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Mediterranean Diet, Body Composition, and Activity Associated with Bone Health in
Women with Fibromyalgia Syndrome

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committees and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained for all participants.

The authors have no conflicts of interest to report.

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Abstract

Background: There is very little scientific literature on the potential relationships between modifiable factors, including body composition, dietary pattern and physical activity (PA), and bone status in patients with fibromyalgia: A musculoskeletal condition characterized by chronic, widespread pain that is often accompanied by a broad spectrum of symptoms.

Objectives: To investigate the impact of body composition parameters, adherence to the Mediterranean diet (Med Diet), and PA on bone health in a population of premenopausal and postmenopausal women with fibromyalgia syndrome (FMS).

Methods: Ninety-five women diagnosed with FMS were included in this cross-sectional study. Body composition, including fat mass (FM), percentage of fat mass (PFM), and lean mass (LM), were calculated using a body composition analyzer. Adherence to the Med Diet was measured through a validated 14-item questionnaire. The International Physical Activity questionnaire was used to assess PA. Bone mass at the calcaneus was estimated through quantitative ultrasound (QUS).

Results: Linear regression analysis revealed that LM had a significant association with broadband ultrasound attenuation (BUA) ($\beta = 0.211$, 95% CI [0.046, 1.259]; $p = 0.035$) and stiffness index (SI) parameters ($\beta = 0.201$, 95% CI [0.019, 1.654]; $p = 0.045$) after adjusting for age and menopausal status. The Med Diet was also significantly associated with BUA ($\beta = 1.693$, 95% CI [0.508, 2.879]; $p = 0.006$).

Discussion: LM and the Med Diet were consistently associated with calcaneal QUS parameters, supporting the hypothesis that LM and adherence to the Med Diet play determinant roles in bone health in FMS women. Training programs to maximize LM and strategies for promoting good adherence to the Med Diet should be considered in order to prevent the development of osteoporosis in FMS women. Since nurses are involved in

implementing preventive programs, their roles in promoting this adherence to the Med Diet and maximizing LM in patients with FMS should help reduce the impact of osteoporosis.

Keywords: bone mass, fibromyalgia, lean mass, Mediterranean diet

Mediterranean Diet, Body Composition, and Activity Associated with Bone Health in Women with Fibromyalgia Syndrome

Fibromyalgia syndrome (FMS) is a musculoskeletal condition characterized by chronic, widespread pain that is often accompanied by a wide spectrum of symptoms, including fatigue, sleep disturbance, memory and concentration problems, irritable bowel syndrome, headaches, and depression (Clauw, 2014). The prevalence of the disease in the general population has been estimated to be 2.7%. The disease is more common among middle-aged women (Queiroz, 2013), and, in fact, FMS is considered the most common cause of musculoskeletal pain in women aged 20–55 (Chinn, Caldwell, & Gritsenko, 2016). The etiology of the disease has not yet been established, but several factors, including dysfunction of the central and autonomic nervous systems, genetic predisposition, immunological vulnerability, and external stressors, seem to be involved (Bellato et al., 2012).

Osteoporosis, defined as a systemic skeletal disease characterized by low bone mineral density (BMD) and a deterioration of bone microstructure that increase the risk of bone fragility (Cosman et al., 2014), has been associated with FMS (Upala, Yong, & Sanguankeeo, 2017). Previous work has explored the relationship between FMS and an increased risk of osteoporosis—although the conclusions are inconsistent (Garip Cimen, Eser, Sayin, Bodur, & Cavusoglu, 2015; Olama, Senna, Elarman, & Elhawary, 2013). The possible mechanisms linking the two diseases are yet to be determined, but it has been proposed that FMS is mediated by the presence of common risk factors (Yunus, Ahles, Aldag, & Masi, 1991).

The available evidence shows that obesity is common in FMS (Gota, Kaouk, & Wilke, 2015). The prevalence of overweight and obesity in FMS patients has been estimated

to be 32%–50% and 21%–28%, respectively (Neumann et al., 2008; Yunus, Arslan, & Aldag, 2002). A large study conducted on 2,596 people with FMS reported that the average BMI of sufferers is in the obese range (Bennett, Jones, Turk, Russell, & Matallana, 2007). A higher BMI seems to be associated to greater pain and disease severity, as well as reduced physical functioning in FMS (Çakit et al., 2018; Okifuji & Hare, 2015). Obesity has also been established as a risk factor for osteoporosis (Gonnelli, Caffarelli, & Nuti, 2014). Additionally, previous researchers investigating the relationship between obesity and osteoporosis—by accounting for the mechanical loading effects of total body weight on bone mass—showed that increasing FM may not have a beneficial effect on bone mass (Kim, Shin, Lee, Im, & Lee, 2010).

On the other hand, a low-quality diet has been reported in patients with FMS (Arranz, Canela, & Rafecas, 2012). Batista et al. (2016) indicated that compared with women with FMS, a control group had a greater intake of carbohydrates, proteins, and lipids, as well as several micronutrients. Healthy dietary patterns and good adherence to the Mediterranean diet (Med Diet) in these patients are important, since it has been demonstrated that a balanced and healthy diet may improve symptoms (Batista et al., 2016; Bjørklund, Dadar, Chirumbolo, & Aaseth, 2018). Likewise, previous evidence gathered on diet and nutrition relating to osteoporosis suggests that balanced dietary patterns and a greater adherence to the Med Diet may be beneficial to bone health (Rivas et al., 2013). However, these associations have not been fully investigated in women with FMS.

Several researchers have reported that FMS patients are physically less active and spend more time in sedentary behavior than age-matched healthy controls (Álvarez-Gallardo et al., 2017; Segura-Jiménez et al., 2015). The evidence strongly supports the fact that regular physical activity has a positive effect, counteracting bone loss and risk of fracture, and resulting in improved bone strength (Moreira et al., 2014). Furthermore, the reduced mobility

reported in FMS patients might result in less exposure to sunlight and, consequently, lower vitamin D levels.; another risk factor for low BMD (Olama et al., 2013). Physical inactivity trends in FMS patients may, therefore, constitute a risk factor for the development of osteoporosis (Yildirim & Yildirim, 2015). Nonetheless, there is very little evidence on the association between physical activity (PA) levels and bone status in FMS sufferers.

Osteoporosis is one of the most classic diseases associated with aging since increasing age leads to a progressive loss in bone loss (Demontiero, Vidal, & Duque, 2012). Further, although osteoporosis has traditionally been considered a disease of postmenopausal women, it has been reported that accelerated bone loss can also occur early in life, leading to premenopausal osteoporosis (Cheng & Gupta, 2013). For this reason, it is important to identify modifiable risk factors that prevent bone loss in both premenopausal and postmenopausal women. Obesity, a low-quality diet, and sedentarism have been recognized as determinants of osteoporosis in the general population (Correa-Rodriguez, Rio-Valle, González-Jiménez, & Rueda-Medina, 2016). Nevertheless, whether these are risk factors in a specific population of FMS women has not previously been analyzed. The published literature supports the need to investigate the relationships between FMS and diet quality, obesity, and PA, together with the relationship between osteoporosis and FMS. In this context, we aimed to investigate the impact of body composition parameters, adherence to the Med Diet, and PA on bone health measured through quantitative ultrasound (QUS) in a population of premenopausal and postmenopausal women with FMS.

Methods

Design and Sample

A cross-sectional study was conducted on a population of 95 Hispanic women, aged between 30 and 70 and diagnosed with FMS, per the 1990 criteria of the American College of Rheumatology (ACR). The women with FMS were recruited from two Spanish fibromyalgia

associations. The exclusion criteria included: (a) any medical condition affecting bone metabolism (renal disease, liver disease, hypogonadism, hyperthyroidism, hyperparathyroidism, etc.); (b) a history of medication known to affect bone health (glucocorticoids, methotrexate, bisphosphonate, calcitonin, estrogen, etc.); (c) any fracture in the past 12 months; and (d) prolonged periods of immobilization in the past 12 months. The participants completed structured questionnaires on their medical history, medication, age when fibromyalgia was diagnosed, menopause status, and previous fractures. Only one study visit was required for each subject. During the visit, informed consent was obtained, the study was explained, and any questions were answered. The study was approved by the ethics committee of a Spanish university. The research was performed in strict compliance with the international code of medical ethics established by the World Medical Association and the Declaration of Helsinki.

Body Composition Measurements

Body composition measurements including body weight, fat mass (FM), percentage of fat mass (PFM), and lean mass (LM) were measured twice (without shoes and in light clothes) to the nearest 0.1 kg using a body composition analyzer (TANITA BC-418MA[®]). Height was measured twice without shoes to the nearest 0.5 cm with a Harpenden stadiometer (Holtain 602VR[®]). The average of the two values for each measurement was used in the analysis. BMI was calculated by dividing body weight (kg) by the square of body height (m²). The same trained research assistant performed all the measurements.

Med Diet

Adherence to the Med Diet was measured using a validated 14-item questionnaire, *Prevención con Dieta Mediterránea* (Prevention with Mediterranean Diet [PREDIMED]) which has previously been described in detail (Martínez-González et al., 2012). Briefly, for each item a score was assigned, either 1 or 0, depending on whether the subjects adhered to

each Med Diet component or not. The Med Diet score therefore ranges from 0 to 14: The higher the score, the higher the degree of adherence to diet pattern. The Med Diet questionnaire has shown to be a valid tool for assessing adherence to this diet when compared to a food frequency questionnaire (FFQ) (Pearson's $r = .52$, $p < .001$; κ statistic = .43) (Schröder et al., 2011). According to the Bland–Altman method, the average Med Diet score estimate was 105% of the FFQ score estimate, and limits of agreement ranged between 57% and 153%. Multiple linear regression analyses demonstrated that a higher Med Diet score related directly ($p < .001$) to high-density lipoprotein (HDL) cholesterol, and inversely ($p < .038$) to body mass index, waist circumference, triglycerides (TG), the TG/HDL ratio, fasting glucose, and the total cholesterol/HDL ratio (Schröder et al., 2011).

Physical Activity

PA levels were assessed using the short version of the International Physical Activity Questionnaire (IPAQ). This questionnaire includes three specific types of activity: walking, moderate intensity activities, and vigorous-intensity activities. The minutes spent every week on each type of activity were computed separately by multiplying the duration and frequency of the activity. A metabolic equivalent (MET) per minute was obtained by multiplying the total minutes and the MET value of vigorous physical activity (VPA) (MET = 8.0), moderate physical activity (MPA) (MET = 4.0), and walking (MET = 3.3), and then adding the three together (Xiang et al., 2017). The questionnaire scores have been shown to be valid and reliable for measuring PA in European adult populations (Craig et al., 2003).

Calcaneal Quantitative Ultrasound (QUS)

Bone mass was assessed through QUS at the calcaneus using the Achilles ultrasound bone densitometer (Lunar Corporation), following the manufacturer's instructions. The QUS method has been postulated as a useful, noninvasive, portable, and inexpensive tool for assessing bone mass as an alternative to dual-energy X-ray absorptiometry (DXA) (Krieg et

al., 2008). Calcaneus QUS provides information on bone microstructure, elasticity, and connectivity through different parameters, including broadband ultrasound attenuation (BUA; dB/MHz), speed of sound (SOS; m/s), and the stiffness index (SI; %). The device was calibrated daily with the physical phantom provided by the manufacturer, and quality-control checks were carried out each day. The nondominant heel was measured unless it was the site of a previous fracture or otherwise unsuitable.

Statistical Analysis

The data were analyzed using SPSS© version 22.0 (IBM Corporation, Armonk, NY). The Kolmogorov–Smirnov test was used to analyse the normality of the distribution of the variables ($p > 0.05$). Linear regression analyses were conducted to determine the association between bone mass status and body composition, dietary patterns, and PA levels after adjusting for covariates. p -values of < 0.05 were considered statistically significant.

Results

Demographic and Clinical Characteristics

Table 1 shows the demographic and clinical data for the women with FMS. The mean age of the patients was 55.76 ± 7.96 . FMS women showed a mean BMI corresponding to overweight status (29.00 ± 6.32). 36.7% of the FMS women reported a previous fracture. 79.5% of the women were postmenopausal, and 20.5% were premenopausal. For body composition parameters, the mean PFM, FM, and LM were 37.11 ± 7.26 , 27.57 ± 10.25 , and 45.09 ± 3.94 , respectively. The total PA reported was 1144.09 ± 1664.68 (MET/min). Medium adherence to the Med Diet was reported (9.37 ± 2.04). The mean values of the BUA and SOS parameters were 105.26 ± 12.48 dB/MHz and 1558.25 ± 38.01 m/s, respectively.

Body Composition, the Med Diet, PA, and Calcaneal QUS

The beta estimates and 95% CI for body composition, the Med Diet, and PA and calcaneus QUS are shown in Table 2. Linear regression analyses revealed that LM was

significantly associated with BUA ($\beta = 0.211$, 95%CI [0.046, 1.259]; $p = .035$) and SI parameters ($\beta = 0.201$, 95%CI [0.019, 1.654]; $p = .045$) after adjusting for age and menopausal status. No significant differences were found between BMI, PFM, and FM and QUS parameters. The Med Diet was significantly associated with BUA ($\beta = 1.693$, 95%CI [0.508, 2.879]; $p = .006$). For PA, we only observed a trend toward significance between MPA and the BUA parameter ($p = 0.083$) adjusted by age and menopausal status.

Discussion

Identifying environmental factors associated with bone mass in FMS women could be a strategy for preventing osteoporosis in these patients. The present study was designed to test the relationships between body composition, adherence to the Med Diet, PA, and bone status in a population of FMS women. Overall, the results presented indicate that LM and adherence to the Med Diet are associated with calcaneal QUS parameters, supporting the hypothesis that LM and the Med Diet are predictors of bone mass in FMS women. The relative contributions of the two body weight components, FM and LM, to bone mass variations are controversial (Chen et al., 2015). Our data suggests that only LM is significantly associated with the BUA and SI parameters after adjusting for confounding factors (age and menopause status) in FMS women. Therefore, the data from this study suggests that promoting training programs for FMS women, to increase LM, could be an effective preventive strategy for reducing the risk of osteoporosis in later life. Similarly to our findings, previous studies conducted on healthy premenopausal and postmenopausal women have suggested that LM, not FM, is related to bone status (Khosla, Atkinson, Riggs, & Melton, 1996; Moon, 2014). Researchers in a two-year prospective study also concluded that LM is the best determinant of BMD in a population of postmenopausal women (Chen et al., 2015). Interestingly, a meta-analysis comparing the magnitude of association between LM, FM, and bone mass concluded that LM exerts the greatest effect on BMD (Ho-Pham,

Nguyen, & Nguyen, 2014). The mechanostat theory proposes that incremental overall weight increases can both increase bone mass and alter bone architecture by inducing an adaptive response to increased mechanical loads (Iwaniec & Turner, 2016). The relevance of LM as a contributor to weight-dependent skeletal loading has been established, since muscles are attached to bones via tendons, and larger and more powerful muscles can deliver greater mechanical loads directly onto bone (Iwaniec & Turner, 2016).

Our findings indicate that the Med Diet is associated with the BUA parameter, highlighting the potential benefits of good adherence to this diet with regards to improved bone health in FMS women. The significant associations identified in this study are consistent with those in other studies (Chen et al., 2015; Rivas et al., 2013). The European Prospective Investigation into Cancer and nutrition (EPIC) study reported that increased adherence to the Med Diet was associated with a 7% decrease in hip fracture incidence per 1-unit increase in Med Diet score in a large cohort of European adults (Benetou et al., 2013). A similar observation was made in a recent systematic review and meta-analysis of observational studies (Malmir, Saneei, Larijani, & Esmailzadeh, 2018). Additionally, Rivas et al. (2013), found significant linear trends between the Med Diet and calcaneus BMD in premenopausal and postmenopausal Spanish women. These studies therefore support the suggestion that a varied diet based on Med Diet patterns may be beneficial in preventing osteoporosis. However, this work demonstrates, for the first time, that good adherence to the Med Diet is also a modifiable environmental factor promoting bone health in FMS women.

PA has been proposed as an important modifiable factor related to osteoporosis (Moreira et al., 2014). Though, in this study, we found a lack of association between PA variables and calcaneal bone mass in FMS patients. These contradictory results might be explained by differences in the study cohorts, since the previous studies were conducted on general populations of older adults, and our study cohort comprised a well-characterized

sample of FMS women. Thus, it could be hypothesized that in FMS women, other modifiable factors, such as LM and dietary patterns, might play more determinant roles in bone health. However, it is also important to note that in this study the assessment of PA was estimated using a self-reported questionnaire. For this reason, further studies involving direct measurements of PA are required to validate our preliminary results.

This study has some limitations that should be noted. Firstly, due to its cross-sectional design we cannot infer causality. Further studies are needed to investigate the mechanisms by which LM and good adherence to the Med Diet could determine higher or lower levels of bone mass in FMS women. As we stated previously, there are also limitations inherent to the assessment of PA using a self-administered questionnaire, as this may be prone to overestimation. Finally, we did not examine serum vitamin D status, and vitamin D levels have also been linked to bone mass. Despite these limitations, this study provides new information on the status of bone mass assessed through ultrasonography, as well as its association with environmental risk factors in a well-characterized population of FMS women.

Conclusion

In conclusion, this study is especially relevant as it provides novel data on bone strength as indicated by QUS measurements in FMS patients. Additionally, we found that LM and the Med Diet were consistently associated with calcaneal QUS parameters, supporting the suggestion that LM and adherence to the Med Diet play determinant roles in bone health in FMS women. Based on this, training programs for maximizing LM and strategies for promoting good adherence to the Med Diet should be considered, in order to prevent the development of osteoporosis in FMS women. Since nurses are involved in implementing preventive programs, their role in promoting adherence to the Med Diet and maximizing LM in FMS sufferers should help reduce the impact of osteoporosis.

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Table 1

Descriptive characteristics of women with FMS

Cases (n = 95)	
Age (years)	55.76±7.96
Height (cm)	158.76±5.91
Weight (kg)	71.94±13.32
BMI (kg/m ²)	29.00±6.32
Previous fracture	29 (36.7)
Postmenopausal women	70 (79.5%)
Body composition	
PFM (%)	37.11±7.26
FM (kg)	27.57±10.24
LM (kg)	45.09±3.93
Physical activity	
MPA (MET/min)	356.77±1424.97
VPA (MET/min)	221.18±652.44
Total PA (MET/min)	1144.09±1664.68
Med Diet	9.37±2.04
Calcaneal QUS	
BUA (dB/MHz)	105.26±12.48
SOS (m/s)	1558.25±38.01
SI (%)	87.91±16.87

Note. BMI= Body Mass Index; FM= Fat mass; PFM= Percentage of fat mass; LM= Lean mass; MPA= Moderate Physical Activity; VPA= Vigorous Physical Activity; Med Diet= Mediterranean Diet; BUA= Broadband Ultrasound Attenuation; SOS= Speed of Sound; SI= Stiffness Index.

^aNumerical variables are shown as mean ± SD (Standard Deviation) and nominal variables as frequencies (%).

Table 2

Body Composition, Med Diet, PA, and Calcaneal QUS

	Calcaneal QUS					
	BUA (dB/MHz)		SOS (m/s)		SI (%)	
	β [95%CI]	<i>p</i> value	β [95%CI]	<i>p</i> value	β [95%CI]	<i>p</i> value
Body composition						
BMI (kg/m ²)	0.097 [-0.199, 0.566]	.343	-0.001 [-1.250, 1.240]	.993	0.094 [-0.276, 0.753]	.359
PFM (%)	-0.026 [-0.391, 0.305]	.806	0.010 [-1.077, 1.177]	.930	0.057 [-0.340, 0.595]	.589
FM (kg)	-0.031 [-0.277, 0.204]	.765	-0.012 [-0.821, 0.737]	.915	0.028 [-0.279, 0.367]	.785
LM (kg)	0.211 [0.046, 1.259]	.035	0.110 [-0.961, 3.049]	.303	0.201 [0.019, 1.654]	.045
Med Diet	1.693 [0.508, 2.879]	.006	1.406 [-3.002, 5.815]	.527	1.292 [-0.552, 3.137]	.167
Physical Activity						
MPA (MET/min)	-0.174 [-0.003, 0.000]	.083	0.162 [-0.001, 0.009]	.126	0.135 [-0.001, 0.004]	.181
VPA (MET/min)	-0.031 [-0.004, 0.003]	.761	0.026 [-0.010, 0.013]	.809	0.008 [-0.005, 0.005]	.938
Total PA (MET/min)	-0.161 [-0.003, 0.000]	.110	0.136 [-0.002, 0.007]	.203	0.112 [-0.001, 0.003]	.270

Note. QUS= Quantitative Ultrasound; BMI= Body Mass Index; FM= Fat mass; PFM= Percentage of fat mass; LM= Lean mass; MPA= Moderate Physical Activity; VPA= Vigorous Physical Activity; Med Diet= Mediterranean Diet; BUA= Broadband Ultrasound Attenuation; SOS= Speed of Sound; SI= Stiffness Index.

^aLinear regression models were adjusted for age and menopausal state