individuales[5].

1.3. Dieta Mediterránea y Salud

Los factores nutricionales juegan un papel tanto en la promoción de la salud como en el desarrollo de la enfermedad[5]. Hasta no hace mucho, la mayoría de los estudios nutricionales se basaban en evaluar nutrientes o alimentos individuales, en lugar de evaluar los patrones dietéticos en su conjunto. Sin embargo, hay varias razones por las que la relación de los hábitos alimentarios y la salud van más allá de una aproximación reduccionista:

- Las personas no comen nutrientes aislados, sino que su dieta está formada alimentos, que son los almacenes de nutrientes, que interaccionan entre sí en los mecanismos de acción y control metabólico[12].
- La dieta constituye una mezcla de muchos alimentos diferentes y estos alimentos están compuestos por miles de productos químicos. Como resultado, hay una

combinación de efectos, interacciones, antagonismos y sinergismos que impiden conocer el efecto del conjunto de la dieta a través de sus componentes individuales[13].

- De toda esta pléyade de componentes individuales (nutrientes o componentes no nutritivos) importantes en la relación de los hábitos alimentarios con la salud, sólo una parte son objeto de los trabajos de investigación. Puede que sean conocidos pero no estudiados, puede que no sean evaluables o incluso que su función no sea totalmente conocida[13].

Por lo tanto, el estudio de la dieta en su conjunto, abarca no sólo el efecto de sus componentes individuales, sino también sus interacciones y combinaciones de efectos, y por tanto aporta una información más completa y relevante de la relación entre los hábitos alimentarios y la salud[14].

La importancia de la Dieta Mediterránea en la salud del individuo no se limita al hecho de que sea una dieta equilibrada, variada y con un aporte de macronutrientes adecuado. A los beneficios de su bajo contenido en ácidos grasos saturados, sal y carbohidratos simples, así como su alto contenido en ácidos grasos monoinsaturados, carbohidratos complejos y fibra, hay que añadir los derivados de su riqueza en sustancias antioxidantes. Una alta adhesión al patrón de Dieta Mediterránea protege, con una alta evidencia, no sólo frente a la enfermedad cardiovascular (ECV), sino también frente a otras enfermedades crónicas tales como el cáncer, la insuficiencia renal, etc.[15–17] y neurodegenerativas[18]. Ha mostrado su claro efecto beneficioso sobre el control y prevención de la obesidad[19,20]. Además, la Dieta Mediterránea se relaciona de forma inversa con la presión arterial sistólica, concentraciones de proteína C reactiva, fibrinógeno[21,22], colesterol total, lipoproteínas de baja densidad (LDL-C) y riesgo de síndrome coronario agudo[20]; al mismo tiempo que se relaciona positivamente con la capacidad antioxidante del organismo[6,19].

Muchos son los estudios que coinciden con estos hallazgos y sugieren una asociación positiva entre la adhesión a la Dieta Mediterránea y una reducción significativa de la mortalidad total, la incidencia de enfermedades cardiovasculares, neurodegenerativas y de cáncer con tan sólo con un ligero aumento en el grado de adhesión a la misma[6,23,24]. Existe evidencia de que componentes específicos de esta dieta pueden desempeñar un papel en la prevención de la osteoporosis y el riesgo de fracturas (alto consumo de frutas, verduras y aceite de oliva, así como el consumo moderado de pescado y alcohol), aunque su efecto sobre la salud ósea como patrón dietético no está aún claro, con un número de estudios que presentan resultados conflictivos[25].

1.4. Adhesión al Patrón Mediterráneo en la Actualidad

La Dieta Mediterránea es un patrimonio cultural inmenso y milenario, evolutivo, dinámico y vital[7], pero que se encuentra en peligro de extinción. Por esto, en el 2010, la UNESCO reconoció a la Dieta Mediterránea como Patrimonio Cultural Inmaterial de la Humanidad, con el objetivo de salvaguardarla.

A pesar de los esfuerzos de organizaciones intergubernamentales (UNESCO, FAO, OMS, etc.) y de los más que documentados beneficios para la salud de este patrón alimentario[5,18], la adhesión a la Dieta Mediterránea ha ido disminuyendo progresivamente en los últimos años[26]. Los últimos estudios epidemiológicos realizados en Europa sugieren un progresivo abandono de este patrón dietético hacia nuevos hábitos y costumbres alimentarias más propias de una dieta occidentalizada, distanciamiento que se hace más evidente en los países del área Mediterránea[27]. Las razones de este distanciamiento son múltiples, como lo son los países mediterráneos afectados. Factores económicos, ambientales y socioculturales contribuyen simultáneamente a este abandono: la actual crisis económica, el desplazamiento de la

población a zonas urbanas, la tecnología, la incorporación de la mujer al mercado laboral o la mayor disponibilidad en el mercado de alimentos de dietas tipo occidental[27]. Por todo esto, se hace necesario el estudio de los hábitos dietéticos y la reevaluación de la adhesión a la Dieta Mediterránea, de manera que se pueda contrastar la tendencia actual en nuestro país (**Artículo I**).

2. Menopausia

2.1. Introducción

La *menopausia* es un estado fisiológico de la mujer determinado por el cese de la secreción ovárica de estrógenos y progestágenos, lo que da lugar al cese del sangrado menstrual junto a la aparición de un conjunto de modificaciones fisiológicas que afectan fundamentalmente al aparato urogenital, sistema cardiovascular, óseo y tejido adiposo[28]. Afecta a todas las mujeres como parte del proceso natural del envejecimiento, apareciendo a una edad que, en España, se sitúa alrededor de los 51 años, con un espectro que va de los 48 a los 51 años[29]. Actualmente, el término menopausia está siendo complementado por un término más preciso: *perimenopausia*. La perimenopausia abarca el período de transición antes y después de la menopausia, pudiendo aparecer 6 años antes de la menopausia y mantenerse de 2 a 5 años después de la menopausia[30]. El período perimenopáusico comienza tan pronto como aparecen las fluctuaciones en la producción hormonal aunque será en último término la reducción de estrógenos la que dará lugar a los síntomas acompañantes, así como a los cambios que ocurren en el organismo. Aunque no deje de ser un proceso fisiológico en la vida de la mujer, éste normalmente lleva asociado numerosos cambios metabólicos que determinan el bienestar personal[31] y la salud general de la mujer[2832].

2.2. Menopausia y Riesgo Cardiovascular

La ECV sigue siendo la primera causa de muerte en todo el mundo[33]. Además, la proporción de muertes que se le atribuyen a la ECV es sustancialmente mayor entre mujeres (51%) que hombres (42%), lo que representa un serio y creciente problema de salud pública que además conlleva una enorme carga para los sistemas públicos y privados de salud[34,35]. Mientras que la ECV es poco frecuente en mujeres jóvenes, lo que se atribuye en parte al efecto protector sobre el sistema vascular de los estrógenos endógenos, conforme la mujer se hace mayor la exposición de ésta a los factores de riesgo cardiovascular aumenta. El hipoestrogenismo característico presente en la postmenopausia promueve una disfunción endotelial, hipertensión, cambios en los lípidos proaterogénicos y resistencia a la insulina, entre otros factores de riesgo cardiovascular[28]. Además, durante el periodo perimenopáusico, la fluctuación de hormonas ya está presente y, por lo tanto, la vulnerabilidad anteriormente mencionada[36]. Por lo tanto si se tiene en cuenta que, debido al aumento de la longevidad, los años en postmenopausia aumentan (de hecho la mujer pasa un tercio de su vida en postmenopausia), es deseable un óptimo estatus cardiometabólico desde la perimenopausia para prevenir o retrasar eventos cardiovasculares prematuras en etapas posteriores[28].

El factor clave para una vida libre de enfermedades crónicas en etapas posteriores es un estilo de vida y una dieta saludable desde edades tempranas e intermedias[37]. Hoy en día, la evidencia epidemiológica de la protección cardiovascular otorgada por la Dieta Mediterránea es fuerte[16,17]. De igual manera, revisiones sistemáticas y metaanálisis de estudios observacionales prospectivos han confirmado que una alta adhesión a la Dieta Mediterránea se asocia con un aumento significativo en el estado de salud y con una disminución, también significativa, de la mortalidad total, así como en la

morbimortalidad por ECV. Sin embargo, no existen estudios previos que se hayan centrado en esta etapa de transición crucial en la vida de la mujer, por lo que sería clínicamente interesante determinar el grado de adhesión en el que se alcanza dicha protección cardiovascular **(Artículo II)**, especialmente cuando los últimos estudios epidemiológicos sugieren un progresivo distanciamiento del patrón mediterráneo[8].

2.3. Menopausia y Osteoporosis

La osteoporosis es una enfermedad metabólica ósea crónica y progresiva que puede afectar a todo el esqueleto, cuya prevalencia es especialmente elevada en mujeres postmenopáusicas. Se define como un trastorno esquelético caracterizado por una fortaleza ósea comprometida que aumenta el riesgo de fractura. La fuerza ósea refleja la integración de la densidad mineral ósea (DMO) y la calidad[38]. La fractura osteoporótica, por su impacto en la mortalidad, deterioro de la calidad de vida y coste para los servicios sanitarios, es un problema de salud de primer orden en la mayoría de los países desarrollados. En Europa se producen anualmente 20,6 millones de fracturas osteoporóticas y en España, se ha estimado que en los próximos 10 años se producirán 714.000, la mayor parte en mujeres mayores de 70 años. Este proceso es prevenible y tratable, pero la falta de signos de alerta antes de aparecer las fracturas, sumado al hecho de que en España no existe consenso en las guías clínicas para su prevención[39], hacen que pocos pacientes sean diagnosticados en fases tempranas y tratados de forma efectiva. Por este motivo, un gran número de personas experimentan dolor, discapacidad y disminución de la calidad de vida a causa de la osteoporosis[40]. La menopausia se asocia con la pérdida de DMO que puede conducir a osteoporosis, generalmente asintomática y, por tanto, no diagnosticada. La pérdida de la función ovárica tiene un gran impacto sobre la salud esquelética y promueve una tasa acelerada de pérdida de masa ósea durante la transición menopáusica[41–43].

Los mecanismos implicados en la patogénesis de la osteoporosis no se conocen completamente, y su desarrollo está influenciado por múltiples factores[43]. Los procesos de modelado y remodelado óseo se rigen no sólo por los rasgos hereditarios sino también por factores nutricionales, mecánicos y hormonales, por lo que una dieta inadecuada y un estilo de vida sedentario pueden reducir la mineralización, sumado al proceso natural de desmineralización por envejecimiento[42]. Una reducción en la densidad ósea en etapas tempranas es probable que aumente el riesgo de osteoporosis y sus secuelas en la edad adulta[44]. Por lo tanto, es importante sensibilizar a la población en general sobre la necesidad de formar y mantener una buena salud ósea desde la infancia a través de la adopción de hábitos saludables. Un adecuado nivel de ejercicio físico se ha asociado a una mejor DMO[45]. Parece que la condición física, y en concreto la fuerza muscular, pueden promover una mayor DMO[46–50]. Sin embargo, algunos estudios no han encontrado asociación entre los diferentes componentes de la condición física y la DMO[51,52]. El peso y la composición corporal parecen también ser importantes determinantes de la DMO, ya que las tasas de pérdida de masa ósea son mayores en mujeres no obesas que en sus homólogas obesas[42,53,54]. Además, numerosos estudios han examinado recientemente el rol de la masa magra y la masa grasa en la DMO, sugiriendo que aumentar la masa magra (más que la masa grasa) podría ser particularmente beneficioso para la salud ósea[55–57]. La menopausia incrementa también los marcadores inflamatorios y la prevalencia de síndrome metabólico[58–60]. La asociación entre el síndrome metabólico y la salud ósea permanece aún poco clara, pero estudios recientes han observado que mujeres con síndrome metabólico presentan mayor DMO, independientemente del índice de masa corporal (IMC)[61,62]. La inflamación también ha mostrado jugar un importante (aunque inconsistente) papel en el remodelado óseo. De hecho, un estudio observó que la proteína C-reactiva mostraba una

relación inversa y dosis dependiente con la DMO[63], mientras que otros autores no han confirmado dicha asociación[64,65]. Numerosos estudios han encontrado también que la Dieta Mediterránea[66] o sus componentes específicos (ej. aceite de oliva, pescado, fruta y verdura) están relacionados con mejoras en la DMO y en la prevención de osteoporosis[67], mientras que otros no han observado claras asociaciones[25,68]. Dado que la perimenopausia es un periodo crítico en lo que respecta a la salud ósea, es de interés público y clínico caracterizar al máximo el grado en el que estos factores modificables (tales como la dieta, la condición física, la composición corporal y los marcadores cardiometabólicos) podrían estar asociados con la DMO en este periodo de la vida de la mujer (**Artículo III**), los cuales podrían tener implicaciones importantes en la implementación de programas más efectivos para la prevención de la pérdida de masa ósea.

3. Fibromialgia.

3.1. Definición

La fibromialgia (FM) es una condición crónica y multidimensional considerada como un trastorno de la regulación del dolor de etiología desconocida, caracterizada por una mayor sensibilidad a los estímulos dolorosos (hiperalgesia) y un umbral de dolor disminuido (alodinia)[69]. Sin embargo, más allá de una condición crónica de dolor generalizado, la FM ha sido definida recientemente como un trastorno dimensional complejo con el dolor como su principal síntoma[70], pero con otros síntomas no dolorosos presumiblemente igual de importantes, como fatiga, rigidez, problemas cognitivos, depresión, ansiedad y problemas cognitivos, entre otros trastornos[70]. La amplia sintomatología y comorbilidades presentes limitan la mayoría de las actividades diarias de los pacientes con FM[71], lo que conlleva un gran impacto sobre la percepción

de la enfermedad[72], causando un deterioro notable en la calidad de vida y la salud mental del paciente[73,74].

3.2 Prevalencia e Impacto Socioeconómico

La prevalencia de FM en la población española es del 2,4%[75], y de éstos el 95% son mujeres[76]. Esta prevalencia es similar a la observada en otros países europeos[77,78],o en Estados Unidos[79]. La FM representa actualmente una importante carga para el sistema de salud pública[80], con importantes costes de atención médica directa e indirecta[81,82]. En España, un estudio[82] reveló que los pacientes con FM incurrieron en 614 € más en costes medios anuales de salud (directos) y en 4.397 € más indirectos en comparación con el grupo de referencia, totalizando un coste medio anual extra de 5.011 € por paciente. Además, tanto los costes directos como los indirectos se han correlacionado significativamente con la gravedad de la enfermedad, el grado de discapacidad funcional, la presencia de síntomas depresivos y la existencia de comorbilidades[83].

Por otra parte, también se ha observado una mayor prevalencia de obesidad y sobrepeso, asociado con la concurrencia de los síntomas y la severidad de la FM[84–86]. En torno al 70% de las mujeres con FM tienen sobrepeso (IMC>25) u obesidad (IMC>30)[87,88]. Los resultados obtenidos en lo referente a la sintomatología de la enfermedad sugieren que las enfermas de FM obesas presentan mayores niveles de ansiedad y depresión, peor calidad de vida y menor vitalidad que las enfermas con normopeso[93]. Si a esto se le suma que la edad media de aparición de la enfermedad se sitúa en periodo menopáusico[78], el riesgo de sufrir sobrepeso u obesidad, se incrementa[94] y por lo tanto el riesgo de empeoramiento de la enfermedad.

3.3. Abordaje de la fibromialgia: El papel de los hábitos dietéticos.

Debido a que la FM es una enfermedad crónica, sin cura conocida[95,96], las guías clínicas más recientes sugieren que el tratamiento óptimo debe consistir en un abordaje multidisciplinar[84,95,96], con una combinación de las modalidades farmacológicas y no-farmacológicas[96]. Entre los tratamientos no-farmacológicos (terapia múltiple, terapia psicológica, ejercicio físico, etc.) la intervención nutricional se presenta como un abordaje prometedor[84]. Numerosos estudios han demostrado la importancia de hábitos dietéticos específicos en el bienestar mental de la población general[97,98]. Una reciente revisión sugiere que un programa de tratamiento que incluya estrategias de pérdida de peso, educación nutricional y el uso de suplementos nutricionales específicos sería recomendable en estos individuos[84]. Sin embargo, es poca la información basada en la evidencia que pueda proporcionar asesoramiento nutricional para esta población[99]. Además, la comunidad científica está preocupada por una gran cantidad de información no-científica relacionada con los beneficios potenciales de algunos productos basados en ingredientes nutricionales o productos botánicos[100], así como dietas específicas con resultados no concluyentes o contradictorios[84,101–103].

Mientras que la mayoría de estudios hasta la fecha se han centrado en el dolor, poca información está disponible sobre la asociación entre los hábitos dietéticos y las esferas psicosociales. Aunque el dolor es el principal síntoma de la FM, la enfermedad ha sido definida como un desorden multidimensional complejo, con otros importantes síntomas psicosociales, que tienen un impacto masivo en la percepción de la enfermedad por parte del individuo así como en la calidad de vida de éste[73]. Por lo tanto, sería de interés evaluar los hábitos dietéticos de esta población y examinar su posible asociación con la salud mental (**Artículo IV**).

En definitiva, la Dieta Mediterránea puede tener un papel relevante en esta etapa fisiológica de la mujer, así como en el tratamiento de la FM, cuyo rango de aparición se sitúa en pleno período perimenopáusico y donde el 95% de los pacientes son mujeres. Por lo tanto, existe la necesidad de una mejor comprensión de la relación entre la Dieta Mediterránea y los determinantes de salud característicos de este período: el riesgo cardiovascular, la osteoporosis y la salud mental.

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OBJETIVOS

General:

El objetivo general de la presente Tesis Doctoral fue analizar el patrón nutricional y de Dieta Mediterránea de un grupo de mujeres perimenopáusicas, y determinar su influencia sobre determinantes de salud asociados a la perimenopausia (riesgo cardiovascular y osteoporosis), así como su relación con el estado de salud mental, depresión y optimismo de un subgrupo de mujeres perimenopáusicas enfermas de fibromialgia.

Específicos:

- Describir y valorar los hábitos dietéticos, el nivel de cumplimiento con las Ingestas de Referencia y el nivel de adhesión al patrón de Dieta Mediterránea de un grupo de mujeres perimenopáusicas del sur de España, así como el impacto y la influencia del estado de peso corporal sobre dichas variables **(Artículo I).**
- Evaluar el nivel de adhesión al patrón de Dieta Mediterránea de una muestra de mujeres perimenopáusicas del sur de España y estudiar la asociación de dicho grado de adhesión sobre los factores tradicionales de riesgo cardiovascular, así como sobre el riesgo cardiometabólico global **(Artículo II).**
- Evaluar, en esta misma población, la asociación de los diferentes componentes de la condición física, composición corporal, marcadores de riesgo cardiovascular y la adhesión a la Dieta Mediterránea con la densidad mineral ósea, y examinar cuáles de estos factores modificables se asocian de manera independiente con la densidad mineral ósea **(Artículo III).**
- Examinar, en una muestra representativa de mujeres perimenopáusicas del sur de España con fibromialgia, la asociación de los hábitos dietéticos de una muestra representativa de mujeres perimenopáusicas del sur de España con fibromialgia con la salud mental, optimismo y depresión **(Artículo IV).**

AIMS:

Overall:

The overall objective of this PhD Thesis was to assess the dietary habits, particularly the Mediterranean dietary pattern, of a group of perimenopausal women, in order to analyze their association with potentially modifiable health markers associated with menopause (cardiovascular disease risk factors and osteoporosis), as well as its relationship with mental health, depression and optimism in a subgroup of perimenopausal women with fibromyalgia.

Specifics:

- To evaluate, in a group of perimenopausal women from Southern Spain, their dietary habits and adherence to the Mediterranean Diet, as well as the impact and influence of weight status on these outcomes (**Paper I**).
- To evaluate, in a Southern Spain population-based sample of perimenopausal women, the level of adherence to the Mediterranean Diet and their influence on traditional cardiovascular disease risk factors along with the clusteredcardiometabolic risk profile (**Paper II**).
- To assess the association of physical fitness, body composition, cardiometabolic markers and dietary patterns with bone mineral density in the same group of perimenopausal women, and to examine which of these modifiable factors are independently associated with bone mineral density in this specific population (**Paper III**).
- To examine, in a representative sample of perimenopausal women from Southern Spain with fibromyalgia, the associations of dietary habits with mental health, optimism and depression (**Paper IV**).

MATERIAL Y MÉTODOS [MATERIAL AND METHODS]

La sección de material y métodos de la presente memoria de Tesis se resume en la siguiente tabla, que incluye la información metodológica más relevante de los artículos que componen la memoria de Tesis.

Table 1. Summary table of the methodology used in the current Thesis

Paper	Study design	Participants	Main variables studied	Methods
I. Mediterranean countries facing Mediterranean diet, are we still on track?	Cross-sectional	206 perimenopausal women aged 53±5 years old	Body composition (weight, height, BMI, body lean and fat mass,), sociodemographic characteristics, dietary patterns, MDS and bone mineral density	BIA, anthropometry, food frequency and Mediterranean diet questionnaires, lifestyle and clinical history questionnaires, BMD
II.Influence of the degree of adherence to the Mediterranean diet on the cardiometabolic risk in peri and menopausal women. The Flamenco Project.	Cross-sectional	194perimenopausal women aged 53±4 years old	Body composition (weight, height, BMI, body lean and fat mass, WC), sociodemographic characteristics, systolic and diastolic blood pressure, resting heart rate, MDS, plasma total cholesterol, HDL-C, LDL-C, triglycerides, C-reactive protein, fasting glucose and physical activity levels	DXA, anthropometry, lifestyle and clinical history questionnaires, Mediterranean diet questionnaire, biochemical analysis, accelerometry"
III. Association of physical fitness, body composition, cardiometabolic markers and adherence to the Mediterranean diet with bone mineral density in perimenopausalwomen. The Flamenco Project.	Cross-sectional	197 perimenopausal women aged 53±4 years old	Body composition (weight, height, BMI, body lean and fat mass, WC), sociodemographic characteristics, physical fitness, MDS, systolic and diastolic blood pressure, resting heart rate, plasma total cholesterol, HDL-C, LDL-C, triglycerides, C-reactive protein and fasting glucose.	DXA, anthropometry, lifestyle and clinical history questionnaires, modified Bruce protocol, handgrip strength, back-scratch test, sit-and-reach test, timed up-and-go test, and Mediterranean diet questionnaire and biochemical analysis.
IV. Association of dietary habits with psychosocial outcomes in women with fibromyalgia: The al-Ándalus Project.	Cross-sectional	485 perimenopausal women aged 52±8 years old with FM	Sociodemographic characteristics, anthropometry and body composition (weight, height, BMI, body lean and fat mass, WC), dietary patterns, mental health and optimism	Lifestyle and clinical history questionnaires, BIA, anthropometry, food frequency questionnaire, SF-36-MCS, BDI-II and LOT-R.

BMI: Body Mass Index, MDS: Mediterranean Diet Score, BIA: Bioelectrical Impedance Analysis, BMD: bone mineral density, FLAMENCO: The Fitness League Against Menopause Costs; WC: waist circumference, MDS: Mediterranean diet score, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, DXA: dual-energy x-ray absorptiometry, FM: Fibromyalgia, SF-36-MCS: mental component of the 36-item Short-Form Health Survey, BDI-II: The Beck Depression Inventory-II, LOT-R: The Life Orientation Test Revised.

RESULTADOS Y DISCUSIÓN [RESULTS AND DISCUSSION]

Los resultados y discusión se presentan en la forma en que han sido previamente publicados en revistas científicas.

1. HÁBITOS NUTRICIONALES Y NIVEL DE ADHESIÓN A LA DIETA MEDITERRÁNEA EN MUJERES PERIMENOPAÚSICAS DEL SUR DE ESPAÑA (ESTUDIO I)

I

Mediterranean countries facing the Mediterranean diet, are we still on track? The example of Southern Spain midlife women

Pilar Ruiz-Cabello Turmo, Virginia A. Aparicio García-Molina, Mª del Mar Fernández Martínez, Natalia Moratalla Cecilia, Eva Gregorio Arenas, Pilar Aranda Ramírez.

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Mediterranean countries facing the Mediterranean diet, are we still on track? The example of Southern Spain midlife women

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Abstract

Introduction and objectives: **the overall intake of a cohort of middle aged women of Granada was studied along with their body composition, anthropometric and sociodemographic characteristics to evaluate if this population does really follow a Mediterranean Diet.**

Methods: **206 women aged 53.3 ± 5.5 years old, were evaluated for their body composition, anthropometric and sociodemographic characteristics, dietary patterns, Mediterranean diet score and bone mineral density. Results were additionally analyzed across weight status categories.**

Results: **86% of the sample was overweight or obese and 14% was normal-weight (no woman was underweight). Mean body fat percentage of the sample was 40.3%. Values of bone mineral density showed a t-score average of -1.26 standard deviations. Energy intake decreased as weight status increased ($p<0.05$), as well as protein intake ($p<0.05$) but no differences were observed for carbohydrates or fat. Deviations from the Daily Recommended Intakes were observed as well as a moderate adherence (23% of the sample) to the Mediterranean Diet with no significant differences among weight status categories.**

Conclusions: **results indicated a progressive distancing from the Mediterranean dietary pattern and an unbalanced diet no correlated to the weight status group, so whether these dietary habits along with the unbalanced diet reported are prolonged over time the overweight and obese population will increase as well as the risk of developing chronic diseases, and will finally concur with the high prevalence of cardiovascular and osteoporosis risk over this population.**

(*Nutr Hosp*. 2015;31:2523-2532)

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Key words: *Women's Health. Mediterranean diet. Obesity. Cardiovascular disease. Osteoporosis.*

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LOS PAÍSES MEDITERRÁNEOS ANTE LA DIETA MEDITERRÁNEA, ¿SEGUIMOS EN EL BUEN CAMINO? EL EJEMPLO DE LAS MUJERES DE MEDIANA EDAD DEL SUR DE ESPAÑA

Resumen

Introducción y objetivos: **se estudió la ingesta dietética de una cohorte de mujeres de mediana edad de Granada, junto a sus características antropométricas y sociodemográficas, para evaluar si esta población sigue una dieta mediterránea.**

Métodos: **se evaluó la composición corporal, características antropométricas y sociodemográficas, patrones dietéticos y adhesión a la dieta mediterránea de 206 mujeres con una edad media de 53.3 ± 5.5 años. Adicionalmente, estos resultados fueron analizados por categorías de peso corporal.**

Resultados: **el 86% de la muestra presentó sobrepeso u obesidad, mientras el 14% presentó normopeso. La masa grasa corporal media fue de el 40.3%. Los valores de densidad mineral ósea presentaron un t-score medio de -1.26 desviaciones estándar. Se observó que la ingesta dietética, así como el consumo de proteína, disminuyeron a medida que aumentó el peso corporal ($p<0.05$ en ambos casos); sin embargo, no se observaron estas diferencias en la ingesta de hidratos de carbono ni de grasas. Existieron desviaciones respecto a las ingestas dietéticas de referencia y una moderada adhesión a la dieta mediterránea, sin observarse diferencias significativas entre las distintas categorías de peso corporal.**

Conclusiones: **los resultados sugieren un distanciamiento progresivo del patrón de dieta mediterránea y una dieta desequilibrada y no correlacionada con el peso corporal, de manera que si estos hábitos dietéticos se mantienen en el tiempo la población con sobrepeso y obesidad se incrementará y, de la misma manera, el riesgo de desarrollar enfermedades crónicas asociadas, coincidiendo finalmente con la elevada prevalencia de riesgo cardiovascular y de osteoporosis observada actualmente en esta población.**

(*Nutr Hosp*. 2015;31:2523-2532)

DOI:10.3305/nh.2015.31.6.8862

Palabras clave: *Salud de la mujer. Dieta mediterránea. Obesidad. Enfermedad cardiovascular. Osteoporosis.*

Abreviaturas

MD: Mediterranean Diet.
CVD: Cardiovascular Disease.
DRIs: Dietary Reference Intakes.
BMI: Body Mass Index.
WHO: Word Health Organisation.
NW/OW/OB: Normalweight/ Overweight/ Obesity.
WC: Waist Circumference.
MDS: Mediterranean Diet Score.

Introduction

Although Spain is one of the countries which represent the Mediterranean Diet (MD), last studies suggest that food consumption patterns and energy and nutrient intakes have changed markedly in the last forty years, differing somewhat at present from the traditional and healthy MD[1-2]. This phenomena is not unique in Spain, other countries traditionally associated to the MD are also experiencing the trend of adopting a more "westernised" lifestyle combined with limited awareness on health issues, poor dietary habits, and a sedentary lifestyle which provides an explanation for the increased risk of cardiovascular diseases (CVD) among the adult Mediterranean population[3-5].

The biological and physiological changes that occur during menopause in midlife women, along with inadequate dietary habits may result in an increased risk of developing health problems leading by obesity and diabetes, CVD, osteoporosis and certain types of cancer[6] which could reduce this population quality of life, increase their morbidity and mortality and as a consequence, increase the healthcare expenditure[7].

In this context, MD is considered a benefit to human health in general and in women in particular, in terms of both primary and secondary prevention of CVD and other chronic diseases[8-9] as well as for its benefits on the physiological and psychological changes that occur in menopause[10]. Many studies suggest a positive association between MD adherence and a significant reduction of overall mortality, cardiovascular, cancer, osteoporotic and neurodegenerative diseases incidence or mortality with just a slight increase of adherence to the MD[3,9,11]. Although not all studies show a protective effect of the MD on body weight and obesity[12-17], the evidence suggests a beneficial role of this dietary pattern and some of these studies show that the MD has a beneficial effect regarding body weight reduction and obesity[18-20].

Therefore the aims of this study are (i) to assess the level of adherence to the MD of a group of midlife south Spanish women as well as their dietary food habits, the level of compliance with the Dietary Reference Intakes (DRIs) and (ii) to study the impact and influence of weight status on these outcomes.

Methods

Participants and study design

The data reported here were obtained within the framework of a large-scaled study in the province of Granada, Andalusia. A cross-sectional epidemiological survey was conducted from February 2010 to June 2013. The recruitment of participants was performed by researchers from the Department of Physiology at the University Granada and by physicians from the main Primary Care Centers via personal interview or information panels. The inclusion criteria were: (a) women, (b) age ranged 45-65 years old, (c) not to have acute or terminal illness, (d) willingness to participate in the research. After being informed of the purpose and procedures of the study, 206 women aged 53.3±5.5 years old were included in the present study.

All the measurements were performed in a single day and by the same qualified and trained researchers to reduce inter-examiners variations. The study was reviewed and approved by the Ethics Committee of the University of Granada and informed consent was obtained from each subject.

Procedures

Anthropometry and body composition

A portable eight-polar tactile-electrode impedanciometer (InBody R20; Biospace, Gateshead, UK) was used to measure weight, body fat and skeletal muscle mass. The validity of this instrument has been reported elsewhere[21]. Height was measured using a stadiometer (Seca 22, Hamburg). Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters) squared and categorized following the World Health Organization (WHO) criteria: underweight (<18.5 kg/m^2), normal-weight (NW) (18.5-24.99 kg/m^2), overweight (OW) (25.0-29.99 kg/m^2) and obese (OB) (≥30.0 kg/m^2)[22]. Waist circumference (WC) was measured with the woman standing at the middle point between the ribs and ileac crest (Harpenden anthropometric tape, Holtain Ltd). Bone mineral density was measured by means of a quantitative portable ultrasound scanner (CUBA Clinical™, Sunlight Omnisense™) which measures absolute and relative values. The average relative value of bone quality used was T-score, which according to experts convened by WHO, has been recommended to define the risk of osteoporosis[23].

Dietary intake

Food consumption was assessed by a 48-h recall method validated by our group in several publications[24-25], in which the participants were interviewed and asked

to recall all foods consumed during the preceding 48 hours[26]. The data recorded concerned the type of food, the amount of food consumed, the method of preparation and the ingredients used. Note was taken of the recipes, condiments, fats or oils used and the brands of the foods[27].

The questionnaire was based on open-ended questions, and photographs were used as a reference for portion size. Food intakes were converted into energy and nutrients with the help of the Spanish Food Composition database[28], using the program *Alimentación y Salud 2120-AYS-48929-40690 Version 2.0*, designed by the Institute of Nutrition and Food Technology, University of Granada. Compliance with the DRIs was calculated using the current guidelines for the Spanish population[29].

Food Frequency questionnaire

It has been used a validated food frequency questionnaire, designed by Mataix et al. in 2000[30]. It consists on a list of 78 foods on which respondent were asked the frequency of consumption (never or number of times per day, week, month or year).

Accordance with the adherence to the MD was evaluated with the Mediterranean Diet Score (MDS), an index created in 2006 by Panagiotakos et al.[17] to evaluate the degree of adherence to the traditional Mediterranean dietary pattern, which represents the traditional MD consumed in Spain at around 1960[31]. It is composed of eleven variables which scores from zero to five depending on the type of food and on de consumption frequency. The MDS ranges from 0 to 55, so that higher values indicate better MD accordance. Cut-off point analysis carried out by the same group of scientists pointed out that the optimal value was 28 as it represented the minimal score at which a decrease in the relative risk of developing coronary syndromes was observed[17]. Furthermore, individuals in the highest tertiles of the MDS[17], had 46% lower odds (odds ratio=0.54, 95% CI 0.44-0.66) of having acute coronary syndromes as compared to the individuals in the lower tertile[17]

Lifestyle and clinical history

The data for this questionnaire were compiled by personal interview with their physicians using a structured questionnaire developed by the National Health Survey (Ministry of Health and Consumer Affairs, 2001)[32].

Statistical analysis

The data were tested for normality before statistical analysis (i.e., skewness and kurtosis tests and histograms for normality), and are presented as means (typical error), unless otherwise indicated. The association between weight status and the study outcomes was examined by one-way analysis of covariance (ANCOVA) after adjustment for age. When significant, pairwise comparisons with Bonferroni's adjustment were performed to keep the experiment wise error rate to α=0.05 and to identify between which groups the differences were significant (e.g. OW vs. OB). Nominal variables such as the differences on obesity status categories were analysed using Chi-squared test All analyses were performed using the Statistical Package for Social Sciences (IBM-SPSS, version 20.0 for Windows), and the level of significance was set at 0.05. Additionally, standardized effect size statistics were estimated in all the comparisons among weight status categories. We used *Cohen's d* and its exact confidence interval for all (parametric) variables. The exact confidence intervals for *Cohen's d* were obtained by means of the non-centrality parameter of the non-central Student's distribution using Wolfram-Mathematica 8.0.

Results

Socioeconomic analysis showed that more than 50% of the individuals had a medium-income status, 80% were housewives, unemployed or retired, had no studies or primary education and 92% live with at least one relative (Table I). A positive relationship between age, occupational and socioeconomic status, household members and weight was found ($p<0.05$).

Anthropometric characteristics of the study participants are shown in Table II. 86% of the sample was OW or OB (no woman was underweight). Mean body fat percentage of the sample was 40.32% with an average value of WC of 91.4 cm. Values of bone mineral density, expressed as t-score, showed an average of -1.26 standard deviations.

Table III shows daily intakes and level of compliance with DRIs of energy and nutrients depending on BMI after being adjusted for age (data from 48-h recall). Energy intake was lower as weight status increased ($p<0.05$). Pairwise analysis showed differences between the NW compared to the OW and OB groups (both $p<0.05$). Likewise protein intake decreased as weight status increased ($p<0.05$) and pairwise analysis showed differences between the NW compared to the OW and OB groups (both $p<0.05$). No differences between weight status groups were observed for carbohydrates, total fat, saturated, monounsaturated or polyunsaturated fats. Regarding DRIs, cholesterol, protein and total fat intakes exceed it while carbohydrate intake remained under the recommendations for all weight groups. Vitamin intakes did not differ among groups except for vitamin B2 and biotin, whose intakes decreased as weight status increased and in which pairwise analysis showed differences between the NW compared to the OB group ($p<0.05$). Mine-

Table I
Sociodemographic characteristics of the study sample

		BMI (kg/m²)			p-value
		≤24.99%	25-29.99%	≥30%	
Age	45-54 years N=129 (62.6%)	11.6	62	26.4	*p<0.001*
	55-65 years N=77 (37.4%)	18.2	33.8	48.1	
	Total	14.1	51.5	34.5	
Occupational Status	Housewife/Retired N=111 (53.6%)	12.4	47.2	40.4	*p=0.038*
	Unemployed/Temporal work N=59 (28.9%)	6.2	64.6	29.2	
	Working N=36 (17.5%)	27.6	41.4	31	
	Total	13.3	51.2	35.5	
Socioeconomic Status	Low income N=76 (37%)	13.1	47.5	39.3	*p=0.045*
	Medium income N=119 (57.6%)	9.5	55.8	34.7	
	High income N=11 (5.5%)	44.4	33.3	22.2	
	Total	12.7	51.5	35.8	
Educational Status	No formal education N=28 (13.6%)	18.2	40.9	40.9	*p=0.144*
	Primary/secondary school N=135 (65.5%)	8.4	54.2	37.4	
	Professional Training/ University N=43 (20.9%)	38.1	20.2	15.5	
	Total	12.9	51.5	35.6	
Household	Alone N=16 (92.1%)	38.5	23.1	38.5	*p=0.008*
	Husband/parents/sons N=190 (7.9%)	10.5	53.9	35.5	
	Total	12.7	51.5	35.8	

BMI, body mass index.

ral intakes showed differences in sodium and chlorine whose intakes decreased as weight status increased and in which pairwise analysis showed differences between the NW compared to the OB group (both *p<0.05*). Nutritional requirements for vitamin D, zinc and iodine intake were below the recommendations for all weight status groups.

Table IV shows the Food Consumption Pattern and the level of compliance with DRIs depending on BMI (data from Food Frequency Questionnaire). No significant differences between weight status groups were observed except for sweet consumption, in which pairwise comparisons showed differences between NW and OB group *(p<0.05)*, and all groups exceed the DRIs. Other results were observed regarding the quality of the diet. None of the groups present an intake of cereals over the DRIs, neither of water, eggs, nor of fruit. Regarding meat, viscera and meat sub products (sausages, salami, etc.) and sweetened beverages, intakes exceed de DRIs.

Finally, MDS values did not show statistical differences across weight status categories and positioned women in the second tertile of the score[33].

Table II
Anthropometry and body composition of the study sample

Anthropometric measures	*Mean (SD)*
Weight, kg	71.62 (12.59)
BMI, kg/m²	29.72 (5.04)
Fat mass, %	40.32 (6.31)
WC, cm	91.36 (11.72)
WC>cutoff limits, %	58.1
WC/Height Ratio	0.58 (0.07)
WC/Height Ratio >cutoff limits, %	91.9
Weight Status, NW/OW/OB (%)	14.1/51.5/34.5
t-score, standard deviations	-1.26 (1.03)

Values expressed as mean (standard deviation), otherwise indicated; SD, standard deviation; BMI, body mass index; WC, waist circumference; NW, normal-weight; OW, overweight; OB obese.

Discussion

The findings of the study should be taken with caution due to the fact that the study sample was relatively small, of convenience, and not represen-

Table III
Energy and Nutrient Intake of the study sample across weight status categories

	Intakes					*%DRI*		
	BMI (kg/m²)					*BMI (kg/m²)*		
	≤24.99 (n=29)	*25-29.99 (n=106)*	*≥30 (n=71)*	*p-value*	*Effect size*	*≤24.99*	*25-29.99*	*≥30*
Kcal	1968.24 (94.98)*†	1688.69 (50.25)*	1645.29 (61.26)†	0.014	0.64 (0.21-1.05)	107.37 (5.92)	93.18 (3.39)	88.12 (3.89)
Proteins, g	91.36 (4.90)*†	77.13 (2.59)*	75.06 (3.16)†	0.017	0.62 (0.21-1.03)	216.76 (13.03)	186.79 (7.47)	181.03 (8.57)
Carbohydrates, g	221.63 (12.20)	193.60 (6.45)	190.51 (7.87)	0.083	0.47 (0.07-0.88)	76.34 (2.88)	76.32 (1.65)	78.69 (1.90)
Total Fat, g	82.39 (5.25)	70.80 (2.78)	69.03 (3.39)	0.090	0.47 (0.07-.088)	126.39 (5.62)	125.17 (3.23)	118.41 (3.70)
SFA, g	19.88 (1.51)	17.27 (0.80)	16.38 (0.97)	0.151	0.43 (0.03-0.84)	89.84 (5.48)	92.28 (2.90)	88.81 (3.54)
MUFA, g	36.42 (2.53)	32.37 (1.34)	31.93 (1.63)	0.298	0.33 (0.07-0.73)	138.58 (8.00)	145.61 (4.23)	145.42 (5.16)
PUFA, g	12.58 (1.55)	10.30 (0.82)	10.36 (1.00)	0.403	0.31 (0.09-0.72)	52.02 (5.21)	48.26 (2.75)	48.54 (3.36)
Cholesterol, mg	234.12 (27.24)	239.65 (14.41)	254.51 (17.57)	0.750	0.10 (0.30-0.50)	119.04 (15.19)	119.65 (8.72)	123.71 (10.00)
Fiber, g	23.06 (1.66)	20.16 (0.88)	20.97 (1.06)	0.301	0.37 (0.03-0.78)	89.68 (8.00)	83.53 (4.59)	87.69 (5.27)
Vit A,μg	1033.61 (177.00)	805.84 (93.64)	850.69 (114.16)	0.525	0.28 (0.13-0.68)	125.20 (29.92)	118.22 (17.17)	112.27 (19.69)
Vit B1,mg	1.77 (0.22)	1.59 (0.11)	1.63 (0.14)	0.764	0.18 (0.22-0.58)	222.91 (35.48)	216.72 (20.36)	212.07 (23.35)
Vit B2,mg	2.54 (0.23)*	1.96 (0.12)	1.88 (0.15)*	0.041	0.53 (0.12-0.94)	200.85 (23.09)	177.75 (13.25)	152.27 (15.20)
Vit B6,mg	2.21 (0.54)	2.33 (0.29)	1.83 (0.35)	0.551	0.19 (0.21-0.59)	133.95 (37.76)	162.00 (26.56)	114.81 (30.46)
Vit B12, μg	6.07 (2.16)	8.52 (1.14)	5.60 (1.39)	0.238	0.28 (0.12-0.68)	357.60 (74.50)	392.11 (42.74)	301.34 (49.02)
Vit C,mg	183.51 (19.64)	161.32 (10.39)	169.49 (12.67)	0.596	0.24 (0.16-0.65)	282.59 (37.56)	279.32 (21.55)	289.07 (24.71)
Vit D, μg	6.12 (1.05)	3.80 (0.56)	3.29 (0.68)	0.075	0.50 (0.09-0.91)	87.02 (19.66)	83.62 (11.28)	58.48 (12.94)
Vit E,mg	12.82 (1.26)	10.97 (0.67)	10.78 (0.81)	0.366	0.30 (0.10-0.71)	103.61 (12.57)	92.71 (7.21)	85.31 (8.27)
Niacin,mg	31.97 (3.25)	26.18 (1.72)	24.08 (2.10)b	0.127	0.45 (0.05-0.86)	230.63 (30.40)	208.71 (17.44)	174.11 (20.00)
Pantotenic Acid	4.82 (0.40)	4.69 (0.21)	4.87 (0.26)	0.861	0.11 (0.29-0.51)	-	-	-
Biotin, μg	14.13 (2.07)*	8.87 (1.10)	8.06 (1.34)*	0.041	0.55 (0.14-0.96)	-	-	-
Folate, μg	302.51 (25.92)	301.49 (13.71)	292.35 (16.71)	0.903	0.07 (0.33-0.47)	142.34 (15.57)	157.08 (8.93)	141.82 (10.24)
Sodium,mg	2357.74 (227.75)*	1832.40 (120.49)	1583.84 (146.89)*	0.014	0.69 (0.27-1.10)	117.36 (11.36)	91.83 (5.99)	79.22 (7.33)

Table III (cont.)
Energy and Nutrient Intake of the study sample across weight status categories

	Intakes					*%DRI*		
	BMI (kg/m²)					*BMI (kg/m²)*		
	≤24.99 (n=29)	*25-29.99 (n=106)*	*≥30 (n=71)*	*p-value*	*Effect size*	*≤24.99*	*25-29.99*	*≥30*
Potasium,mg	3247.18 (194.61)	2910.21 (102.96)	2865.11 (125.51)	0.233	0.37 (0.04-0.77)	92.78 (5.58)	83.55 (2.94)	81.91 (3.60)
Calcium,mg	910.71 (57.06)	876.34 (30.19)	834.10 (36.80)	0.480	0.25 (0.15-0.65)	104.19 (8.31)	107.55 (4.77)	98.82 (5.47)
Phosphorus,mg	1308.45 (69.22)	1153.60 (36.62)	1141.34 (44.64)	0.102	0.45 (0.04-0.86)	182.40 (10.63)	165.19 (5.40)	164.72 (6.65)
Magnesium,mg	347.16 (21.75)	309.06 (11.51)	292.36 (14.03)	0.109	0.47 (0.06-0.88)	107.08 (7.33)	103.77 (4.21)	94.48 (4.82)
Iron,mg	14.97 (3.29)	16.27 (1.74)	16.77 (2.12)	0.899	0.07 (0.33-0.48)	122.29 (40.61)	150.68 (23.30)	162.66 (26.72)
Zinc,mg	8.51 (0.68)	7.60 (0.36)	6.94 (0.44)	0.142	0.43 (0.02-0.84)	54.01 (7.27)	51.78 (4.17)	49.50 (4.78)
Iodine, μg	102.73 (14.41)	101.13 (7.62)	85.67 (9.29)	0.392	0.22 (0.18-0.62)	77.27 (13.37)	87.89 (7.67)	77.32 (8.80)
Cooper, μg	12.08 (5.56)	7.67 (2.94)	4.98 (3.59)	0.558	0.24 (0.16-0.64)	-	-	-
Chlorine,mg	2648.73 (318.62)*	2028.76 (168.57)	1705.00 (205.50)*	0.046	0.55 (0.14-0.96)	-	-	-
Manganese,mg	12.84 (4.89)	8.27 (2.59)	3.67 (3.16)	0.318	0.35 (0.05-0.75)	-	-	-
Selenium, μg	83.22 (5.70)	67.38 (3.02)	71.28 (3.67)	0.073	0.60 (0.18-1.01)	149.51 (10.38)	123.07 (5.47)	129.69 (6.69)

Values expressed as mean (standard error).SFA, Satuarted Fatty Acids; MUFA, Monounsaturated Fatty Acids; PUFA, Poliunsaturated Fatty Acids.
*,† Common superscripts in a same row indicate a significant difference (P<0.05) between the groups with the same symbol; Pairwise comparisons were performed with Bonferroni's adjustment.

tative of the region studied. On the other hand, the findings of the present study have highlighted some aspects which deeply differ from the nutrition goals for this population and concur with the general trend in Spain as well in other Mediterranean countries of showing a dangerous departure from the traditional MD which, from the 60s, has characterized this area[2,34-37]. Concretely, our results indicated that, despite than more than 93.1% of the sample was over the cut-off limits[33] only the 23% were in the highest tertiles of the MDS.

Rates of OW and OB and central adiposity (as measured through the WC and WC/height ratio) were extremely high. In fact 60% and 91.4% of the sample were over the cutoff limits respectively[38]. However, these alarming values do not differ from other epidemiological studies developed in Spain[4,39-42], neither from data from the WHO[43]. Indeed, Andalusia stands out for being one of the communities with higher prevalence of OB in the country what clearly position these women at an increased CVD risk[38,44].

The macro and micronutrients analysis of the diet showed clear deviations from the Food Consumption Guidelines developed by the Spanish Society of Community Nutrition[29]. We have observed an unbalanced daily intake of energy and macronutrients in favor of a higher consumption of proteins (190% of DRIs) and fat (122% of DRIs) and the low percentage of carbohydrates (76% of DRIs) (Fig. 1) which, as expected, is a general trend in the Spanish population[1,37,45]. This concurs with the results observed regarding to the dietary patterns in which cereals, main source of this macronutrient, were below the recommendations in all weight status groups. As expected, the contrary has been observed in meat, viscera and sub products, which were far away from the recommended intakes. This may explain the high total cholesterol intake found too, and could agree with the high prevalence of OW and OB aforementioned. The lack of cereals in the diet, mainly whole grain cereals, is in accordance with the general trend observed in other studies in Spain[1,45-46], even if in this group the intakes are slightly higher respect to

Table IV
Food frequency patterns of the study sample across weight status categories

	Intakes					*%DRI*		
	BMI (kg/m²)					*BMI (kg/m²)*		
	≤24.99 (n=29)	*25-29.99 (n=106)*	*≥30 (n=71)*	*p-value*	*Effect size*	*≤24.99*	*25-29.99*	*≥30*
Cereals ,svg/d	3.65 (0.24)	3.44 (0.12)	3.55 (0.15)	0.697	0.19 (0.21-0.60)	73.02 (4.77)	68.84 (2.44)	71.00 (2.99)
Dairy products svg/d	2.95 (0.22)	2.74 (0.11)	2.61 (0.14)	0.436	0.29 (0.11-0.70)	98.37 (7.45)	91.54 (3.81)	87.18 (4.66)
Vegetables (svg/d)	4.15 (0.30)	3.73 (0.15)	3.76 (0.18)	0.447	0.31 (0.09-0.71)	207.34 (14.78)	186.66 (7.55)	188.08 (9.25)
Fruits, svg/d	1.99 (0.23)	2.20 (0.12)	1.98 (0.15)	0.459	0.15 (0.55-0.25)	66.36 (7.79)	73.24 (3.98)	65.88 (4.88)
Meat and subproducts, svg/w	4.04 (0.36)	3.77 (0.18)	3.90 (0.22)	0.781	0.17 (0.23-0.57)	115.39 (10.21)	107.82 (5.22)	111.37 (6.39)
Fish, svg/w	5.12 (0.43)	4.40 (0.22)	4.83 (0.27)	0.245	0.37 (0.04-0.77)	146.29 (12.39)	125.72 (6.33)	137.87 (7.75)
Eggs, svg/w	2.32 (0.20)	2.04 (0.10)	2.19 (0.12)	0.389	0.31 (0.09-0.72)	66.36 (5.69)	58.40 (2.91)	62.73 (3.56)
Pulses, svg/w	2.94 (0.23)	2.77 (0.12)	2.71 (0.15)	0.701	0.18 (0.22-0.59)	117.64 (9.33)	111.00 (4.77)	108.37 (5.84)
Viscera and meat subproducts, svg/w	6.86 (0.84)	5.75 (0.43)	6.18 (0.53)	0.481	0.11 (0.51-0.29)	342.88 (41.98)	287.46 (21.46)	308.95 (26.28)
Sugar and Sweets, svg/w	9.99 (1.40)	8.81 (0.72)*	6.63 (0.88)*	0.036	0.49 (0.08-0.89)	666.23 (93.50)	587.16 (47.79)	441.86 (58.53)
Fats, svg/w	3.04 (0.15)	2.88 (0.08)	2.98 (0.09)	0.537	0.14 (0.55-0.26)	-	-	-
Alcoholic beverages, svg/w	3.70 (0.69)	2.58 (0.41)	2.06 (0.50)	0.221	0.32 (0.73-0.08)	-	-	-
Non-alcoholic beverages, svg/w	2.88 (1.12)	3.15 (0.57)	3.71 (0.70)	0.759	0.14 (0.54-0.26)	192.27 (74.47)	209.77 (38.06)	247.46 (46.61)
Water (ml/day)	1205 (130)	1310 (65)	1317 (80)	0.737	0.18 (0.58-0.22)	60.24 (6.48)	65.54 (3.31)	65.85 (4.05)
MDS	34.04 (0.95)	33.14 (0.49)	33.64 (0.60)	0.651	0.20 (0.19-0.61)	-	-	-

Values expressed as mean (standard error). MDS, Mediterranean Diet Score
*,† Common superscripts in a same row indicate a significant difference (P<0.05) between the groups with the same symbol; Pairwise comparisons were performed with Bonferroni's adjustment.

those previously mentioned. Since the 1960's, cereals and its derivates have shown a marked decreased (434 g/day in 1964 vs. 214 g/day in 2006)[1] and still is bread the most important food within this group in which has been observed that white bread consumption represented 2/3 of total bread intake while whole bread represented 1/3. Although last studies have demonstrated that the consumption of dietary fiber and whole grain intake is inversely related to obesity, type two diabetes, cancer and CVD[47-48], it seems like the message has not been taken hold onto the general population, who is still in the wrongly believe that bread contributes to weight gain, which is not true in the case of whole grain type[46]. In the same trend is the consumption of eggs which was under the recommendations in all weight status groups following a decreased since the 2000 (4.6 medium-size eggs/week vs 3.7 medium-size eggs/week in 2006)[1,49]. The decline in egg consumption is probably due to the general concern that eggs are 'unhealthy', based on their cholesterol content. Although it is true that eggs contain cholesterol, it must be remembered that the consumption of saturated fatty acids has a higher influence on cholesterol levels than dietary cholesterol[1]. Fruits consumption still remained under the recommendations accordingly to other Spanish studies[1,45]. Nevertheless, its consump-

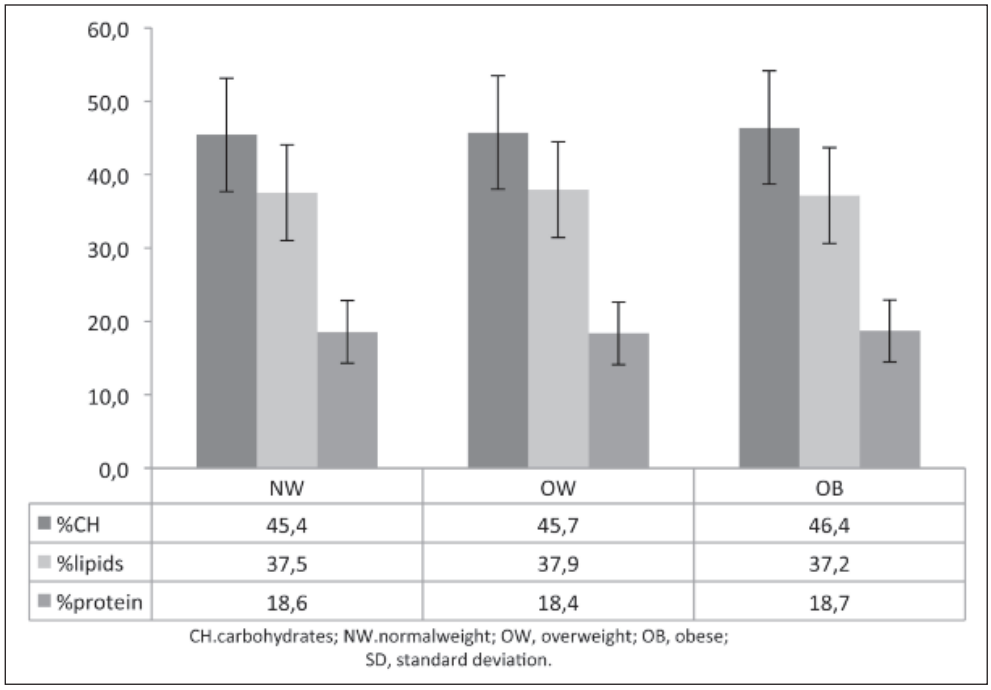

Fig. 1.—Percentaje of Kcal provided by macronutrients across weight status categories.

tion, when compared with 1964 data, has nearly doubled[1,45,49]. Finally water consumption it has been also found to be inadequate with almost the whole sample below the 2/3 of the recommendations. Nonetheless, comparisons with other studies have been difficult to conduct due to the lack of consensus about the methodology used[50-51] and the scarcity of them[52]. Since water is considered an essential nutrient for life it should be taken into account in every nutrient assessment study. Unfortunately, most studies underestimate water collection as part of the diet, since it contributes with no calories and no nutrients.

In contrast, it has been observed a marked rise on total food intake, far away from recommendations especially based on viscera and meat sub products, sugar, sweets and sweetened beverages[2]. The high meat consumption observed in this study concurs with the general trend in Spain which has remained constant in the last decade[52]. Despite sweet consumption greatly exceeded the DRIs for all weight status groups, its consumption and its relation with OW and OB status is still uncertain, as studies provide a lack of consensus and inconsistent results[53]. Indeed, the results observed showed a negative correlation with BMI, as well as for Energy intake, which should be considered cautiously since it is well known that overweight and obese persons are likely to underreport intake during dietary recall[54], representing one potential limitation of our study. Nevertheless, the relationship between the consumption of sugar-sweetened beverages and body weight has become a matter of much public and scientific interest[55]. Added sugar has been evidenced as a contributor to weight gain in children and adults[53] and probably to the risk of diabetes, fractures, and dental caries[55]. The lack of a significant difference in the present study between groups may be due to the effect size, characterised by a small sample size representing the NW group.

When analysing these results as a whole and comparing it with similar studies[1], is observed that MD is at risk precisely in the Mediterranean population, and that risk does exist not only in the OW and OB population but throughout the study sample independently of their weight status, so whether these dietary habits along with the unbalanced diet reported are prolonged over time the overweight and obese population will increase as well as the risk of developing any of the aforementioned chronic diseases, and will finally concur with the high prevalence of cardiovascular[40] and osteoporosis risk over this population[56].

There are several limitations inherent in our study design. The study was observational in its nature and, although likely to be reflective of usual dietary patterns, may be subject to selection bias. Results may be biased by the use of a convenience sample and by the selection of patients who consented to the study. The study results are partially based on patient self-report, which is subject to the influence of memory and other subjective factors as the general trend of underreport by obese and overweight patients[54]. In addition, the study lacked of a high sample size and it was carried out only in midlife women, so that future studies should be replicated in other age groups. On the other hand, this study examined a complete range of nutritional behaviors and patterns in a single report, it was corrected by a potential confounder (age), with the use of published validation studies for most of the measurements[5,24-25] including dietary assessment, which

allowed us to deeply explore nutritional status. Finally, the present study, further categorized the sample by weight status categories (i.e. NW, OW and OB) in order to test the presence or absence of significant differences between dietary habits and nutrient intake across weight status categories.

Conclusions

Despite that dietary guidelines warn against unhealthy-related eating behaviors, these results point to a deficient dissemination and implementation of these guidelines, as well as a progressive distancing from the Mediterranean dietary pattern. This study should stimulate further research, involving larger sample sizes, on MDS and other health indicators in understudied populations because it may in effect have the potential to find out the main deviations of the traditional MD and healthy patterns that have characterized the Mediterranean countries, and could be the key to the development of customized educational programs aimed to be effective. Indeed, initiatives such as improving nutritional education and lifestyle in this population from primary care centers could help reduce the burden of chronic diseases and their associated costs.

Finally, taking into account that in Spain most of midlife women have an important role in education and nutritional habits of their household, the beneficiaries of these initiatives could be extended and reach beyond the purpose of this project.

Conflict of interest

The authors report no conflict of interest.

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2. DIETA MEDITERRÁNEA Y OTROS FACTORES QUE PUEDEN INFLUIR SOBRE LA SALUD CARDIOVASCULAR Y LA DENSIDAD MINERAL ÓSEA DURANTE LA PERIMENOPAUSIA (ESTUDIOS II Y III)

Influence of the degree of adherence to the Mediterranean diet on the cardiometabolic risk in peri and menopausal women. The Flamenco Project.

II

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Influence of the degree of adherence to the Mediterranean diet on the cardiometabolic risk in peri and menopausal women. The Flamenco project

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KEYWORDS
Cardiovascular disease;
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Tobacco

Abstract *Background and aims:* The Mediterranean diet (MD) has been associated with reduced morbidity from cardiovascular diseases in the general population. The aim of this study was to assess whether different degrees of adherence to the MD were associated with the cardiometabolic risk in peri and menopausal women.
Methods and results: This cross-sectional study included 198 peri and menopausal women participating in the Flamenco project. Validated questionnaires were used to assess menopause health-related quality of life and degree of adherence to the MD (low, medium and high). The following cardiometabolic risk factors were assessed: fat mass percentage, waist circumference, blood pressure and resting heart rate, plasma markers (total cholesterol, high and low-density lipoprotein cholesterol [HDL-C and LDL-C, respectively], total cholesterol/HDL ratio, triglycerides, C-reactive protein and fasting glucose), Physical activity levels and smoking status. The degree of adherence to the MD among the study sample was 27%, 40% and 30% for low, medium and high adherence, respectively. After controlling for potential confounders, women with a high adherence to the MD showed lower plasma total cholesterol ($p = 0.025$), resting heart rate ($p = 0.005$), LDL-C ($p = 0.019$), triglycerides ($p = 0.046$) and C-reactive protein ($p = 0.009$) compared to those with a low adherence. Likewise women with high adherence to the MD showed lower total cholesterol/HDL-C ratio ($p = 0.020$) compared to those with a medium adherence. The high MD adherence group also showed lower clustered cardiometabolic risk ($p = 0.004$). Moreover, when analysing specific MD components, whole grain cereals, pulses (both $p < 0.05$) and red wine ($p < 0.01$) consumption were inversely associated with the clustered cardiometabolic risk.
Conclusion: The present findings suggest that a high but not medium adherence to the MD is associated with a cardioprotective effect in peri and menopausal women. As a low percentage of the sample showed a high adherence to the MD, future research aimed at increasing the adherence to this dietary pattern for a better cardiometabolic status during peri and menopause is warranted.

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Introduction

Cardiovascular diseases (CVD) remain the leading cause of death around the world [1]. The proportion of all deaths attributable to CVD are substantially greater among women (51%) than men (42%), representing a serious and growing public health problem, and placing an enormous burden on global healthcare systems and resources [1,2]. While CVD is generally rare in young women, as women get older the vulnerability to CVD risk factors rises [1]. The characteristic hypoestrogenism present in postmenopause promotes endothelial dysfunction, hypertension, proatherogenic lipid changes and insulin resistance, among other CVD risk factors [3]. Furthermore, during the perimenopausal period, which may appear 6 years before menopause and subside 2–5 years later, fluctuation of hormones already exists and therefore, the aforementioned vulnerability [4]. Finally, due to the fact that with increasing longevity post-menopausal years increase [5], an optimum cardiometabolic status during peri and menopause is desirable to prevent or delay premature cardiovascular events in the elderly [3].

Healthy lifestyle and diet at younger and middle ages are key factors for a life free of chronic diseases at later ages [6]. Nowadays, the epidemiologic evidence on the CVD protection afforded by the traditional Mediterranean diet (MD) is strong [7,8]. Likewise, systematic reviews and meta-analyses of observational prospective studies have confirmed that a greater adherence to the MD is associated with a significant improvement in health status and a significant reduction in overall mortality, as well as in morbidity and mortality from CVD in the general population [9,10]. However, no previous studies have focused, so far, on this transitional and crucial physiological stage of women. Thus, it may be clinically relevant to determine the appropriate degree of adherence on which the aforementioned cardiovascular protection could be reached, especially when recent studies suggest a progressive distancing of the MD pattern in this specific population [11,12].

Therefore, the objectives of the present study were to evaluate, in a southern Spain population-based sample of peri and menopausal women: (1) their degree of adherence to the MD, (2) the influence of the aforementioned degree of adherence with CVD risk factors, and (3) the influence of the degree of adherence to the MD on the clustered cardiometabolic risk.

Methods

Study population

The recruitment and procedures of the subjects for the present study (The Fitness League against Menopause Costs, Flamenco project) are described elsewhere [13]. Women were contacted through primary care centres from Granada (Southeast Spain) and press releases. The total sample for present analyses comprised 198 peri and menopausal women (age range 45–60 years) who were informed about the aims and study procedures and signed a written informed consent before being enrolled in the study.

The procedures have been reviewed and approved by the Ethics Committee for Research Involving Human Subjects at the University of Granada.

Procedures

Assessment protocol was completed in two non-consecutive days (e.g. Monday and Wednesday). Socio-demographic, dietary and clinical characteristics, blood pressure, resting heart rate and body composition (in the same order as presented here) were assessed on day one. Participants completed self-reported questionnaires about their clinical and socio-demographic characteristics. On day two, participants attended the primary care centre for the biochemical analysis.

Socio-demographic and clinical information

Socio-demographic (including age, educational status and current occupational status, among others) and health-related information (e.g. smoking habit and history of illness) was collected using a questionnaire.

The Cervantes Scale [14] is a validated questionnaire specific for Spanish middle-aged women to quantify menopause health-related quality of life. It contains 31 items or questions (positive and negative ones) grouped into four domains: ‘Menopause and Health’; ‘Psychological’; ‘Sexuality’ and ‘Couple Relationship’. Global Cervantes scores range from 0 to 155 points where higher global and domain Cervantes scores denoting worse quality of life.

Body composition

Weight (kg) was assessed with a scale (InBody R20, Biospace, Seoul, Korea). Lean and fat mass of the whole body was measured using a dual-energy X-ray absorptiometry device (Hologic Discovery QDR, Nasdaq: HOLX). Height (cm) was measured using a stadiometer (Seca 22, Hamburg, Germany). Waist circumference (cm) was assessed at the middle point between the ribs and the ileac crest, with the participant standing (Harpenden anthropometric tape, Holtain Ltd). Height and weight were used to calculate body mass index (BMI) (weight [Kg]/height [m^2]) and categorized following the World Health Organization criteria: normal-weight (18.5–24.99 kg/m2), overweight (25–29.99 kg/m2) and obese ($\geq$30 kg/m2) [15].

Vascular function

Systolic and diastolic blood pressure, as well as resting heart rate, were measured after 5 min of rest, on two separate occasions (with 2 min between trials), with the person seated (Omron Health Care Europe B.V. Hoofddorp). The lowest value of the two trials was selected for the analysis.

Dietary patterns

A validated food frequency questionnaire, designed by Mataix et al. [16] has been employed to study dietary

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habits. It consists of a list of 78 foods wherein participants were asked about the frequency of consumption (never or number of times per day, week, month or year) for the different foods. Compliance with the Dietary recommended intakes (DRIs) was calculated using current guidelines for Spanish population [17]. The adherence to the MD was evaluated with the Mediterranean diet score (MDS), an index created by Panagiotakos et al. [18] to evaluate its predictive ability on cardiovascular disease risk and markers. It is composed of eleven variables scoring from zero to five depending on their position in the MD pyramid [19]. Thus, for the consumption of items presumed to be close to this pattern (e.g. non-refined cereals) it was assigned a score of 0 when a participant reported no consumption, a score of 1 with consumption 1–4 servings/month, a score of 2 with 5–8 servings/month, a score of 3 with 9–12 servings/month, a score of 4 with 13–18 servings/month and a score of 5 for more than 18 servings/month. In contrast, for consumption of foods presumed to differ from this diet (e.g. meat and cured meats) we assigned the scores on a reverse scale. The MDS ranges from 0 to 55, with higher values indicating better MD accordance. Both questionnaires were administered to participants by trained interviewers. Based on the MDS, participants were categorized into three groups: low adherence (MDS $\leq$ 29.99), medium adherence (MDS 30–33.99) and high adherence (MDS $\geq$ 34) groups [18,20].

Biochemical markers

Venous blood samples after overnight fasting were collected. Plasma total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides, C-reactive protein and glucose were assessed with standard procedures using an autoanalyzer (Hitachi-Roche p800, F. Hoffmann-La Roche Ltd. Switzerland).

Physical activity levels

Accelerometry was used to objectively measure moderate-vigorous physical activity. Women were asked to wear a tri-axial accelerometer (Actigraph GT3X+, Pensacola, Florida, US) for 9 consecutive days, starting the next morning after they received the monitor. The first and last day were excluded from the analyses, accounting for a total of 7 complete days of recording.

Statistical analysis

Descriptive statistics were used to characterize participants' socio-demographic, clinical and nutritional information (objective 1). The data were tested for normality before statistical analysis (e.g. skewness and kurtosis tests and histograms). Nominal variables were analysed by the Chi-squared test. The association between the degree of adherence to the MD and CVD risk factors (objective 2) was examined by one-way analysis of covariance (ANCOVA) after adjusting for age, BMI, regular menstruation, smoking habit and use of hormone replacement therapy, additionally adjusted for physical activity levels in the multivariate model. A clustered cardiometabolic risk (z-score) was created as the mean of the standardized scores [(value - mean)/standard deviation] of waist circumference, the average between systolic and diastolic blood pressure, plasma triglycerides, HDL-C, C-reactive protein and fasting glucose [21]. This clustered cardiometabolic risk was compared across MD adherence groups by ANCOVA after adjusting for age, BMI, regular menstruation, smoking habit, use of hormone replacement therapy and physical activity levels (objective 3). Post-hoc multiple comparisons with the Bonferroni's correction were applied to examine pairwise differences between groups (e.g. low vs. high MD adherence).

To test which specific components of the MD were associated with the clustered cardiometabolic risk, a linear regression analyses was carried out including the clustered cardiometabolic risk as dependent outcome and all the MD components as independent outcomes.

All the analyses were performed using the Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, version 20.0, Armonk, New York) and the level of significance was set at $\alpha = 0.05$ two-tailed.

Results

The descriptive characteristics of the study participants across MD adherence groups are shown in Table 1. Thirty-two percent of women were normal-weight, 41% were overweight, 22% of women were obese and there were no underweight women. None of the anthropometric, menopausal health-related quality of life or the socio-demographic characteristics differed between MD adherence groups (all $p > 0.05$).

Food consumption patterns and MDS are shown in Table 2. Cereals, fruits and vegetables consumption met the DRIs for Spanish population, while non-refined cereals and pulses were consumed below the DRIs. Fish and shellfish, red meat and cured meats, poultry and dairy products were consumed over the DRIs. The MDS, measured as the sum of the individual scores for each food or food group, showed a mean score of 31, reflecting a moderate adherence to the MD in this population [20].

Table 3 shows cardiometabolic markers by the three degrees of MD adherence after adjusting for age, BMI, regular menstruation, smoking habit and use of hormone replacement therapy (objective 2). The degree of adherence to the MD was not associated with body composition, systolic and diastolic blood pressure, HDL-C, triglycerides, fasting glucose and smoking habit (all $p > 0.05$). Adherence to the MD was found to be associated with resting heart rate ($p = 0.026$), total cholesterol ($p = 0.028$), LDL-C ($p = 0.027$), total cholesterol/HDL-C ratio ($p = 0.030$), and C-reactive protein levels ($p = 0.011$). Pairwise comparisons showed that the group with a high adherence to the MD had lower resting heart rate, total cholesterol, LDL-C and C-reactive protein levels

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Table 1 Descriptive characteristics of the study participants according to the degree of adherence to the Mediterranean diet (n = 198).

		All participants (N = 198)	Mediterranean diet score			p
			Low adherence (≤29.99) N = 64 (32.2%)	Medium adherence (30–33.99) N = 80 (40.4%)	High adherence (≥34) N = 54 (27.3%)	
Age, years		52.6 (4.5)	52.0 (4.8)	53.1 (4.4)	52.9 (4.1)	0.315
Weight, kg		69.5 (12.2)	72.4 (14.4)	68.4 (11.6)	68.6 (10.0)	0.120
Cervantes global score		52.7 (23.9)	54.7 (25.7)	53.3 (24.4)	51.2 (22.2)	0.742
Menopause and health domain		26.0 (13.9)	27.3 (14.4)	26.4 (13.9)	26.8 (12.1)	0.921
Psychical domain		9.4 (8.1)	10.8 (8.3)	9.2 (8.1)	9.5 (7.5)	0.472
Sexuality domain		11.2 (5.5)	10.6 (5.6)	11.4 (5.2)	10.5 (5.4)	0.549
Couple relationship domain		6.2 (5.5)	6.1 (5.6)	6.3 (5.2)	4.8 (5.0)	0.244
Body mass index	Normal-weight, ≤24.9 (36.9%)	27.1 (4.6)	28.6	42.8	28.6	0.725
	Overweight, 25–29.9 (40.9%)		33.7	36.4	29.9	
	Obese, ≤30 (22.2%)		36.4	43.1	20.5	
Fat mass	Normal, ≤35 (6.6%)	41.3 (5.2)	33.2	42.8	23.7	0.930
	High, >35 (93.4%)		32.4	40.0	27.6	
Waist circumference	No risk, ≤88 cm (29.3%)	93.6 (11.0)	26.7	41.3	32.0	0.472
	Risk, >88 cm (70.7%)		34.8	40.0	25.2	
Occupational status	Working, full-time (36.6%)	–	28.6	50.0	21.4	0.107
	Working, partial-time (14.7%)		46.4	21.5	32.1	
	Unemployed/housewife (48.7%)		31.2	38.7	30.1	
Educational status	No studies/primary school (25.8%)	–	44.9	36.7	18.4	0.112
	High school/professional training (37.4%)		22.5	46.5	31.0	
	University degree (36.8%)		32.9	37.1	30.0	
Smoking habit	No smoker (76.5%)	–	28.5	42.3	29.2	0.124
	Currently smoking (23.5%)		44.4	35.6	20.0	

Values shown as mean (standard deviation) for continuous variables and as percentage for categorical variables.

than the group with a medium adherence. Likewise, pairwise comparisons showed that the group with a high adherence to the MD presented lower total cholesterol/HDL-C ratio than the group with a low adherence (overall $p < 0.05$). After additional adjustment for physical activity (min/week), differences between groups were significantly stronger and new significant differences emerged, i.e., plasma triglycerides ($p = 0.046$), which showed a reduction across degrees of MD adherence. Pairwise comparisons showed that the group with a high adherence to the MD presented lower plasma triglyceride levels than the group with a medium MD adherence ($p < 0.05$).

Table 2 Food frequency patterns and Mediterranean diet score of the study sample (n = 198).

Food groups	Intake		DRI	MDS	
	Mean	(SD)	%	Mean	(SD)
Cereals, svgs/day	2.9	(1.2)	95.7	–	–
Non-refined cereals, svgs/day	0.9	(0.8)	27.3	3.2	(2.1)
Potatoes, svgs/wk	2.2	(1.9)	–	2.2	(1.2)
Fruit, svgs/day	2.3	(1.4)	116.4	4.7	(1.2)
Vegetables, svgs/day	4.6	(2.8)	153.2	4.9	(0.4)
Pulses, svgs/wk	2.6	(1.4)	87.5	2.8	(1.2)
Fish/shellfish, svgs/wk	6.2	(3.1)	310.3	4.1	(1.2)
Red and cured meats, svgs/wk	7.6	(4.3)	254.3	0.5	(1.0)
Poultry, svgs/wk	5.6	(3.3)	277.9	0.9	(1.2)
Dairy products, svgs/day	2.7	(1.4)	134.9	–	–
Whole-fat dairy products, svgs/day	0.8	(0.8)	–	1.6	(1.7)
Olive oil, svg/day	2.0	(1.1)	–	5.0	(0.0)
Red wine, ml/day	45.6	(57.2)	–	0.4	(1.3)
Mediterranean diet score	–	–	–	31.1	(4.2)

%DRI, percentage of compliance with dietary recommended intakes [17] (for Spanish population); MDS, Mediterranean diet score; SD, standard deviation; svgs/day, servings per day; svgs/wk, servings per week.

The clustered cardiometabolic risk profile (z-score) by the three degrees of MD adherence is shown in Fig. 1 (objective 3). After adjusting for age, BMI, regular menstruation, smoking habit, use of hormone replacement therapy and physical activity levels, adherence to the MD was found to be associated with a reduced cardiometabolic risk, in which pairwise comparisons showed that the group with a high adherence to the MD had a lower clustered cardiometabolic risk than the groups with low or medium adherence (overall $p = 0.004$). In a complementary linear regression analysis, associations between individual MD food groups and the clustered cardiometabolic risk were also examined. Whole grain cereals ($\beta = -0.246$, $B = -0.006$, $SE = 0.003$, $p = 0.046$), pulses ($\beta = -0.221$, $B = -0.026$, $SE = 0.013$, $p = 0.049$) and red wine ($\beta = -0.429$, $B = -0.004$, $SE = 0.001$, $p = 0.005$) showed a significant inverse association with the clustered cardiometabolic risk. The intake of fruit and potatoes showed a borderline significant inverse association ($p = 0.087$ and $p = 0.069$, respectively, data non-shown).

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Table 3 Cardiometabolic markers according to adherence to the Mediterranean diet (n = 198).

	Mediterranean diet score						P^a	P^b
	Low adherence (≤29.99) N = 64 (32.2%)		Medium adherence (30–33.99) N = 80 (40.4%)		High adherence (≥34) N = 54 (27.3%)			
Body composition								
Fat mass, %	42.1	(0.7)	41.2	(0.6)	40.7	(0.7)	0.350	0.259
Waist circumference, cm	95.7	(1.4)	93.2	(1.2)	91.3	(1.5)	0.105	0.084
Blood pressure and heart rate								
Systolic blood pressure, mmHg	123.4	(2.0)	118.6	(1.8)	121.1	(2.2)	0.218	0.277
Diastolic blood pressure, mmHg	77.0	(1.2)	74.7	(1.1)	73.9	(1.3)	0.220	0.166
Resting heart rate, bpm	74.7	(1.3)	77.6[c]	(1.2)	72.7[c]	(1.4)	0.026	0.005
Plasma markers								
Total cholesterol, mg/dL	219.8	(5.6)	233.8[c]	(4.9)	214.0[c]	(5.9)	0.028	0.025
LDL-cholesterol, mg/dL	137.8	(5.2)	148.9[c]	(4.5)	130.1[c]	(5.4)	0.027	0.019
HDL-cholesterol, mg/dL	57.9	(2.4)	62.2	(2.0)	64.5	(2.4)	0.156	0.121
Total cholesterol/HDL	3.9[c]	(0.1)	3.9	(0.1)	3.4[c]	(0.1)	0.030	0.020
Triglycerides, mg/dL	112.8	(8.5)	116.1	(7.6)	88.7	(9.1)	0.054	0.046
C-reactive protein, mg/L	3.5	(0.6)	4.3[c]	(0.5)	1.8[c]	(0.6)	0.011	0.009
Fasting glucose, mg/dL	85.6	(2.1)	88.0	(1.8)	88.4	(2.2)	0.616	0.493
Smoking habit								
No cigarettes/day	10.8	(1.7)	12.6	(2.2)	8.8	(2.4)	0.503	0.518

Values shown as mean (standard error); MDS, Mediterranean diet score; LDL, low density lipoprotein; HDL, high density lipoprotein.
[a] Model adjusted for age, body mass index, regular menstruation, smoking habit and use of substitutive hormone therapy.
[b] Model additionally adjusted for physical activity (min/week). Pairwise comparisons between groups were performed with Bonferroni's adjustment.
[c] Common superscript indicates a significant difference ($P < 0.05$) between groups with the same letter.

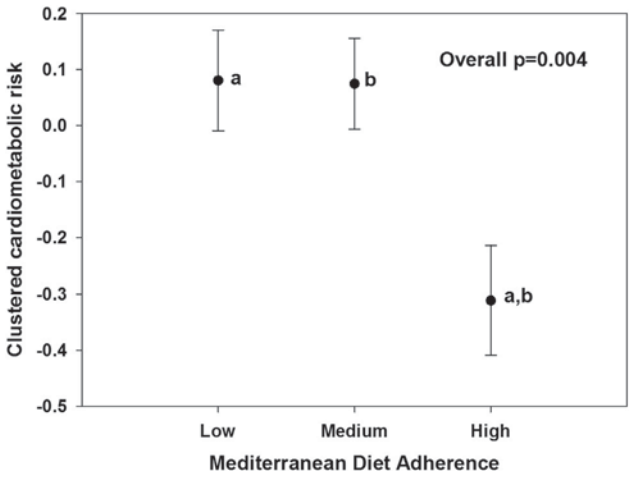

Figure 1 Clustered cardiometabolic risk (z-score) by Mediterranean Diet adherence groups. Dots represent mean and bars standard error (SE). [a,b] Common superscript indicates a significant difference ($p < 0.05$) between groups with the same letter. Pairwise comparisons were performed with Bonferroni's adjustment.

Discussion

The main findings of the present study suggest that a high adherence to the MD promotes a reduced cardiometabolic risk among peri and menopausal women, independently of various factors. Nevertheless, less than one third of the study sample showed a high MD adherence (MDS ≥ 34). Indeed, a clear cardioprotective effect was observed only when a high adherence was reached, regardless of potential confounders as age, BMI, regular menstruation, smoking habit, use of hormone replacement therapy and physical activity. Although some components of the MD as whole grain cereals, pulses and red wine were associated with lower clustered cardiometabolic risk, individual associations were less significant than the association between the MD adherence groups and the clustered cardiometabolic risk.

Menopause health-related quality of life, as assessed with the Cervantes questionnaire, and body composition of the study sample were similar than those observed in previous epidemiological studies conducted in Spanish populations with the same age range [11,22,23]. The sample showed a high prevalence of overweight-obesity and central adiposity, which positions these women at increased CVD risk [22]. However, in Spain, as well as in other Mediterranean countries, those risk factors have not always been linked to a higher incidence of cardiovascular events [24,25]. In fact, Spain stands out as one of the countries with the lowest incidence of cardiovascular events across Europe [1], and a clear attributable reason is the diet followed by most population in this country. This phenomena has been called the "Mediterranean paradox": low risk of CVD despite a high prevalence of known cardiovascular risk factors [25,26]. Mediterranean diet is an aggregation of foods positively associated with cardioprotective lipid profile, better glucose metabolism and lower inflammation [24]. Our results are in line with this argument, as a high adherence to this dietary pattern showed improved cardiometabolic risk markers, which remained significant even after correction for potential confounders.

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In the present sample, the significant associations between MD adherence groups and the clustered cardiometabolic risk were observed in the high compared to the low and medium adherence groups. A large number of meta-analyses of epidemiologic studies [9,10], also adjusted for multiple confounders, compared the highest versus the lowest category of adherence to the MD. These studies also highlighted the importance of increasing the adherence to the MD in order to prevent CVD even in the group of moderate adherence in which, as observed in the present study, cardiometabolic markers significantly differed from those observed in the high adherence group [27]. Although pathophysiological pathways of protection provided by the MD are not fully understood, there is no doubt about the richness of this dietary pattern in antioxidant and anti-inflammatory molecules, which prevent the expression of several proatherogenic genes involved in vascular inflammation, foam cell formation, and thrombosis [8]. In light of these results, the beneficial association of a high adherence to the MD over the consequences of menopausal transition and chronological ageing could protect peri and menopausal women against the endothelial dysfunction.

The MD is arguably the best-studied and most evidence-based diet to prevent not only CVD but also other chronic diseases, as it has become the standard for healthy eating [28]. In the present study, whole grain cereals, pulses and red wine emerged as the only MD components associated with a lower clustered cardiometabolic risk. There is no doubt that a high consumption of whole grain cereals and pulses, as well as a moderate intake of red wine can assure a better cardiovascular health and a reduced risk of CVD or cardiovascular events (regardless of other factors, nutritional or not) [10,29]. However, increasing evidence indicates that the synergy among the nutrient-rich foods included in the MD fosters favourable changes in intermediate pathways of cardiometabolic risk, which has been linked with reduced CVD incidence and mortality [9,30]. Therefore, the lack of associations between other MD components and the clustered cardiometabolic risk as well as the higher association of the MD index with the clustered cardiometabolic risk support the mentioned synergistic effect [9,30].

Nevertheless, southern European countries are rapidly abandoning the MD, orienting their food choices toward products typical of the Western dietary pattern, rich in refined grains, animal fats, sugars, processed meat and poor in legumes, cereals, fruits and vegetables [26,31]. Our results, not dissimilar from previous similar studies carried out by our group [11], point to a similar trend, with a low and moderate adherence to the MD in 32% and 40% of the study population, respectively, and with only 27% of women reaching high adherence. Lifestyles contribute far more heavily than biological factors to poor cardiovascular health [32]. It highlights the need to strengthen the role of public health efforts in the management of CVD risk. In recent years, several prevention campaigns have been conducted to increase physical activity, improve diet, and reduce smoking habit, major determinants for the development of CVD, since they can be modified [33]. Nevertheless, literature has shown difficulty in changing lifestyles [34–36]. Therefore, targeting these campaigns to specific population groups, such as the one shown in the present study, with specific and personalized messages derived from their specific deviations from the traditional MD, could potentially increase their success.

Strengths and limitations

This study has some limitations that should be underlined. First, the cross-sectional study design precluded establishing causal relationships. Second, we have no clinical information about the menopause status of the women (through hormonal assessments) despite a validated questionnaire was used to measure menopause health-related quality of life. Several strengths must be also recognized. Firstly, this study included inflammation (C-reactive protein) as part of the clustered cardiometabolic risk profile, and the multivariate model was also corrected for physical activity levels. In addition, our measurement tools to assess body composition (e.g. dual-energy X-ray absorptiometry), cardiometabolic markers, objective measurement of physical activity (accelerometry) and adherence to the MD, are widely valid and reliable and thus, the accuracy of the results are guaranteed. Moreover, the equally distributed sample across degrees of adherence to the MD participating in this study provided proper comparisons between MD adherence groups.

Conclusions

The results from the present study suggest that a high adherence to the MD could be associated with a cardioprotective effect in peri and menopausal women. At the same time, the assessment of dietary patterns showed some deviations from the traditional MD. Future intervention studies to determine whether peri and menopausal women in the lowest MD adherence group might particularly benefit from intervention programs aimed at increasing the adherence to this dietary pattern for a better cardiometabolic status during and after menopause are warranted.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.numecd.2016.10.008.

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Association of physical fitness, body composition, cardiometabolic markers and adherence to the Mediterranean diet with bone mineral density in perimenopausal women.The Flamenco Project.

III

Virginia A. Aparicio, Pilar Ruiz-Cabello, Milkana Borges-Cósic, Ana Andrade, Irene Coll-Risco, Pedro Acosta-Manzano & Alberto Soriano-Maldonado

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Association of physical fitness, body composition, cardiometabolic markers and adherence to the Mediterranean diet with bone mineral density in perimenopausal women. The FLAMENCO project

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ABSTRACT

This study aimed to analyse the association of different components of physical fitness, body composition, cardiometabolic markers and the Mediterranean diet with bone mineral density (BMD) in perimenopausal women, and to test which of these components are independently associated with BMD. The sample comprised 197 perimenopausal women (52.6 ± 4.5 years). Physical fitness was assessed with the "Senior Fitness Test" battery and the handgrip strength and Bruce tests. Fat and lean mass and BMD were measured using dual-energy X-ray absorptiometry. We analysed the markers of metabolic syndrome, C-reactive protein, and components of the Mediterranean diet. Handgrip muscle strength ($\beta = 0.212$, $P = 0.005$), body weight ($\beta = 0.244$, $P = 0.001$), BMI ($\beta = 0.180$, $P = 0.011$) and lean mass ($\beta = 0.379$, $P < 0.001$) were positively associated with BMD. No associations were observed between cardiometabolic markers or the Mediterranean diet with BMD (all $P > 0.05$). When all relevant indicators of BMD were simultaneously considered, lean mass was the only 1 showing an independent association with BMD ($\beta = 0.392$, $P < 0.001$), explaining 14% of the BMD variability. In conclusion, muscle strength might be a marker of BMD in perimenopausal women. However, lean mass was the only factor independently associated with BMD. Future research to determine whether increasing lean mass through specific exercise-based interventions contributes to increasing BMD is warranted.

ARTICLE HISTORY
Accepted 27 May 2016

KEYWORDS
Lean mass; handgrip strength; Mediterranean diet; alcohol; tobacco; weight status; strength; C-reactive protein

Introduction

Osteoporosis is defined as a skeletal disorder characterised by compromised bone strength that increases the risk of fracture (Lorentzon & Cummings, 2015). The bone strength primarily reflects the integration of bone mineral density (BMD) and quality (Lorentzon & Cummings, 2015). Half of Caucasian women will suffer an osteoporotic fracture during their life (Ström et al., 2011), which increases morbidity and economic burden within the ageing female population (Lo, Burnett-Bowie, & Finkelstein, 2011). Loss of ovarian function has a big impact on female skeletal health and promotes accelerated rate of bone loss during the menopausal transition (Gerber et al., 2015; Lo et al., 2011; Seifert-Klauss et al., 2012; Sowers et al., 2010).

Although sometimes inconclusive, there is evidence suggesting that a number of potential modifiable factors might have a positive impact on BMD. Higher levels of physical activity or exercise are associated with better physical fitness (Teoman, Özcan, & Acar, 2004). It seems that physical fitness, and especially muscle strength, may promote greater BMD (Cheung et al., 2012; Di Monaco, Di Monaco, Manca, & Cavanna, 2000; Dixon et al., 2005; Iida et al., 2012; Kim, Lee, & Cho, 2012; Shin, Liu, Panton, & Ilich, 2014). However, some studies found no association between different components of fitness and BMD (Foley, Owings, Pavol, & Grabiner, 1999; Furrer, van Schoor, de Haan, Lips, & de Jongh, 2014; Tucker, Nokes, Bailey, & Lecheminant, 2014). Weight status and body composition also appear to be important determinants of BMD as the rates of bone loss during perimenopause are greater in non-obese women than in their obese counterparts (Finkelstein et al., 2008; Lo et al., 2011; Sowers et al., 2010). In addition, several studies have recently examined the role of fat and lean mass on BMD, suggesting that increasing lean mass (rather than fat mass) might be particularly beneficial for bone health (Namwongprom et al., 2013; Salamone et al., 1995; Sotunde et al., 2015).

Menopause also increases inflammatory markers and the prevalence of metabolic syndrome (Cagnacci et al., 2015; Figueroa-Vega, Moreno-Frías, Malacara, & Bolego, 2015; Janssen, Powell, Crawford, Lasley, & Sutton-Tyrrell, 2008). The association between metabolic syndrome and bone health remains unclear, but recent studies observed that women with metabolic syndrome present higher BMD, independently of body mass index (BMI) (Heidari et al., 2015; Muka et al., 2015). Inflammation has also been shown to play an important (although inconsistent) role in bone remodelling, with C-reactive protein showing an inverse and independent dose–response relationship with BMD (de Pablo, Cooper, & Buckley, 2012), whereas others found no association (Manghat et al., 2010; Nabipour et al., 2009). Several studies

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have also found that the Mediterranean diet (Rivas et al., 2013), or its specific components (e.g., olive oil or fish) are related to increases in BMD and the prevention of osteoporosis (García-Martínez, Rivas, Ramos-Torrecillas, De Luna-Bertos, & Ruiz, 2014; Tagliaferri et al., 2014), while others have failed to find clear associations (Kontogianni et al., 2009; Romero Perez & Rivas Velasco, 2014).

Since perimenopause is a rather critical period in women's bone health (Lo et al., 2011; Sowers et al., 2010), it is of clinical and public health interest to further characterise the extent to which several modifiable factors (such as physical fitness, body composition, cardiometabolic markers and the diet) might be associated with BMD in this period of women's life, which may have important implications for the implementation of more efficient bone-loss prevention programmes.

Consequently, the aims of the present study were: (1) to assess the association of different components of physical fitness, body composition, cardiometabolic markers and the Mediterranean diet with BMD in perimenopausal women and (2) to examine which of these modifiable factors are independently associated with BMD in this specific population.

Methods

Participants

The complete methodology of the FLAMENCO study is published elsewhere (Carbonell-Baeza et al., 2015). Women were contacted through primary care centres from Granada (Southeast Spain) and press releases published in local newspapers and social media. Inclusion criteria for the current cross-sectional study were: (1) aged 45–60 years old; (2) not to have severe somatic or psychiatric disorders. Exclusion criteria were: (1) acute or terminal illness; (2) to have suffered a major cardiovascular event (i.e., myocardial infarction, angina or ictus) in the past 6 months; (3) unable to ambulate; (4) unstable cardiovascular disease or other medical condition; (5) upper or lower extremity fracture in the past 6 months; (6) unwillingness to complete the study requirements; (7) presence of neuromuscular disease or drugs affecting neuromuscular function; (8) to have *osteoarticular prosthesis, which* could interfere in the dual-energy X-ray absorptiometry analysis results.

The total sample for the present analyses comprised 197 women (age range 45–60 years) who were informed about the aims and study procedures and signed written informed consent before being enrolled in the study.

This study has been reviewed and approved by the Ethics Committee of the "Hospital Virgen de las Nieves" (Granada, Spain).

Procedures

The assessment protocol was completed on 2 nonconsecutive days (e.g., Monday and Wednesday). Socio-demographic, dietary and clinical characteristics, blood pressure, resting heart rate, body composition and physical fitness (in the same order as presented here) were assessed on day 1. Participants were interviewed in a private room and completed self-reported questionnaires about their clinical and socio-demographic characteristics. On day 2, participants attended the primary care centre for the biochemical analysis.

Socio-demographic and clinical information

Socio-demographic (including age, educational status and current occupational status among others) and other health-related information was collected using a questionnaire. This anamnesis included questions regarding smoking and alcohol habits, history of illness (as osteoporosis, hypertension or diabetes), menopause status, indicators of socio-economic status (such as personal and household income, educational level etc.), marital status and number of children.

Systolic and diastolic blood pressure, as well as resting heart rate, were measured in a sitting position (Omron Health Care Europe B.V. Hoolddorp) after 5 min of rest, on 2 separate occasions (with 2 min between trials). The lowest value of the 2 trials was selected for the analysis.

Body composition

Weight (kg) was assessed with a scale (InBody R20, Biospace, Seoul, Korea). Lean, fat and bone mass of the whole body was measured using a dual-energy X-ray absorptiometry device (Hologic Discovery QDR, Nasdaq: HOLX). Height (cm) was measured using a stadiometer (Seca 22, Hamburg, Germany). Waist circumference (cm) was assessed at the middle point between the ribs and the ileac crest, with the participant standing (Harpenden anthropometric tape, Holtain Ltd.). Height and weight was used to calculate BMI (weight [Kg]/height [m^2]).

Physical fitness

Participants' physical fitness status was assessed by means of the following tests:

Cardiorespiratory fitness. The *modified Bruce protocol* (Bruce, Kusumi, & Hosmer, 1973) was performed to estimate maximal oxygen uptake (VO_{2max}), and was used as a measure of cardiorespiratory fitness. The test consists of 5 increasing workload stages of 3 min each (stage 1: 2.7 km/h, 10% inclination; stage 2: 4 km/h, 12% inclination; stage 3: 5.5 km/h, 14% inclination; stage 4: 6.8 km/h, 16% inclination; stage 5: 8 km/h, 18% inclination). The test concludes when the 85% of the individual's heart rate reserve is accomplished. VO_{2max} was estimated with the formula by Bruce et al. (Bruce et al., 1973): VO2max = 6.70−2.82 × 2 + 0.056 × duration of the test (s).

Muscular strength. *The handgrip strength* test was employed as measure of overall muscle strength. Grip strength measured by dynamometry is a well established, quick and easy indicator of muscle status (Bohannon, 2015) that provides useful information about overall muscular strength in multiple populations and diseases (Barichella et al., 2016; Silva Neto et al., 2016) and is considered nowadays an important part of the evaluation of frailty and physical functioning in clinical settings (Chainani et al., 2016; Volaklis et al., 2016). Handgrip strength was measured using a digital dynamometer (TKK 5101 Grip-D;Takey, Tokyo, Japan) as described elsewhere (Ruiz-Ruiz, Mesa, Gutiérrez, & Castillo, 2002). The participants

performed (alternately with both hands) the test twice. The best value of 2 trials for each hand was chosen and the average of both hands was used in the analyses.

Flexibility. The *back-scratch test* (Rikli & Jones, 1999) was used as a measure of overall shoulder range of motion (upper-body flexibility). This test involves measuring the distance between (or overlap of) the middle fingers behind the back with a ruler. The best score of 2 attempts for each arm was recorded and the average of both arms was used in the analyses. The *sit-and-reach test* required the use of the sit-and-reach standardised box with a slide ruler attached to the top (Rodriguez et al., 1998). The participant is required to sit with knees straight and legs together, and feet placed against the box. The participant slowly reaches forward as far as possible (lower-body flexibility). The final position that the participant reaches is the test score. The best score of 2 attempts was recorded and used in the analyses.

Motor agility/dynamic balance. The *timed up-and-go test* was performed to assess dynamic balance. The participant, seated in a chair with arms and trunk supported, stands up on the word "go" and walk 3 m in a straight line, turn 180°, walks back to the chair and sits down again in the chair. Each participant performed 1 trial to become familiar with the test. The test was performed twice separated by 1-min rest. The time from the start until the participant sits down in the chair with back support was measured and the best of the 2 attempts was used in the analyses.

Mediterranean diet

The *Mediterranean diet score* (Panagiotakos, Pitsavos, & Stefanadis, 2006) was used to evaluate the degree of adherence to the traditional Mediterranean diet. It consists of 11 items (non-refined cereals, potatoes, fruits, vegetables, legumes, fish, olive oil, red meat and derivate, poultry, full-fat dairy products and alcohol), which scores ranging from 0–5 based on frequency of consumption and on the level of adequacy to this Mediterranean pattern. Thus, the total score ranges from 0–55, with higher scores indicating greater adherence to the Mediterranean diet.

Biochemical parameters

Venous blood samples after all night fasting were collected. Immediately after the blood collections, the samples were brought to the hospital's biochemical analysis laboratory, where they were centrifuged and pipetted. Plasma alkaline phosphatase, C-reactive protein, HDL cholesterol, triglycerides and glucose concentrations were estimated using an autoanalyser (Hitachi-Roche p800, F. Hoffmann-La Roche Ltd.).

Statistical analysis

Linear regression analysis was used to assess the association of different components of physical fitness, body composition, cardiometabolic and inflammatory markers and dietary patterns (independent variables in separate models) with BMD (dependent variable; objective 1). We controlled for potential confounding using 2 consecutive models. The basic model (model 1) was adjusted for age. The multivariable model (model 2) was further adjusted for menstrual status (Gerber et al., 2015), hormonal therapy, smoking status, educational and occupational status. Dietary and cardiometabolic markers were further adjusted for BMI. The variables significantly associated with BMD in objective 1 were used to assess which modifiable factors were independently associated with BMD (objective 2). A forward stepwise regression analysis was undertaken including BMD as dependent variable. The above-mentioned potential confounders were included and kept fixed into the model (step 1). In step 2, variables significantly associated with BMD were simultaneously introduced into the model by using a stepwise procedure. This procedure introduces the studied components step by step into the model (when $P < 0.05$) according to the strength of their association with the outcome. The model was reassessed with the addition of every new component and variables were left out of the model if $P > 0.10$.

We further characterised the association of the factors independently associated with BMD (i.e., in objective 2), by dividing the sample into age-specific quartiles of the specific factor (e.g., lean mass). One-way analysis of covariance (ANCOVA) was used to assess the differences on BMD across the different quartiles, after adjustment for age, educational status, marital status, smoking status, regular menstruation and hormonal therapy. The Bonferroni's correction for multiple comparisons across quartiles was applied, and the difference between quartile 1 and quartile 4 was used to assess the potential clinical relevance of the association under study. *Cohen's d* and its exact confidence interval (CI) were used to estimate the standardised effect size between quartile 1 and quartile 4. The statistical analysis was performed with SPSS (IBM SPSS Statistics for Windows, version 20.0; Armonk, NY, USA) and the statistical significance was set at $\alpha = 0.05$.

Results

The socio-demographic and clinical characteristics of the study sample are shown in Table 1. The sample was, on average, 53 years old, and had a mean BMI of 27 kg/m^2 (overweight), waist circumference of 94 cm and 41% body fat. Mean bone *T*-score was 0.45, with an 11% prevalence of osteopenia–osteoporosis. Most of the participants lived with a partner, had finished secondary studies or a University degree, and presented irregular menstruation. The sample showed a mean score of 31 in the *Mediterranean diet score*, reflecting a moderate adherence to the Mediterranean diet (Beunza et al., 2010), and a 25% presented metabolic syndrome.

Linear regression analysis assessing the association of physical fitness, body composition, cardiometabolic markers and the Mediterranean diet with BMD in perimenopausal women (objective 1) are shown in Table 2. Cardiorespiratory fitness, flexibility or motor agility were not associated with BMD (all, $P > 0.05$). Higher handgrip strength was significantly associated with higher BMD ($\beta = 0.212$, $P = 0.005$ for the multivariate model). Likewise, higher body weight ($\beta = 0.244$,

Table 1. Descriptive characteristics of the study participants (n = 197).

Variable			Mean (SD)
Age (years)			52.6 (4.5)
Weight (kg)			69.4 (12.3)
Height (cm)			159.8 (5.9)
Body mass index (kg/m^2)			27.1 (4.6)
Weight status (NW/OW/OB) (%)			34/43/23
Waist circumference (cm)			93.9 (10.8)
Body fat (%)			41.3 (5.3)
Lean mass (kg)			39.9 (5.0)
Bone status			
Bone mineral density (g/cm^2)			1.15 (0.098)
Bone mineral density *T*-score			0.45 (1.19)
Bone mineral density *Z*-score			0.51 (0.94)
Normal/osteopenia/osteoporosis (%)*			89.3/9.1/1.5
Plasma alkaline phosphatase (UI/L)			74.6 (23.1)
Physical fitness			
Cardiorespiratory fitness		*Bruce test (VO_2max)*	20.8 (5.4)
Muscle strength		*Handgrip strength (kg)*	26.5 (4.0)
Flexibility	Upper body	*Back-scratch (cm)*	−2.8 (8.1)
	Lower body	*Sit-and-reach (cm)*	26.2 (7.8)
Dynamic balance and agility		*Timed up-and-go (s)#*	4.9 (0.61)
Mediterranean diet score			30.9 (4.4)
Educational status			***n* (%)**
No studies			6 (3.0)
Primary or professional training			76 (38.6)
High-school			42 (21.3)
University degree			73 (37.1)
Marital status			
Single			26 (12.7)
With partner/married			137 (70.1)
Separated/divorced/widow			34 (17.2)
Metabolic syndrome presence (yes/no)			(25.2/74.8)
Regular menstruation (yes/no)			(28.4/71.6)
Smoking status (yes/no)			(22.7/77.3)

SD, Standard deviation; NW, normal weight; OW, overweight; OB, obese; *Normal bone is defined as a *T*-score of −1.0 or higher, osteopenia is defined as between −1.0 and −2.5, osteoporosis is defined as −2.5 or lower; #Lower scores indicate better performance; Metabolic syndrome was defined following the American Heart Association criteria.

P = 0.001), BMI (β = 0.180, P = 0.011) and lean mass (β = 0.379, P < 0.001) were associated with higher BMD. Neither of the cardiometabolic risk markers under study (vascular, lipid, glycaemic and inflammatory markers) was associated with BMD (all P > 0.05 for the multivariate model). Similarly, adherence to the Mediterranean diet and its components were not associated with BMD (all P > 0.05).

The independent association of the different factors with BMD (objective 2) is presented in Table 3. Lean mass was independently associated with BMD (β = 0.392, P < 0.001) and explained 14% of the variability in BMD (P < 0.001).

Bone mineral density by quartiles of lean body mass is shown in Figure 1. Bone mineral density increased across lean mass quartiles in a dose-response manner, after adjustment for age, educational status, marital status, smoking status, regular menstruation and hormonal therapy (overall, P < 0.001). Pairwise comparisons showed significant differences between quartile 1 of lean mass and the rest of quartiles. Women in quartile 2 also presented lower BMD than those in quartile 4 (P < 0.05). Participants with the highest lean mass levels (quartile 4) had, in average, 0.11 g/cm^2 higher BMD than participants with the lowest lean mass levels (quartile 1; P < 0.001, effect size *Cohen's d* = 1.19, CI 0.74–1.63). As expressed in *T*-score, this difference is equal to −0.23 (CI −0.55–0.09) versus 1.09 (CI 0.78–1.41).

Discussion

The main findings of the present study indicate that neither cardiorespiratory fitness, flexibility, motor agility, cardiometabolic markers (blood pressure, lipids, fasting glucose or C-reactive protein), nor the Mediterranean diet are associated with BMD in perimenopausal women. By contrast, muscle strength, body weight, BMI and lean mass are significantly associated with BMD in this population. Among them, lean mass was the only factor independently associated with BMD, explaining 14% of the BMD variability. Bone mineral density was higher across quartiles of lean mass, and the difference on BMD between the groups with the highest and the lowest lean mass was clinically meaningful.

It has been suggested that physical fitness is positively associated with BMD (Iida et al., 2012) but it is important to know which specific fitness components are particularly associated in order to design more efficient exercise-based intervention studies to improve BMD. Our results suggest that muscle strength is the only fitness component significantly associated with BMD in perimenopausal women, concurring with the results reported by prior studies with smaller sample sizes (Di Monaco et al., 2000; Marin, Pedrosa, Moreira-Pfrimer, Matsudo, & Lazaretti-Castro, 2010; Shin et al., 2014). Moreover, there is consistent evidence that handgrip strength is associated with BMD in this population (Cheung et al., 2012; Di Monaco et al., 2000; Dixon et al., 2005; Kim et al., 2012; Lamprinoudi et al., 2014; Marin et al., 2010; Shin et al., 2014), and it might be an indicator of fracture and falls as a marker of general muscle strength (Di Monaco et al., 2000; Kim et al., 2012; Rikkonen et al., 2012). Therefore, further prospective research to determine the potential of handgrip strength to predict BMD in clinical settings is warranted.

In agreement with our results, several studies have confirmed that greater weight and BMI are positively associated with BMD (Finkelstein et al., 2008; Lo et al., 2011; Marin et al., 2010; Muka et al., 2015; Sowers et al., 2010). Notwithstanding, the incidence of fractures has been found to be similar for all weight statuses and, consequently, obesity might not be protective against fractures (Copês et al., 2015). Therefore, body weight alone may not be associated with increased BMD unless a significant proportion of that weight comprises lean mass (Salamone et al., 1995). To note is that lean mass is composed mainly of muscle mass, which can be increased through muscular strength training. Interestingly, the correlation of muscle strength with lean mass in this study was r = 0.371 (P < 0.001). A potential explanation for the noticeable association of both muscle and lean mass with BMD is given by the fact that optimum bone remodelling needs of mechanical loads and stimuli (Pereira, Javaheri, Pitsillides, & Shefelbine, 2015; Tobias et al., 2014). In fact, sarcopenia is strongly associated with lower BMD and osteoporosis (Kim & Won, 2014). As a clinically meaningful difference on BMD was observed between extreme lean mass quartiles, one could speculate that increasing lean mass through muscle strength training could result in improvements on BMD in perimenopausal women, which requires further prospective research.

Of interest is the lack of association observed between fat mass and BMD. A similar study also found that body weight

Table 2. Linear regression analysis assessing the association of physical fitness, anthropometry and body composition, cardiometabolic markers and the Mediterranean diet with bone mineral density in perimenopausal women.

	Bone mineral density (g/cm^2)							
	Age-adjusted				Multivariate adjusted[a]			
Physical fitness	β	B	SE	*P*	β	B	SE	*P*
Bruce test (VO_2max)	−0.072	−0.001	0.001	0.314	−0.084	−0.001	0.001	0.245
Handgrip strength (kg)	0.192	0.005	0.002	0.010	0.212	0.005	0.002	0.005
Back-scratch (cm)	−0.107	−0.001	0.001	0.142	−0.059	−0.001	0.001	0.449
Sit-and-reach (cm)	−0.104	−0.001	0.001	0.133	−0.115	−0.001	0.001	0.102
Timed up-and-go (s)#	0.052	0.008	0.012	0.493	0.004	0.001	0.012	0.960
Body composition								
Weight (kg)	0.205	0.002	0.001	0.003	0.244	0.002	0.001	0.001
Height (m)	0.064	0.001	0.001	0.366	0.069	0.001	0.001	0.337
Body mass index (kg)	0.145	0.003	0.001	0.036	0.180	0.004	0.002	0.011
Fat mass (%)	−0.060	−0.001	0.001	0.390	−0.042	−0.001	0.001	0.560
Lean mass (kg)	0.344	0.007	0.001	<0.001	0.379	0.008	0.003	<0.001
Cardiometabolic markers*								
Metabolic syndrome presence	0.039	0.009	0.021	0.664	0.009	0.002	0.021	0.921
Glucose (mg/dL)	0.178	0.001	0.001	0.061	0.115	0.001	0.001	0.240
Triglycerides (mg/dL)	0.048	0.000	0.000	0.622	0.036	0.000	0.000	0.706
HDL-cholesterol (mg/dL)	−0.113	−0.001	0.001	0.255	−0.043	0.000	0.001	0.666
Systolic blood pressure (mm/Hg)	0.168	0.001	0.000	0.017	0.125	0.001	0.000	0.091
Diastolic blood pressure (mm/Hg)	−0.009	0.000	−0.001	0.893	−0.029	0.000	0.001	0.684
Waist circumference (cm)	0.091	0.001	0.001	0.191	0.118	0.001	0.001	0.097
C-reactive protein (mg/dL)	−0.050	−0.001	0.002	0.607	−0.078	−0.002	0.002	0.430
Mediterranean diet*								
Mediterranean diet score	−0.117	−0.003	0.002	0.113	0.065	0.001	0.002	0.375
Dairy products (servings/week)	0.017	0.000	0.001	0.808	−0.020	0.000	0.001	0.855
Red meat (servings/month)	0.074	0.000	0.000	0.301	0.081	0.000	0.000	0.253
Fish (servings/month)	0.006	0.000	0.001	0.927	0.006	0.000	0.001	0.929
Olive oil (servings/week)	−0.073	−0.001	0.001	0.311	−0.069	−0.001	0.001	0.341
Alcohol (ml/week)	−0.122	0.000	0.000	0.084	−0.118	0.000	0.000	0.105
Tobacco (smoker)	−0.170	−0.042	0.028	0.138	−0.099	−0.023	0.017	0.163

SE, Standard Error; β, standardised regression coefficient; B, nonstandardised regression coefficient; #Lower scores indicate better performance; [a]Model adjusted for age, educational status, marital status, smoking status, regular menstruation and hormonal therapy; *Model additionally adjusted for body mass index; Metabolic syndrome was defined following the American Heart Association criteria.

Table 3. Stepwise regression analysis assessing which physical fitness and body composition components were independently associated with bone mineral density in perimenopausal women.

	Bone mineral density (g/cm^2)						
	β	B	SE	*P*	Adjusted R^2	R^2 change	*P*
Step 1					0.062		0.010
Age	−0.198	−0.004	0.002	0.027			
Educational status	−0.071	−0.008	0.008	0.326			
Marital status	−0.037	−0.003	0.007	0.608			
Hormonal therapy	−0.057	−0.024	0.030	0.429			
Regular menstruation	−0.070	−0.015	0.019	0.429			
Smoking	−0.104	−0.024	0.017	0.148			
Step 2					0.200	0.138	<0.001
Age	−0.128	−0.003	0.002	0.160			
Educational status	−0.070	−0.008	0.008	0.321			
Marital status	−0.042	−0.004	0.007	0.557			
Hormone therapy	−0.070	−0.029	0.030	0.321			
Regular menstruation	−0.051	−0.011	0.019	0.554			
Smoking	−0.114	−0.027	0.016	0.107			
Lean mass	0.392	0.008	0.001	<0.001			

SE, Standard Error; β, standardised regression coefficient; B, nonstandardised regression coefficient; R^2, adjusted coefficient of determination, expressing the percent variability of the dependent variable explained by each model; R^2 change, additional percent variability explained by the model due to the inclusion of the new term.

was associated to BMD, but the most important component was lean mass while fat showed no association (Marin et al., 2010). Consequently, our findings suggest that increasing lean rather than fat mass might potentially be beneficial to bone health (Namwongprom et al., 2013; Salamone et al., 1995; Sotunde et al., 2015), but also that fat mass might have a weak influence on the bone. Contrary, Liu, Ilich, Brummel-Smith, and Ghosh (2014) found a negative association between fat mass and BMD, and they concluded that overweight/obesity after certain amount of fat mass, may not be protective against osteoporosis.

Another major finding of this study was the lack of association of BMD with the cardiometabolic, inflammatory and dietary parameters assessed. Some studies have found a relationship between metabolic syndrome and BMD (Heidari et al., 2015; Muka et al., 2015) and data of the Rotterdam Study

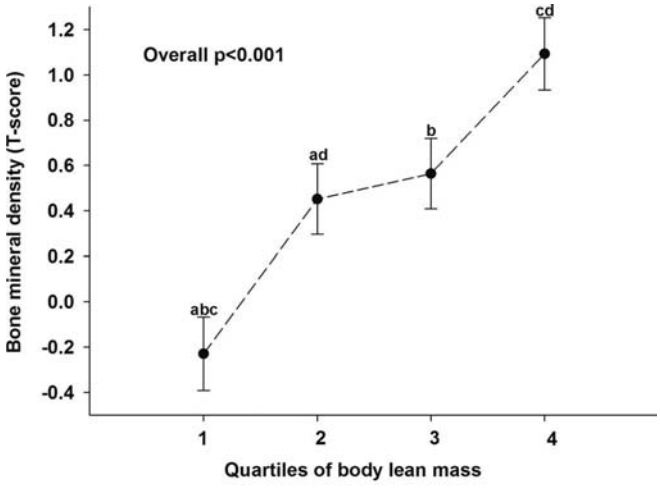

Figure 1. Graphic representation of the association between quartiles of lean mass and bone mineral density in perimenopausal women.

[abcd] Common superscript indicate a significant difference ($P < 0.05$) between groups with the same letter. Model adjusted for age, educational status, marital status, smoking status, regular menstruation and hormonal therapy. Pairwise comparisons were performed with Bonferroni's adjustment. Quartile 1 represents the group with the lowest lean mass.

showed that it was positively associated with higher femoral neck BMD, especially mediated by the glucose component (unrelated to diabetes) (Muka et al., 2015). Although we have observed the similar borderline trend in glucose, which could highlight the need of adequate glucose levels for a better bone health, our data do not concur with the rest of markers and further research in this issue is required. We did not confirm a negative association between inflammation and BMD. In a large sample of perimenopausal women, de Pablo et al. (2012) observed that C-reactive protein levels were inversely and independently associated with BMD. However, in agreement with our results, other studies failed to find association between inflammatory markers and BMD (Manghat et al., 2010; Nabipour et al., 2009) or this association disappeared in multivariate analysis (Ganesan, Teklehaimanot, Tran, Asuncion, & Norris, 2005). Consequently, inflammation and other cardiometabolic markers may act as a surrogate for other primary factors associated with BMD, such as obesity.

Finally, although the Mediterranean diet has been robustly linked to better overall health and longevity in the literature, its relationship with bone status is still inconclusive (Rivas et al., 2013). Some observational studies reported that a moderate consumption of fish (Calderon-Garcia et al., 2013) and olive oil (García-Martínez et al., 2014; Kontogianni et al., 2009; Tagliaferri et al., 2014), and a low consumption of red meat (Kontogianni et al., 2009) was associated with higher BMD and lower fracture risk. However, others, like us, did not find associations, especially regarding the level of adherence to this dietary pattern (Kontogianni et al., 2009; Romero Perez & Rivas Velasco, 2014). We have not confirmed an inverse association between alcohol consumption and BMD, which is not surprising since none of the participants consumed alcohol above the recommendations.

The positive association observed between lean but not fat mass with BMD could potentially be attributed to differences in determinants of muscle mass, such as exercise, lifestyle factors, oestrogens or a combination of these factors (Kim et al., 2012). Hence, experimental studies are warranted to determine whether exercise programmes focused on enhancing muscle mass (Bailey & Brooke-Wavell, 2010; Menzel et al., 2015; Tobias et al., 2014) in perimenopausal women with low lean mass levels can prevent BMD loss. In this line, future studies should address the extent to which treatment strategies based on resistance training and vertical load impacts instead of the classical nutritional-based interventions could allow women the achievement of a better bone status in this stage.

This study has limitations that must be underlined. The cross-sectional design precludes determination of causality. Information on plasma bone and hormonal biomarkers, which could have been of interest for the better interpretation of the present results, was lacking. Finally, the perimenopausal women included in this study were not particularly affected by osteopenia (9.1%) or osteoporosis (1.5%). It is possible that the high prevalence of overweight–obesity (66%) observed in this sample played a role in such low prevalence (Finkelstein et al., 2008; Lo et al., 2011; Sowers et al., 2010). As a result, these findings might not be generalisable to other populations of perimenopausal women with higher rates of BMD loss. This study has also several strengths that need to be highlighted. Firstly, this study provided a comprehensive examination of the association of several potential modifiable factors that have been inconsistently associated with BMD in this population within the same report. In addition, our measurement tools to assess body composition (i.e., dual-energy X-ray absorptiometry), cardiometabolic markers, muscle strength (i.e., handgrip dynamometry) and adherence to the Mediterranean diet, are widely valid and reliable and thus, the accuracy of the results are guaranteed.

Conclusion

The findings of the present study indicate that muscle strength, weight, BMI and lean mass are positively associated with BMD in perimenopausal women. On the other hand, body fat mass and none of the cardiometabolic markers studied, the Mediterranean diet or its components was associated with BMD in this population. Lean body mass showed a moderate an independent association with BMD, explaining 14% of its variability. Importantly, women with the highest levels of lean body mass (quartile 4) showed a significantly higher BMD than those with the lowest lean body mass levels (quartile 1), and this difference resulted to be clinically meaningful. Further prospective research and experimental studies are warranted to determine the extent to which increasing lean mass through exercise programmes can enhance BMD in this critical period of women's life.

Disclosure statement

None of the authors have any conflict of interests.

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3. HÁBITOS DIETÉTICOS Y SU RELACIÓN CON LA SALUD MENTAL EN MUJERES CON FIBROMIALGIA (ESTUDIO IV)

Association of dietary habits with psychosocial outcomes in women with fibromyalgia: The al-Ándalus Project.

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IV

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Association of Dietary Habits with Psychosocial Outcomes in Women with Fibromyalgia: The al-Ándalus Project

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ABSTRACT

Background Fibromyalgia (FM) is a complex multidimensional disorder with pain as its main symptom. Fibromyalgia imposes a psychosocial burden on individuals that negatively impacts quality of life. The relationship of dietary habits with these psychosocial aspects is still unclear.

Objective The purpose of this cross-sectional study was to assess dietary habits in a representative sample of women with FM and to explore their association with mental health, depression, and optimism in this population.

Design A cross-sectional study was conducted between November 2011 and January 2013.

Participants The study sample comprised 486 women (ages 35 to 65 years) with FM from Andalucía (southern Spain).

Main outcome measures Mental health, depression, and optimism were evaluated by means of the mental component scale of the 36-item Short-Form Health Survey, the Beck Depression Inventory (BDI-II), and the Life Orientation Test Revised, respectively. A short form of a validated food frequency questionnaire was used to assess dietary habits.

Statistical analyses performed Analysis of covariance was used to assess associations between dietary habits and mental health, depression, and optimism. The presence of severe depression (BDI-II $\geq$29) as a function of dietary habits was examined with logistic regression.

Results A daily or almost-daily consumption of fruit and vegetables and a moderate consumption of fish (2 to 5 servings per week) were associated with higher scores in mental health ($P<0.001$, $P<0.05$, and $P<0.001$, respectively) and lower levels of depression ($P<0.001$, $P<0.01$, and $P<0.01$, respectively). A daily or almost-daily consumption of vegetables and a moderate consumption of dairy products and fish were associated with higher levels of optimism ($P<0.05$, $P<0.05$, and $P<0.001$, respectively). A daily or almost-daily consumption of cured meats and sweetened beverages were associated with higher levels of depression and lower levels of optimism, respectively (both $P<0.05$).

Conclusion The results this study suggest that a daily or almost-daily intake of fruit and vegetables and a moderate intake of fish may be associated with more favorable psychosocial outcomes in women with FM. Conversely, excessive intake of cured meats and sweetened beverages was related to worse scores in optimism and depression outcomes. Future research analyzing dietary patterns as well as intervention studies evaluating the effects of healthy dietary patterns on psychosocial and physical outcomes in individuals with FM are warranted.

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FIBROMYALGIA (FM) IS A DISEASE CHARACTERIZED BY widespread pain[1] and a constellation of other symptoms and comorbidities[2] that cause a marked deterioration of Health Related Quality of Life (HRQoL), mental well-being, and depression.[3] Consequently, FM represents an important public health issue.[3] Individuals with FM have a remarkably consistent pattern of health status impairment marked by deterioration in physical and psychosocial well-being.[3-5] Moreover, a greater prevalence of overweight and obesity has also been observed,[6] and this finding has been found to be associated with the concurrence of FM symptoms and severity.[2,7,8]

Because no cure is available for FM,[5,9] recent guidelines suggest that the optimal treatment consists of a multidisciplinary approach[5,7,9] with a combination of pharmacological and nonpharmacological treatment modalities.[5] Among

nonpharmacological treatments, dietary intervention is a promising approach.[7] Several studies have demonstrated the importance of specific dietary habits on the mental well-being of the general population.[10-12] A recent review suggests that a treatment program including weight-loss strategies, nutritional education, specific dietary interventions, and the use of targeted nutritional supplements is recommended for individuals with FM.[7] However, little evidence-based information is available to provide nutritional advice for this specific population.[13] Furthermore, the scientific community is concerned about anecdotal nonscientific information related to the potential benefits of some products based on nutritional ingredients or botanicals[14] as well as specific diets with either no conclusive or contradictory results.[7,15-17]

Although most studies have focused on pain, little information is available about the association of dietary habits with psychosocial outcomes. Although pain is the main FM symptom, the disease has been defined as a complex multidimensional disorder, with other important psychosocial symptoms that have a massive impact on the individual's illness perception and quality of life.[18]

Therefore, the aims of this cross-sectional study were (1) to assess the dietary habits in a representative sample of women with FM from southern Spain, and (2) to examine the associations of dietary habits with mental health, depression, and optimism in this population.

METHODS

Study Sample and Design

The study assessments were carried out between November 2011 and January 2013. Briefly, a total of 617 women with FM were recruited through local associations of people with FM (via e-mail, letters, telephone, and University press) from Andalusia (southern Spain). After receiving detailed information about the aims and study procedures, participants signed informed consents before taking part in the study. Inclusion criteria for women with FM were: (1) to be previously diagnosed by a rheumatologist, (2) to meet the 1990 American College of Rheumatology fibromyalgia classification criteria,[1] and (3) to not have acute or terminal illness, or a severe dementia (Mini-Mental State Examination score <10).[19] Thirty-eight women with FM were not previously diagnosed, 92 did not meet the 1990 American College of Rheumatology criteria, and one had severe cognitive impairment. The final sample resulted in a sample size of 486 women with an age range from 35 to 65 years. The study was reviewed and approved by the local Ethics Committee ('Hospital Virgen de las Nieves,' Granada, Spain).

PATIENTS AND PROCEDURES

Sociodemographic Data

Sociodemographic information was recorded using a self-report questionnaire that included date of birth, marital status, educational level, current occupational status, and time since FM diagnosis, among other questions such as smoking status, household members, menstrual status, use of contraceptives, use of hormone replacement therapy, number of children, number of miscarriages, household tasks, and the use of nutritional supplements such as naturalistic (eg, *Plantago ovata*, omega-3 capsules, and so forth) or homeopathic products (eg, *Aconitum* 7CH, *Arnicum* 6CH, 20CH, and so forth).

Anthropometry and Body Composition

A portable eight-polar tactile-electrode bioelectrical impedance device (InBody R20; Biospace) was used to measure weight (kg), body fat (%), and skeletal muscle mass (kg). Height (cm) was measured using a stadiometer (Seca 22). Body mass index was calculated as weight (in kilograms) divided by height squared (in meters) and categorized following the World Health Organization criteria.[20] Waist circumference (cm) was measured, with the participant standing, at the middle point between the ribs and iliac crest (Harpenden anthropometric tape, Holtain Ltd). All measurements were conducted by trained researchers.

Dietary Habits

Dietary habits for the previous year were self-reported through completion of a short form of a validated food frequency questionnaire,[21] in which participants indicated the frequency of consumption (number of times per day, week, month, or year) of 34 foods divided by food groups: fruit, vegetables, dairy products, fish, cereals, pulses, eggs, meat, fats, sweets, beverages, and nuts. Questionnaires were reviewed by research staff, and study participants were asked to fill in any missing responses. Based on this food frequency questionnaire (see Figure 1, available at www.andjrnl.org), the answers were categorized to create three levels of food consumption: a *low-consumption group* for frequencies from never up to 1 serving per week, a *moderate-consumption group* for frequencies from 2 up to 5 servings per week, and a *high-consumption group* for a daily or almost-daily frequency (from 6 servings per week to daily consumption of at least 1 serving).

Mental Health

Mental health was self-reported with the Mental Component of the 36-Item Short-Form Health Survey (SF-36),[22] which has been validated in Spanish populations[23] for the evaluation of HRQoL. The Mental Component is measured by the following dimensions: vitality, mental health, social functioning, and emotional role. The final score for each dimension ranges from 0 to 100, with higher scores corresponding to better mental health.

Depression

The Beck Depression Inventory-II (BDI-II) is a 21-item questionnaire used to assess (self-reported) depressive symptomatology.[24] Participants rated each item from 0 ("not present") up to 3 ("severe") in the context of the past 2 weeks. Thus, the BDI-II score ranges from 0 to 63, with a higher score indicating greater depression. Clinical cutoff scores have been described as follows: a score from 0 to 13 represents none or minimal depression, from 14 to 19 represents mild depression, 20 to 28 represents moderate depression, and $\geq$29 represents severe depression.[25]

Optimism

The Life Orientation Test Revised (LOT-R)[26] assessed the participants' expectations about their future and their

general sense of optimism. This self-reported test comprises 10 items rated on a 5-point Likert scale. The LOT-R score ranges from 6 to 30, with higher scores indicating higher levels of dispositional optimism. Reference values for women aged 45 to 50 years of age are 15.2±3.8 and for women aged 51 to 60 years, 14.4±4.0.[26]

Participants received instructions on how to complete all of the self-administered questionnaires (sociodemographic data, dietary habits, SF-36, BDI-II and LOT-R) by trained researchers.

STATISTICAL ANALYSIS

Descriptive statistics were used to assess the dietary habits, derived from the food frequency questionnaire, of women with FM from the study population. The associations between dietary habits (eg, fish consumption) and mental health, depression, and optimism were examined by one-way analysis of covariance with age and percent body fat as covariates. Whenever there was a significant association, pairwise comparisons with the Bonferroni's correction for multiple comparisons were performed to identify differences across food-frequency groups (ie, low-, moderate-, and high-consumption groups). In addition, standardized effect size statistics were estimated in all of the comparisons among compliance with food consumption categories. Cohen's *d* and its exact confidence interval was used for all (parametric) variables and was interpreted as small (~0.25), moderate (~0.5), or large (~0.8 or greater).[27] The exact confidence intervals for Cohen's *d* were obtained by means of the non-centrality parameter of the noncentral Student's distribution using Wolfram-Mathematica 8.0.[28] The association of dietary habits (independent variables in separate models) was further assessed with the presence of severe depression (BDI-II≥29; dependent variable) with logistic regression after adjustment for age and percent body fat. All analyses were performed using the Statistical Package for Social Sciences[29] and statistical significance was set at α=.05.

RESULTS

A total of 486 women with FM met the inclusion criteria and were included in this study. Data were missing (<3%) on some items of the food frequency questionnaire. The descriptive characteristics of the participants are presented in Table 1. Seventy-three percent of the sample were overweight or obese. Dietary aspects indicated that 21% of the sample followed a diet. Of these individuals, 43% reported following a diet because of a disease or health problem, and 31% reported following a diet for weight-loss reasons. The use of vitamins or other type of supplementation ranged from 8% to 18% of the sample.

The dietary habits of the study participants are shown in Table 2. A daily or almost-daily (6 to 7 times per week) consumption of fruit, dairy products, cereals group (bread, rice, pasta, potatoes), and olive oil were observed in more than 50% of the participants, as well as a moderate consumption (from 2 up to 5 servings per week) of vegetables, fish, pulses, eggs, and meat. Cured meats, sweets, sweetened beverages, butter or margarine, mayonnaise, and alcoholic beverages were occasionally consumed (never or less than 1 serving per week) by most of the sample (53.1%, 45.3%, 74.9%, 81.5%, 99.8%, and 80.0%, respectively). Nut consumption presented a high variability, being slightly higher in the moderate-consumption group (39.5% of participants).

Table 1. Anthropometric, sociodemographic, and dietary characteristics of women with fibromyalgia (n=486) participating in the al-Ándalus project

Anthropometric and body composition	*mean±SD*[a]
Age (y)	52.2±8.0
Body mass index	28.6±5.5
Waist circumference (cm)	90.6±13.1
Body fat (%)	40.2±7.7
Muscle mass (kg)	22.7±3.3
	%
Weight status, NW/OW/OB[b]	27.2/36.1/36.7
	n (%)
Follow a diet since fibromyalgia diagnosis, yes	100 (20.6)
Reasons to follow a diet	
Lose weight	31 (31)
Maintain current weight	8 (8)
Live more healthily	15 (15)
Disease or health problem	43 (43)
Other reasons	3 (3)
Vitamins or minerals supplementation, yes	76 (15.6)
Naturalist products supplementation, yes	89 (18.3)
Homeopathic products, yes	38 (7.8)
SF-36[c], Mental Component	*mean±SD*
Social functioning	43.4±25.0
Emotional role	55.9±28.6
Mental health	45.4±20.3
Vitality	22.4±17.7
Mental Component Scale	35.6±11.9
BDI-II[d] total score	26.4±11.6
LOT-R[e] total score	13.4±4.4

[a]SD=standard deviation.
[b]NW/OW/OB=normal weight/overweight/obese.
[c]SF-36=Short-Form-36 Health Survey. The final score for each dimension ranges from 0 to 100, with higher scores corresponding to better mental health.
[d]BDI-II=Beck Depression Inventory, 2nd edition. The final score ranges from 0 to 63, with higher scores indicating greater depression.
[e]LOT-R=Life Orientation Test Revised. The LOT-R score ranges from 6 to 30, with higher scores indicating higher levels of dispositional optimism.

Table 3 shows the association of dietary habits with mental health, optimism, and depression after adjusting for age and percent body fat. Dairy products, cereals, pulses, eggs, meat, cured meats, sweets, sweetened beverages, butter or margarine, mayonnaise, olive oil, alcoholic beverages, and nut consumption were not associated with mental health (all $P>0.05$). Consumption of fruit ($P<0.001$), vegetables ($P<0.05$), and fish ($P<0.001$) were associated with mental health. Pairwise comparisons showed that the group with a

Table 2. Dietary habits of women with fibromyalgia (n=486) participating in the al-Ándalus Project assessed by a food frequency questionnaire[a]

	Low Consumption[b]		Moderate Consumption[c]		High Consumption[d]	
	Number	%	Number	%	Number	%
Fruit	41	8.6	118	24.7	319	66.7
Vegetables	35	7.3	265	55.6	177	37.1
Dairy products	56	11.7	80	16.7	342	71.5
Fish	78	16.3	388	81.2	12	2.5
Cereals[e]	34	7.1	81	17.0	361	75.8
Pulses	107	22.0	348	73.4	19	4.0
Eggs	119	24.9	354	74.2	4	0.8
Meat	41	8.6	407	85.1	30	6.3
Cured meats	252	53.1	191	40.2	32	6.7
Sweets	215	45.3	168	35.4	92	19.4
Sweetened beverages	356	74.9	84	17.7	35	7.4
Butter / margarine	388	81.5	58	12.2	30	6.3
Mayonnaise	476	99.8	1	0.2	0	0.0
Olive oil	6	1.3	2	0.4	470	98.3
Alcoholic beverages	380	80.0	58	12.2	37	7.8
Nuts	156	33.0	187	39.5	130	27.5

[a]Results are expressed as number of women and percentages of the study population (%). Total sample size does not add up to N=486 because of missing data.
[b]Low consumption=frequencies from 0 to 1 serving per week.
[c]Moderate consumption=frequencies from 2 to 5 servings per week.
[d]High consumption=from 6 servings per week to daily consumption of at least 1 serving.
[e]Cereals=cereals group represents bread, rice, pasta, and potato consumption.

daily or almost-daily consumption of fruit had higher scores in mental health than the low- ($P<0.001$) and moderate-consumption groups ($P<0.05$), and the group with a moderate consumption of fish presented higher scores in mental health than the low-consumption group ($P<0.05$).

Dairy products, cereals, pulses, eggs, meat, sweets, sweetened beverages, butter or margarine, mayonnaise, olive oil, alcoholic beverages, and nut consumption were not associated with depression. Consumption of fruit ($P<0.001$), vegetables ($P<0.01$), and fish ($P<0.01$) was inversely associated with BDI-II total score. Pairwise comparisons showed that the group with a daily or almost-daily consumption of fruit and vegetables had lower levels of depression than the low-consumption group (all $P<0.01$), and the group with a moderate consumption of fish had lower levels of depression compared with the low- and high-consumption groups (all $P<0.01$). The group with a daily or almost-daily consumption of cured meats showed higher levels of depression than the moderate-consumption group ($P<0.05$). Additional analyses (Table 4) showed that eating fruit every day or almost every day, in comparison with never or 1 serving per week, was associated with 60% lower risk of severe depression (odds ratio [OR]=0.40; $P=0.007$). Similarly, a moderate fish consumption, in comparison with never or 1 serving per week, was associated with 48% lower risk of severe depression (OR=0.52; $P=0.010$).

Fruit, cereals, pulses, eggs, meat, cured meats, sweets, butter or margarine, mayonnaise, olive oil, alcoholic beverages, and nut consumption were not associated with optimism (all $P>0.05$). Consumption of vegetables ($P<0.05$), dairy products ($P<0.05$), fish ($P<0.001$), and sweetened beverages ($P<0.05$) were associated with levels of optimism (Table 3). Pairwise comparisons indicated that the group with a daily or almost-daily consumption of vegetables had higher levels of optimism than the moderate-consumption group ($P<0.05$), the group with a moderate consumption of dairy products had higher levels of optimism than the daily or almost-daily consumption group ($P<0.05$), the group with a moderate consumption of fish had higher levels of optimism than the low- and high-consumption groups (both $P<0.001$), and the group with a daily or almost-daily consumption of sweetened beverages had lower levels of optimism than the low- and moderate-consumption groups (both $P<0.05$).

Finally, Figure 2 shows the association of fruit, vegetables, and fish consumption on the four dimensions that compose the score of the SF-36 Mental Component. A daily or almost-daily consumption of fruit was positively associated with social functioning ($P<0.01$), emotional role ($P<0.001$), and mental health ($P<0.05$), and a daily or almost-daily consumption of vegetables was positively associated with mental health and vitality (both $P<0.05$). Likewise, a moderate consumption of fish was positively associated social functioning

Table 3. Association between different food consumption groups and mental health, optimism, and depression for women with fibromyalgia (n=486) participating in the al-Ándalus project[a]

	Low consumption[b]	Moderate consumption[c]	High consumption[d]	*P* value	Effect size[e]
	←——— *mean (SE)* ———→				
SF-36 MCS score[f]					
Fruit	29.9 (1.90)*	33.5 (1.11)**	37.1 (0.69)*,**	<0.001	0.59 (0.38-0.81)
Vegetables	32.2 (2.08)	34.9 (0.75)	37.1 (0.91)	<0.05	0.41 (0.13-0.69)
Dairy products	36.3 (1.62)	36.9 (1.39)	35.2 (0.67)	0.480	0.17 (−0.01-0.37)
Fish	31.0 (1.38)*	36.6 (0.61)*	30.5 (3.76)	<0.001	0.64 (0.43-0.84)
Cereals[g]	32.4 (2.19)	35.3 (1.36)	36.0 (0.65)	0.282	0.29 (0.09-0.49)
Pulses	36.7 (1.20)	35.6 (0.67)	30.4 (2.78)	0.115	0.50 (0.15-0.87)
Eggs	34.9 (1.16)	35.8 (0.66)	34.8 (6.04)	0.770	0.08 (−0.13-0.29)
Meat	32.9 (1.95)	35.9 (0.61)	34.7 (2.23)	0.303	0.24 (0.06-0.43)
Cured meats	35.2 (0.79)	36.7 (0.90)	31.6 (2.16)	0.075	0.43 (0.15-0.70)
Sweets	35.4 (0.85)	36.7 (0.97)	34.2 (1.28)	0.279	0.20 (−0.04-0.44)
Sweetened beverages	35.9 (0.65)	36.2 (1.34)	30.6 (2.18)	0.062	0.45 (0.07-0.83)
Butter/margarine	35.6 (0.63)	34.1 (1.64)	37.5 (2.20)	0.440	0.27 (−0.14-0.70)
Mayonnaise	35.7 (0.57)	42.5 (12.00)	—	—	0.54 (0.36-0.76)
Olive oil	28.7 (4.85)	36.0 (8.34)	35.5 (0.56)	0.378	0.61 (−1.06-2.29)
Alcoholic beverages	35.6 (0.63)	35.8 (1.65)	35.4 (2.13)	0.988	0.03 (−0.37-0.44)
Nuts	36.8 (0.99)	34.27 (0.89)	36.49 (1.12)	0.120	0.21 (0.00-0.42)
BDI-II[h]					
Fruit	30.6 (1.80)*	29.1 (1.06)**	24.9 (0.66)*,**	<0.001	0.49 (0.27-0.69)
Vegetables	30.1 (1.96)*	27.3 (0.72)**	24.5 (0.88)*,**	<0.01	0.48 (0.21-0.76)
Dairy products	26.7 (1.56)	25.3 (1.32)	26.7 (0.64)	0.633	0.12 (−0.07-0.31)
Fish	29.6 (1.34)*	25.6 (0.59)*,**	34.4 (3.48)**	<0.01	0.76 (0.56-0.96)
Cereals[g]	27.5 (2.10)	27.8 (1.03)	26.2 (0.62)	0.803	0.14 (−0.04-0.33)
Pulses	25.2 (1.14)	26.7 (0.63)	27.6 (2.70)	0.476	0.20 (−0.15-0.56)
Eggs	26.8 (1.09)	26.2 (0.63)	34.2 (5.84)	0.381	0.67 (0.46-0.89)
Meat	29.0 (1.87)	26.3 (0.58)	25.5 (2.17)	0.348	0.29 (−0.18-0.77)
Cured meats	26.5 (0.75)	25.7 (0.86)*	31.2 (2.06)*	<0.05	0.49 (0.22-0.75)
Sweets	26.4 (0.81)	25.5 (0.91)	28.5 (1.22)	0.153	0.25 (0.01-0.50)
Sweetened beverages	26.1 (0.63)	26.8 (1.29)	29.5 (1.97)	0.241	0.28 (0.08-0.48)
Butter / margarine	26.1 (0.60)	28.9 (1.57)	26.9 (2.17)	0.240	0.23 (0.05-0.43)
Mayonnaise	26.4 (0.54)	11.8 (11.7)	—	0.213	1.23 (1.04-1.43)
Olive oil	25.8 (4.75)	29.1 (8.21)	26.6 (0.54)	0.943	0.28 (−1.36-1.93)
Alcoholic beverages	26.5 (0.61)	24.9 (1.55)	27.7 (1.98)	0.516	0.23 (−0.17-0.64)
Nuts	25.0 (0.94)	27.4 (0.85)	26.4 (1.05)	0.166	0.20 (0.00-0.42)
LOT-R[i]					
Fruit	12.3 (0.76)	12.9 (0.28)	14.2 (0.34)	0.072	0.30 (0.10-0.52)
Vegetables	12.6 (0.76)	13.0 (0.27)*	14.1 (0.33)*	<0.05	0.35 (0.08-0.62)
Dairy products	13.0 (0.59)	14.6 (0.50)*	13.2 (0.24)*	<0.05	0.37 (0.03-0.72)
Fish	12.2 (0.51)*	13.7 (0.22)*,**	9.6 (1.38)**	<0.001	0.87 (0.66-1.08)
Cereals[g]	13.7 (0.82)	13.5 (0.50)	13.3 (0.24)	0.836	0.08 (−0.11-0.28)

(*continued on next page*)

Table 3. Association between different food consumption groups and mental health, optimism, and depression for women with fibromyalgia (n=486) participating in the al-Ándalus project[a] (*continued*)

	Low consumption[b]	Moderate consumption[c]	High consumption[d]	*P* value	Effect size[e]
Pulses	13.6 (0.44)	13.4 (0.24)	11.5 (1.05)	0.174	0.46 (0.10-0.82)
Eggs	13.5 (0.42)	13.4 (0.24)	11.5 (2.22)	0.672	0.43 (0.08-0.80)
Meat	13.4 (0.72)	13.5 (0.22)	12.3 (0.83)	0.392	0.26 (0.08-0.46)
Cured meats	13.4 (0.28)	13.6 (0.33)	11.7 (0.79)	0.078	0.46 (0.18-0.73)
Sweets	13.4 (0.31)	14.1 (0.35)	12.3 (2.47)	0.762	0.12 (−0.12-0.37)
Sweetened beverages	13.5 (0.24)*	13.6 (0.49)**	11.3 (0.79)***	<0.05	0.52 (0.14-0.90)
Butter/margarine	13.4 (0.23)	13.8 (0.60)	12.1 (0.81)	0.228	0.37 (−0.05-0.80)
Mayonnaise	13.4 (0.21)	17.9 (4.37)	—	0.296	0.98 (0.79-1.17)
Olive oil	11.9 (1.81)	14.3 (3.13)	13.4 (0.21)	0.706	0.54 (−1.12-2.21)
Alcoholic beverages	13.4 (0.23)	13.5 (0.60)	13.1 (0.77)	0.940	0.08 (−0.32-0.49)
Nuts	13.7 (0.37)	13.2 (0.33)	13.4 (0.41)	0.637	0.10 (−0.10-0.32)

[a]Results are expressed as mean (standard error, SE) after adjusting for age and % body fat.
[b]Low consumption=frequencies from 0-1 serving per week.
[c]Moderate consumption=frequencies from 2-5 servings per week.
[d]High consumption=from 6 servings per week to daily consumption of at least 1 serving.
[e]Effects size statistics are expressed as Cohen's *d* (95% exact confidence interval).
[f]SF-36 MCS score=Short-Form-36 Health Survey Mental Component Scale score. The final score for each dimension ranges from 0 to 100, with higher scores corresponding to better mental health.
[g]Cereals=Cereals group represents bread, rice, pasta, and potato consumption.
[h]BDI-II=Beck Depression Inventory-second edition. The final score ranges from 0 to 63, with higher scores indicating greater depression.
[i]LOT-R=Life Orientation Test Revised. The LOT-R score ranges from 6 to 30, with higher scores indicating higher levels of dispositional optimism.
*,**,***Common superscripts in a same row indicate a significant difference ($P<0.05$) between the groups with the same symbol. Pairwise comparisons were performed with Bonferroni's adjustment.

($P<0.05$), emotional role ($P<0.01$), and mental health ($P<0.05$).

DISCUSSION

This cross-sectional study presents descriptive data on the dietary habits in a representative sample of women with FM and reveals the association of dietary habits with important psychosocial outcomes in this population. The main findings indicate that a daily or almost-daily consumption of fruit is positively associated with better mental health and a lower risk of severe depression. Similarly, daily or almost-daily consumption of vegetables and moderate consumption of fish are positively associated with better mental health and optimism and inversely associated with depression levels. Furthermore, a moderate but weekly consumption of fish is associated with a lower risk of severe depression. Finally, a moderate but weekly consumption of dairy products is positively associated with more optimism. In contrast, a daily or almost-daily consumption of cured meats and sweetened beverages are associated with less favorable psychosocial outcomes.

Current scientific evidence supports an association between nutrition and health and the importance of healthy dietary habits on the well-being of the population.[11,30] However, in FM, neither observational nor prospective studies have been conducted to date to assess dietary habits of this population, although several intervention trials have been conducted to facilitate and evaluate dietary habit modification.[14-16,31,32] Most of these dietary interventions, which have not shown conclusive results, have focused on isolated nutrients, or supplements, and others on restrictive diets, which might promote long-term deficiencies,[9,16] as well as being unsustainable over time.[7] A recent review study highlights the importance of nutrition in the multidisciplinary treatment approach of this disease.[7]

The direct association observed in this study between the daily or almost-daily consumption of fruit and vegetables and mental health and the inverse association with depression in women with FM is not surprising, but it is promising. Eating fruit every day as well as fish from 2 to 5 times per week was associated with a reduced risk of major depression. The postulated ability of certain nutrients contained in fruit and vegetables (complex carbohydrates, B vitamin complex, folate, antioxidants, minerals, and so forth) to influence mental health[33] may partially explain the observed association. Folate and vitamins B-12 and B-6, through methionine conversion, are involved in 1-carbon metabolism that acts in several methylation reactions, such as those that involve serotonin and other monoamine neurotransmitters. Folate is required for the synthesis of methionine from homocysteine, and vitamins B-12 and B-6 also serve as cofactors for enzymes involved in homocysteine metabolism.[33,34] The findings observed in the current study are in line with previous studies that have shown a direct association between the intake of the recommended 5 daily servings of fruit and vegetables (as defined by the Mediterranean diet[35]) and lower psychological distress,[36] as well as lower levels of

Table 4. Association between different food consumption groups and the presence of severe depression (BDI-II[a] ≥29) in women with fibromyalgia (n=486) involved in the al-Ándalus project

Food frequency	OR[b]	SE[c]	95% CI[d]	*P* value[e]
Fruit				
Low consumption[f]	Ref[g]			
Moderate consumption[h]	0.678	0.250	0.330, 1.396	0.292
High consumption[i]	0.398	0.136	0.204, 0.778	0.007
Vegetables				
Low consumption	Ref			
Moderate consumption	0.758	0.274	0.373, 1.540	0.443
High consumption	0.495	0.186	0.237, 1.034	0.061
Dairy products				
Low consumption	Ref			
Moderate consumption	1.166	0.415	0.581, 2.344	0.666
High consumption	1.012	0.301	0.565, 1.812	0.968
Fish				
Low consumption	Ref			
Moderate consumption	0.516	0.132	0.313, 0.851	0.010
High consumption	1.540	1.036	0.412, 5.754	0.521
Cereals[j]				
Low consumption	Ref			
Moderate consumption	0.806	0.338	0.354, 1.835	0.608
High consumption	0.632	0.233	0.307, 1.304	0.215
Pulses				
Low consumption	Ref			
Moderate consumption	1.356	0.313	0.862, 2.132	0.187
High consumption	0.896	0.483	0.312, 2.577	0.839
Eggs				
Low consumption	Ref			
Moderate consumption	0.924	0.203	0.600, 1.422	0.720
High consumption	1.482	1.517	0.199, 11.026	0.701
Meat				
Low consumption	Ref			
Moderate consumption	0.583	0.195	0.303, 1.123	0.107
High consumption	0.444	0.225	0.164, 1.199	0.109
Cured meats				
Low consumption	Ref			
Moderate consumption	0.903	0.182	0.608, 1.342	0.614
High consumption	1.414	0.535	0.673, 2.968	0.360
Sweets				
Low consumption	Ref			
Moderate consumption	1.072	0.230	0.704, 1.632	0.746
High consumption	1.285	0.327	0.780, 2.116	0.325

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Table 4. Association between different food consumption groups and the presence of severe depression (BDI-II[a]≥29) in women with fibromyalgia (n=486) involved in the al-Ándalus project (*continued*)

Food frequency	OR[b]	SE[c]	95% CI[d]	*P* value[e]
Sweetened beverages				
Low consumption	Ref			
Moderate consumption	1.064	0.267	0.651, 1.739	0.804
High consumption	1.257	0.451	0.622, 2.540	0.524
Butter/margarine				
Low consumption	Ref			
Moderate consumption	1.608	0.461	0.917, 2.820	0.097
High consumption	0.920	0.366	0.421, 2.001	0.834
Mayonnaise				
Low consumption	Ref			
Moderate consumption	0.980	0.012	0.958, 1.004	0.105
High consumption	—	—	—	—
Olive oil				
Low consumption	Ref			
Moderate consumption	5.211	9.331	0.156, 174.161	0.356
High consumption	3.313	3.650	0.382, 28.709	0.277
Alcoholic beverages				
Low consumption	Ref			
Moderate consumption	0.912	0.266	0.515, 1.617	0.754
High consumption	1.253	0.448	0.622, 2.524	0.528
Nuts				
Low consumption	Ref			
Moderate consumption	1.428	0.321	0.919, 2.219	0.113
High consumption	1.169	0.293	0.715, 1.911	0.533

[a]BDI-II=Beck Depression Inventory-second edition. The final score ranges from 0 to 63, with higher scores indicating greater depression.
[b]OR=odds ratio.
[c]SE=standard error.
[d]CI=confidence interval.
[e]*P* value adjusted for age and % body fat.
[f]Low consumption=frequencies from 0 to 1 serving per week.
[g]Ref=reference.
[h]Moderate consumption=frequencies from 2 to 5 servings per week.
[i]High consumption=from 6 servings per week to daily consumption of at least 1 serving.
[j]Cereals=Cereals group represents bread, rice, pasta, and potato consumption.

depression[37] with a "fruit and vegetables–rich diet." The largest study conducted to date examining the association of fruit and vegetable consumption with psychosocial well-being[38] showed an inverse association with depression, psychological distress, the presence of mood and anxiety disorders, and self-perceived poor mental health status in the general population.

In the same context, the significant association of moderate fish consumption with mental health, optimism, and reduced depression observed in this study also concurs with the conclusions derived from a recent systematic review[37] in which moderate fish consumption was shown to be protective against depression, although an intake above a designated threshold seemed to have the opposite effect. A recent meta-analysis has shown an inverse relationship between fish consumption and depression,[39] especially when the fish were rich in omega 3 fatty acids. Although Spanish dietary recommendations suggest 4 servings of fish per week,[40] higher intakes could lead to an accumulation of mercury compounds, polychlorinated biphenyls, and dioxins, exerting a toxicological effect that could increase the risk of depression[41] and also may have adverse effects on cardiometabolic health.[42]

Finally, in previous studies conducted in different populations, a significant adverse linear trend was observed for cured meats and sweetened beverages,[34,43] which is in line

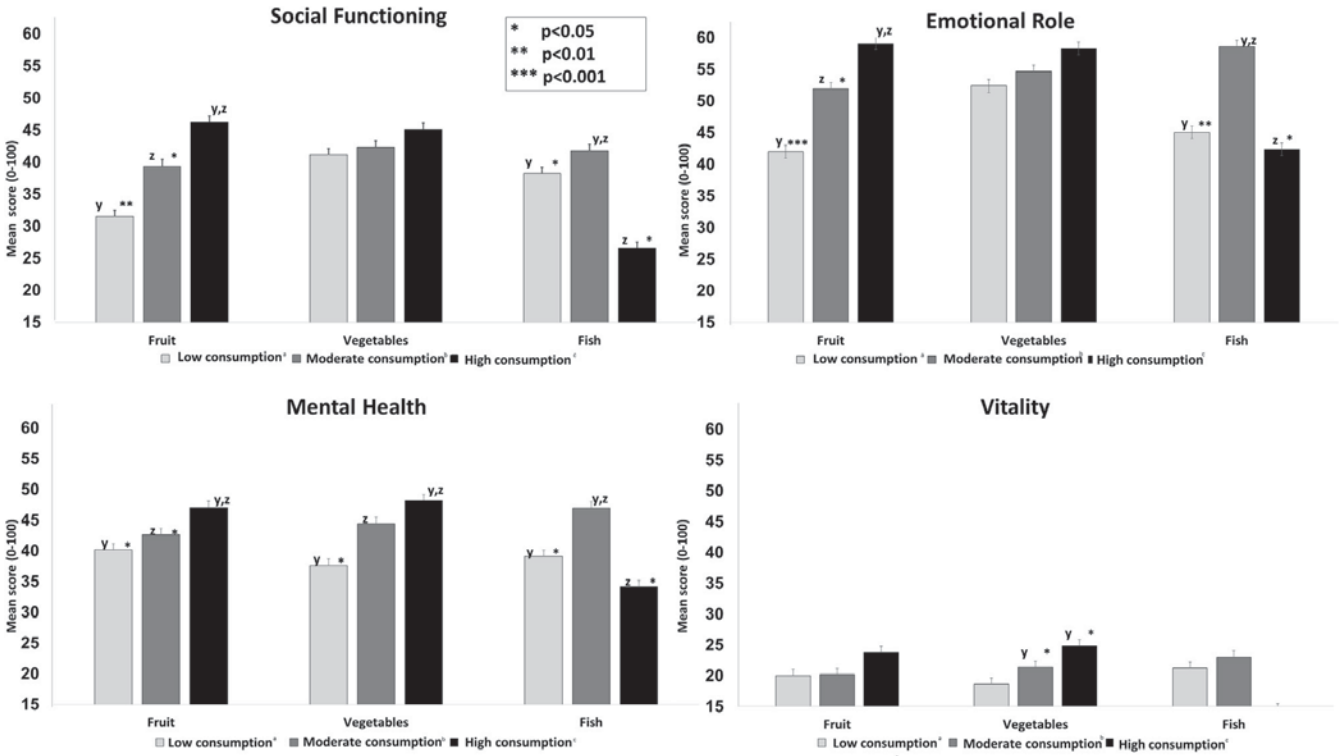

Figure 2. Association between fruit, vegetables, and fish consumption on the four dimensions of the Mental Component of the 36-item Short-Form Health Survey (SF-36) in women with fibromyalgia (n=486) participating in the al-Ándalus project: Social functioning, emotional role, mental health, and vitality. Bars represent mean and 95% confidence intervals after adjusting for age and % body fat. The final score for each dimension of the SF-36 Mental Component Scale ranges from 0 to 100, with higher scores corresponding to better mental health. [a]Low consumption=frequencies from 0 to 1 serving per week; Moderate consumption=frequencies from 2 to 5 servings per week; High consumption=from 6 servings per week to daily consumption of at least 1 serving. [yz]Common superscripts in the same consumption group indicate a significant difference (*$P<0.05$; **$P<0.01$; ***$P<0.001$) between the groups with the same letter.

with the present findings, and supports the idea that a western dietary pattern, characterized by consumption of processed meats, sugar, flavored drinks, pizza, and so forth, increases the odds for severe depression.[43]

The assessment of dietary habits in a representative sample of women with FM from southern Spain showed some deviations from dietary guidelines.[44] One-third of the study sample reported not eating fruit on a daily basis, whereas the figure for vegetables rose to nearly two-thirds of the sample. Notwithstanding, nearly half of the population overate cured meats and sweets.[44] The rest of the food groups assessed appear to be close to dietary guidelines.[44] These results are in line with the general trend observed in Spain[45] in which an insufficient dissemination and implementation of these guidelines as well as a progressive distancing from the Mediterranean diet[45,46] has been observed. The Mediterranean diet (characterized by an abundance of plant-based foods such as fruit, vegetables, whole-grain cereals, nuts and legumes; olive oil as the main source of fat; moderate amounts of fish, poultry, dairy products, and eggs; relatively low amounts of red meat and sweets; and moderate consumption of red wine with meals[30]) has extensive scientific evidence for its role in general health, showing a direct relationship with better SF-36 Mental Components.[12,30,36,47] The main elements of the Mediterranean diet ensure an adequate intake of several nutrients that negatively correlate with depression and mental disorders.[11,12] We hope that the results of the current study will stimulate future research in the FM population, assessing dietary patterns as a whole and not just individual nutrients or foods. Future research is also needed to provide a complete picture of the relationship of diet with HRQoL and well-being, taking into account the complex interactions among nutrients.[48]

This study has some limitations that should be noted. First, a specific questionnaire assessing the Mediterranean dietary pattern was not used. Thus, studying associations with Mediterranean diet adherence was not possible. Second, the cross-sectional study design precluded establishing causal relationships. Further prospective research is needed to better understand the interrelationships between diet and psychosocial outcomes in fibromyalgia. Finally, this study was carried out only in women, and future studies should be conducted in men with FM. The main strength of this study was the relatively large and representative sample size, which enabled assessment of dietary habits and their association with relevant psychosocial outcomes in this population. In addition, this study used a clinical measure of depression to evaluate the relationship between dietary patterns and psychosocial outcomes, unlike most studies, which employ only QOL measures as primary outcomes for mental health.

CONCLUSION

The results of this study suggest that a daily or almost-daily intake of fruit and vegetables and a moderate intake of fish may be associated with more favorable psychosocial outcomes in women with fibromyalgia. Conversely, excessive intake of cured meats and sweetened beverages were related to worse scores for depression and optimism. Future research analyzing dietary patterns as well as intervention studies evaluating the effects of healthy dietary patterns on psychosocial and physical outcomes in individuals with FM are warranted.

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STATEMENT OF POTENTIAL CONFLICT OF INTEREST

No potential conflict of interest was reported by the authors.

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FOOD FREQUENCY QUESTIONNAIRE (Short-Form)

FOOD GROUPS	NEVER	SERVINGS/DAY	SERVINGS/WEEK	SERVINGS/MONTH	SERVINGS/YEAR
MEAT					
Meat					
Cured meats					
FISH					
Fish					
Shellfish (shrimps, clams, mussels, etc)					
EGGS					
Fried, boiled, omelet, etc					
PULSES					
Lentils					
Chickpeas					
White beans					
Green peas					
CEREALS					
Bread					
Rice					
Pasta (noodles, spaghetti, pizza)					
Potatoes (fried, boiled, grilled, in omelet, etc)					
DAIRY PRODUCTS					
Milk					
Yoghurt					
Pudding/Flan					
Cheese					
FATS					
Butter / Margarine					
Mayonnaise					
Olive Oil					
VEGETABLES					
Servings of vegetables					
FRUITS					
Number of fresh fruit servings per day					
Canned fruit					
SWEETS					
Sugar					
Chocolate					
Cookies, cakes, pastries					
BEVERAGES					
Water					
Packaged fruit juices					
Fresh fruit juices					
Sweetened beverages (soda, sweetened tea...)					
Beer					
Wine Red.....White.....					
Distilled alcoholic beverages (rum, whisky, gin...)					
NUTS					
Servings (a handful)					

Figure 1. Translated short form of the Spanish validated Food Frequency Questionnaire (FFQ). Participants indicate the frequency of consumption (times per day, week, month, or year) of 34 foods divided by food groups: fruit, vegetables, dairy products, fish, cereals, pulses, eggs, meat, fats, sweets, beverages, and nuts.

CONCLUSIONES

I. Existe un progresivo distanciamiento del patrón de Dieta Mediterránea entre las mujeres perimenopáusicas del sur de España, cuya adhesión es mayoritariamente moderada y donde sólo un tercio presenta alta adhesión.

II. El consumo de cereales no refinados y legumbres por debajo de las recomendaciones, así como el excesivo consumo de proteína animal resultan en una dieta hipoglucídica, hiperproteica e hiperlipídica.

III. Una alta adhesión al patrón de Dieta Mediterránea podría favorecer un perfil cardiometabólico más saludable en mujeres perimenopáusicas, caracterizado por una menor frecuencia cardíaca basal, menores concentraciones plasmáticas de colesterol total, colesterol LDL, ratio colesterol total/HDL, triglicéridos y proteína C-reactiva, independientemente de la edad, índice de masa corporal, menstruación regular, hábito tabáquico, uso de terapia hormonal sustitutiva y niveles de actividad física.

IV. Una alta adhesión al patrón de Dieta Mediterráneapodría reducir el riesgo cardiometabólico global, mientras que dicho efecto no se observa cuando la adhesión es moderada o baja. Aunque algunos de los componentes de la Dieta Mediterránea, como cereales integrales, legumbres y vino tinto muestran una asociación inversa con el riesgo cardiometabólico global, estas asociaciones individuales no son tan fuertes como la observada con la Dieta Mediterránea estudiada en su conjunto.

V. La fuerza muscular, el peso, el índice de masa corporal y la masa magra se asocian positivamente con la densidad mineral ósea en mujeres perimenopaúsicas, no presentando asociación la adhesión a la Dieta Mediterránea, la masa grasa, ni ninguno de los marcadores cardiometabólicos estudiados.

VI. La masa magra muestra una asociación fuerte e independiente con la densidad mineral ósea, explicando el 14% de la variabilidad y mostrando una diferencia clínicamente relevante entre las mujeres perimenopaúsicas en el primer y cuarto cuartil de masa magra.

VII. El estudio de los hábitos dietéticos en una muestra representativa de mujeres perimenopáusicas del sur de España con fibromialgia muestra que un consumo diario de fruta y verdura, así como un consumo moderado (2-5 raciones/semana) de pescado se asocia con mejor salud mental y optimismo y menor depresión. Por otro lado, un consumo diario o casi diario de embutidos y bebidas azucaradas se asocian a menor optimismo y mayor depresión.

Conclusión general:

Los resultados de la presente memoria de Tesis ponen de manifiesto la importancia, en esta población, de mantener una alta adhesión al patrón de Dieta Mediterránea para reducir el riesgo cardiometabólico, así como una adecuada fuerza y masa muscular que preserve la densidad mineral ósea. Asimismo, en la mujer perimenopáusica con fibromialgia, la ingesta diaria de fruta y verdura y el consumo semanal, pero moderado (2-5 raciones/semana), de pescado pueden mejorar su salud mental.

CONCLUSIONS

I. There is a progressive distancing from the Mediterranean dietary pattern among the perimenopausal women from Southern Spain, whose adherence is mostly moderate, with less than one third of the study population showing a high adherence.

II. The lack of cereals, mainly whole grain cereals, and pulses in the diet in favor of a higher consumption of animal proteins determine a hypoglycemic, hyperproteic and hyperlipidemic diet.

III. A high adherence to the Mediterranean Dietary pattern promote a better cardiometabolic profile among perimenopausal women, characterized by lower resting heart rate, plasma total cholesterol, LDL-C, total cholesterol/HDL-C ratio, triglycerides and C-reactive protein compared to those with a low adherence, regardless of potential confounders as age, body mass index, regular menstruation, smoking habit, use of substitutive hormone therapy and physical activity levels.

IV. Women with a high adherence to the Mediterranean Dietary pattern showed a lower clustered cardiometabolic risk, a protection that was not afforded when adherence was low or medium. Although some of the components of the Mediterranean Diet, such as whole grains, legumes and red wine show an inverse association with the clustered cardiometabolic risk, these individual associations are not as strong as those observed when the Mediterranean Diet is studied as a whole.

V. Muscle strength, body weight, body mass index and lean mass are significantly associated with bone mineral density in perimenopausal women. By contrast, neither cardiorespiratory fitness, flexibility, motor agility, cardiometabolic

markers (blood pressure, plasma lipids, fasting glucose or C-reactive protein), nor the Mediterranean Diet are associated with bone mineral density.

VI. Lean mass is the only factor independently associated with bone mineral density, explaining 14% of its variability. The difference in bone mineral density between the groups with the highest and the lowest quartiles of lean mass is clinically meaningful.

VII. The study of the dietary habits in a representative sample of perimenopausal women from Southern Spain with fibromyalgia indicate that a daily consumption of fruit and vegetables as well as a moderate but weekly (2-5 servings/week) consumption of fish is positively associated with better mental health, optimism and a lower risk of severe depression. In contrast, a daily or almost-daily consumption of cured meats and sweetened beverages are associated with less favorable psychosocial outcomes.

Overall Conclusion:

These findings of the present Thesis highlight that, among the perimenopausal women studied, the Mediterranean Diet adherence is mainly low or moderate, with an overconsumption of animal protein and refined carbohydrates and an intake below recommendations for non-refined cereals and pulses. These results also show the importance of maintaining a high adherence to the Mediterranean Diet in order to reduce the cardiometabolic risk, as well as an adequate lean mass to preserve bone mineral density. Likewise, in perimenopausal women with fibromyalgia, a daily intake of fruit and vegetables and a weekly, but moderate (2 -5 servings/week), consumption of fish can improve the patient's mental health.