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HIGH FREQUENCY OF FRAGILITY FRACTURES IN POSTMENOPAUSAL WOMEN WITH DYSMOBILITY SYNDROME: A SINGLE-CENTER CROSS-SECTIONAL STUDY

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Abstract

Purpose: To assess the frequency of dysmobility syndrome (DS) in a group of postmenopausal women, to determine the frequency of fragility fractures in these patients, and to compare the frequency of fragility fractures and other clinical, biochemical, densitometric, and muscle health characteristics between patients with and without DS.

Methods: Postmenopausal women aged ≥ 60 years were invited to participate in a muscle health study program in our bone clinic. The diagnosis of DS was considered when at least three of the following factors were present: osteoporosis, ≥1 fall in the preceding year, low muscle mass, slow gait speed, low grip strength, and high-fat mass. The cohort was divided into patients with DS and without DS.

Results: The mean age in the study cohort (n = 250) was 70.36± 7.72 years. DS was diagnosed in 77 patients (30.8 %). A history of falls in the preceding year and the prevalence of fragility fractures were more frequent in patients with DS in comparison with the control group (60% vs. 19%, p <0.001 and 42% vs 17%, p <0.001, respectively). Furthermore, the history of fragility fractures was significantly associated with the presence of DS (OR 4.92, 95% CI 2.3-10.4, p <0.001).

Discussion: A significant association was found between DS and a history of fragility fractures. Although this new concept needs further investigation, it seems that the identification of various compartments affected by the aging process results in an opportunity to better predict major adverse events in the elderly.

Keywords: Dysmobility syndrome. fragility fractures, risk of falls, osteoporosis

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ALTA FRECUENCIA DE FRACTURAS POR FRAGILIDAD EN MUJERES POSTMENOPÁUSICAS CON SÍNDROME DE DISMOVILIDAD: ESTUDIO DE DISEÑO TRANSVERSAL DE UN SOLO CENTRO

Resumen

Propósito: Evaluar la frecuencia del síndrome de dismovilidad (SD) en un grupo de mujeres posmenopáusicas, determinar la frecuencia de fracturas por fragilidad en estas pacientes y comparar la frecuencia de fracturas por fragilidad y otras características clínicas, bioquímicas, densitométricas y de salud muscular entre pacientes con y sin SD.

Métodos: Se invitó a mujeres posmenopáusicas de edad ≥60 años a participar en un programa de estudio de la salud muscular en nuestra clínica ósea. Se consideró el diagnóstico de SD cuando estaban presentes al menos tres de los siguientes factores: osteoporosis, ≥1 caída en el año anterior, baja masa muscular, velocidad de marcha lenta, baja fuerza de prensión y masa grasa elevada. La cohorte se dividió en pacientes con SD y sin SD.

Resultados: La edad media de la cohorte de estudio (n = 250) fue de 70,36± 7,72 años. Se diagnosticó SD en 77 pacientes (30,8%). Los antecedentes de caídas en el año anterior y la prevalencia de fracturas por fragilidad fueron más frecuentes en los pacientes con SD en comparación con el grupo de control (60% frente a 19%, p <0,001 y 42% frente a 17%, p <0,001, respectivamente). Además, el antecedente de fracturas por fragilidad se asoció significativamente con la presencia de SD (OR 4,92; IC 95% 2,3-10,4; p <0,001).

Discusión: Se encontró una asociación significativa entre el SD y los antecedentes de fracturas por fragilidad. Aunque este nuevo concepto requiere más investigación, parece que la identificación de diversos compartimentos afectados por el proceso de envejecimiento brinda la oportunidad de predecir mejor los principales acontecimientos adversos en los ancianos.

Palabras clave: *Síndrome de dismovilidad. fracturas por fragilidad, riesgo de caídas, osteoporosis.*

Introduction

Advancing age is accompanied by a decrease in the function of various systems, including the musculoskeletal system.[1-4] The term "sarcopenia" was proposed in 1989 to describe the loss of muscle mass that occurs with age.[5] Later, this concept evolved to include other parameters such as muscle quality and function.[6-10] This multifactorial and progressive phenomenon is associated with increased morbidity and mortality, falls, fractures, disability, and hospitalization.[3,11-15]

Additionally, the bone tissue is also affected by aging, resulting in an increased risk of fracture.[16-18] Multiple studies identify a bidirectional relationship between bone and muscle tissue ("the muscle-bone unit") which involves mechanical and biochemical factors.[19-24]

In 2013, Binkley et al. described the term "dysmobility syndrome" (DS), which includes osteoporosis, falls in the preceding year, obesity/high-fat mass, low lean mass, slow gait speed, and low grip strength. DS was considered when three or more of these factors were present.[24] This new and extended concept, which includes bone, muscle, and adiposity, may be a better predictor for adverse events in the elderly.[24]

However, there is a lack of consensus on the parameters to be evaluated in DS, and the cut–off points to be used, representing a need for further research and validation in different populations. Therefore, in this study

we aimed: i) to assess the frequency of DS in a group of postmenopausal women referred to our institution. ii) to determine the prevalence of fragility fractures in these patients, and iii) to compare the prevalence of fragility fractures and other clinical, densitometric, and muscle health characteristics between patients with and without DS.

Methods

This is a single-center cross-sectional study analyzing data from medical records of post-menopausal women aged ≥ 60 years who were invited to participate in a muscle health study program in our bone clinic. Patients using walking aids, those with neuromuscular illnesses who were not able to perform the physical performance tests, and patients with chronic conditions associated with low muscular mass (history of cancer, renal failure, chronic obstructive pulmonary disease, and insulin-dependent diabetes) were excluded from the study. Informed consent was obtained from all individual participants included.

The following parameters were collected at our institution through medical records and/or questionnaires: age, regular physical activity, risk factors for osteoporosis, history of fragility fractures (wrist, spine, hip, and humerus) assessed by X-rays, and 25-hydroxyvitamin D values in the previous 6 months. Weight and height were determined using a mechanical scale and a wall-mounted height rod.

We evaluated the following predicting factors of DS:

Bone mineral density: BMD was measured by dual-energy X-ray absorptiometry (DXA) with GE Lunar Prodigy equipment (General Electric Lunar, Madison, WI, USA) at the lumbar spine (LS) (L1-L4), femoral neck (FN), and total hip (TH). Diagnosis of osteoporosis was based on a T score of ≤-2.5 at any region, using the manufacturer's database (USA, Lunar).

History of falls: At least one fall in the preceding year, assessed by self-report.

Lean mass: Lean mass was assessed by DXA total body scan. The body composition software analyzes total lean mass (kg), arms and legs lean mass (kg), appendicular skeletal muscle mass (ASM) (the sum of the lean mass of the 4 limbs), and appendicular skeletal mass index (ASMI) (ASM/height^2) (kg/m^2). Low muscle mass was considered with an ASMI <5.5 kg/m^2 or an ASM <15 kg, as proposed by the European Working Group on Sarcopenia in Older People 2 (EWGSOP2).[14]

Gait speed: Gait speed was defined as the time it takes to walk in a straight line over a flat surface at a comfortable speed. Low gait speed was defined using a value ≤ 0.8 m/s as proposed by EWGSOP2.[14]

Muscle strength: Muscle strength was evaluated by hand-grip strength assessment (Jamar Hydraulic Hand Dynamometer, USA). The best result of three trials performed in both hands was recorded. Low strength was defined as <20 kg as proposed by Binkley et al.[24]

Fat mass: Total fat mass was assessed by body composition derived from DXA. High-fat mass was defined as > 40 %.[25]

We considered patients with DS those who presented with at least 3 of the following factors: osteoporosis, one or more falls in the preceding year, low muscle mass, slow gait speed, low grip strength, and high-fat mass. We divided the study population into patients with DS and without DS (control group).

Statistical analysis

Quantitative data were presented as the mean ± standard deviation (SD), and categorical data were presented as frequencies and percentages (%). The normal distribution of continuous data was assessed using the Shapiro-Wilks test. To compare quantitative data, the Student's t-test was used for parametric variables and the Wilcoxon Rank Sum Test for non-parametric variables. Comparisons between qualitative variables were assessed using a chi-squared test. A

p-value <0.05 was considered statistically significant. Statistical analysis was performed using STATISTICS 7.0 Copyright ©1995, 2000 Analytical software (Statsoft).

Results

The basal characteristics of the 250 women included in the study are presented in Table 1. The mean age of the cohort was 70.36 ± 7.72 years. DS was diagnosed in 77 patients (30.8%). Out of these patients, 55% presented with 3 factors of DS, 34% with 4, 6% had 5 and 5% presented with the 6 clinical factors. The relative frequency of each factor is detailed in Table 2. The frequency of prevalent fragility fractures in patients with DS was 42%.

Table 1. General characteristics of the total cohort (n=250).

Age (years)	70.36 ± 7.72
Weight (kg)	61.80 ± 11.02
Height (m)	1.57 ± 0.06
BMI (kg/m^2)	25.08 ± 4.38
Lumbar spine	
BMD (g/cm^2)	0.963 ± 0.162
T-score	-2.0 ± 1.3
Femoral neck	
BMD (g/cm^2)	0.755 ± 0.096
T-score	-2.0 ± 0.8
Total hip	
BMD (g/cm^2)	0.792 ± 0.108
T-score	-1.8 ± 0.9
Fat mass (%)	38.66 ± 7.88
25 hydroxyvitamin D (ng/ml)	31.68 ± 11.26
ASMI (kg/m^2)	5.85 ± 0.66
MM in arms (kg)	3.376 ± 0.551
MM in legs (kg)	11.142 ± 1.586
Hand grip (kg)	22 ± 4
Sit-to-stand test (s)	12.4 ± 3.9
Gait speed test (m/s)	1.0 ± 0.2

BMI (body mass index), LS (lumbar spine), FN (femoral neck), TH (total hip), ASMI: (appendicular skeletal mass index), MM (muscle mass)
Data presented as mean and SD

In Table 3, we compare the demographic, clinical, bone densitometry, vitamin D, and muscle health data between patients with and without DS. Women with DS were older (p <0.001), had shorter stature (p <0.001), and presented lower FN (p =0.007) and TH BMD (p =0.046) than the group without DS. Regarding body composition, women with DS had higher fat mass and lower lean mass. A history of falls in the preceding year and the frequency of fragility fractures were more frequent in patients with DS in comparison with the control group (60% vs. 19%, p <0.001 and 42% vs. 17%, p <0.001, respectively). There were no statistical differences regarding vitamin D levels and reported physical activity (Table 3).

In the multivariate analysis, the history of fragility fractures was significantly associated with the presence of DS (Odds ratio 4.92, 95% confidence interval: 2.3-10.4, p <0.001) (Table 4).

Discussion

In this cohort of postmenopausal women over 60 years attending our bone clinic, DS was frequent, present in 30.8%. According to a systematic review by Hill et al., the prevalence of DS varied from 22 to 34%.[26] Besides, an increased prevalence of DS has been reported with increasing age.[24,26,27] Similar to our study, Ribeiro dos Santos et al found a prevalence of 27%, in a cohort of 375 subjects aged ≥60 years (70% women, recruited from two Public Health Services and from the general population).[29] On the other hand, population-based studies in elderly subjects reported a lower prevalence (between 5.1 and 20%).[25,26]

Importantly, almost half of the women with DS from our research group had suffered a fragility fracture in the preceding year.

Table 2. Frequency of each factor from the dysmobility syndrome in our cohort.

Factor	Frequency (n, %)	
	Within the total cohort (n=250)	Within patients with DS (n=77)
Osteoporosis (T-score ≤ -2.5)	111 (44.4%)	44 (57.1%)
High fat mass (> 40%)	103 (41.2%)	44 (57.1%)
Falls in the preceding year	78 (31.2%)	45 (58.4%)
Low lean mass (ASMI < 5.5 kg/m^2 or an ASM <15 kg)	74 (29.6%)	39 (50.6%)
Low grip strength (< 20 kg)	67 (26.8%)	47 (61.0%)
Slow gait speed (≤ 0.8 m/s)	56 (22.4%)	44 (57.1%)

ASMI: (appendicular skeletal mass index), ASM: (appendicular skeletal mass)

Table 3. Comparison of demographic, clinical, bone densitometry, laboratory, and muscle health data between patients with and without dysmobility syndrome.

	Patients with dysmobility syndrome (n = 77)	Patients without dysmobility syndrome (n = 173)	p
Age (y)	73.26 ± 8.47	69.17 ± 7.08	<0.001
Weight (kg)	61.11 ± 11.36	62.09 ± 10.89	0.484
Height (mts)	1.54 ± 0.05	1.58 ± 0.06	<0.001
BMI (kg/m^2)	25.63 ± 4.73	24.85 ± 4.22	0.168
BMD			
Lumbar spine (g/cm^2)	0.958 ± 0.208	0.964 ± 0.139	0.283
Femoral neck (g/cm^2)	0.728 ± 0.100	0.766 ± 0.093	0.007
Total hip (g/cm2)	0.769 ± 0.112	0.801 ± 0.105	0.046
Fat mass (%)	40.74 ± 7.80	37.77 ± 7.77	<0.001
Vitamin D (mg/ml)	30.46 ± 12.91	32.21 ± 10.49	0.175
ASMI (kg/m^2)	5.60 ± 0.70	5.95 ± 0.62	<0.001
Arms MM (kg)	3.117 ± 0.503	3.484 ± 0.535	<0.001
Legs MM (kg)	10.258 ± 1.284	11.509 ± 1.557	<0.001
Hand grip (Kg)	19 ± 4	24 ± 4	<0.001
Sit-stand test (s)	14.6 ± 5.0	11.5± 2.9	<0.001
Gait speed (m/s)	0.9 ± 0.2	1.1 ± 0.2	<0.001
History of falls (previous year)	60% (44)	19% (34)	<0.001
Fragility fractures	42% (31)	17% (31)	<0.001

BMI (body mass index), LS (lumbar spine), FN (femoral neck), TH (total hip), ASMI: (appendicular skeletal mass index), MM (muscle mass)
Data presented as mean and SD

Table 4. Multivariate analysis for factors predicting history of fragility fractures.

	OR	95% CI	P
Age	1.01	0.9-1.1	0.752
Dysmobility syndrome	4.96	2.3-10.4	<0.001
Falls in the preceding year	1.14	0.4-2.2	0.735
Osteoporosis	1.43	0.7-3.0	0.213

OR (Odds ratio), CI (Confidence interval)

Moreover, the presence of DS was significantly associated with a history of fragility fractures, meaning that the current classification of DS seems accurate to help us determine the risk of this serious adverse health outcomes in the elderly.[24,29,30] The fracture frequency in our cohort seems to be higher in comparison to other studies.[24,26,28] The group of Binkley et al. reported that in patients with DS, 30% had had a previous fragility fracture.[24] Burgueno-Aguilar et al., in a study conducted in Mexico, reported that 30% of women who met the DS criteria had a history of fragility fractures.[31] Finally, in an elderly community-based population from Korea, the prevalence of fragility fractures in patients with DS was 25%.[27]

Considering that postmenopausal women showed higher frequencies of fragility fractures in comparison to men and younger women, our research focuses on this population group.[24,26] However, among men enrolled in the Osteoporotic Fractures in Men (MrOS) prospective cohort study, the presence of DS was independently associated with a higher risk of major osteoporotic fracture during a 14-year follow-up (Hazard ratio 3.45, 95% CI: 2.78-4.29). Moreover, when the DS criteria were combined with the Fracture Risk Assessment Tool (FRAX) score, it resulted in a better prediction of major osteoporotic fractures in men.[32]

In our group, when compared with women who did not have DS, patients with DS presented less muscle mass in upper and lower limbs, lower strength, and physical performance (sit-stand and walk). In line with this observation, more than half of the women with DS had a higher frequency of falls during the previous year. Other studies have linked DS with falls.[29-31] Consistent with our study, Burgueno-Aguilar et al. reported a frequency of falls of around 60%.[32] In the above-mentioned study by Binkley et al, 36% of older adults with DS had had a fall in the preceding year.[24] In clinical practice, recognizing people at risk of falling is crucial, since falls are an independent risk factor for fragility fractures.[33] What is more, falls represent a significant cause of morbidity and mortality in the elderly.[34]

Additionally, the introduction of adipose tissue in the diagnostic criteria for DS collaborates with the detection of those individuals at risk. A higher fat mass is associated with lower muscle quality, and it predicts an accelerated loss of lean mass.[35,36] Therefore, it is important to highlight that these criteria recently proposed by Binkley identify those individuals at risk of fragility fractures and other comorbidities associated with old age.[24] From a clinician's point of view, this syndrome reminds us of the importance of having a broader view, integrating different systems that, mistakenly, have in the past been considered separately when evaluating these patients.

Our investigation has several limitations, one being the small number of subjects and lack of biochemical studies. Second, given the lack of national reference values, we used

the cut-off points proposed in the literature. Additionally, the patients in our cohort were evaluated at a reference center and this might overestimate the real prevalence of DS (referral bias). Indeed, the prevalence of DS seems to be lower in community-based studies.[27,29] It should be noted that the diagnosis of DS does not have a defined methodology. Indeed, in the original publication, Binkley et al. established the importance of comparing the cut-off points and approaches with other studies to define the best-fit factors capable of predicting adverse musculoskeletal outcomes in older adults.[24] This cohort was previously evaluated using only the concepts of sarcopenia without considering other parameters.[3]

These findings may encourage comprehensive evaluation of patients by adding the importance of fat compartment and previous falls.

In conclusion, 30% of our patients complied with the definition of DS. A significant association between DS and a history of fragility fractures was described. Although this new concept needs further investigation, it seems that the identification of various compartments affected by the aging process (bone, muscle, and adipose tissue) results in a better prediction of fracture prevalence.

In the future, we strongly believe that DS criteria would be a useful tool for physicians aiming to identify patients at risk and therefore reduce morbidity and mortality in these patients.

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Ethics declarations

Conflicts of interest: Rubén Abdala, Mariana Gonzalez Pernas, Fernando Jerkovich, and María Belén Zanchetta declare that they have no conflict of interest regarding this publication.

Ethics approval: The study was in accordance with the ethical standards of the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication: Written informed consent was obtained from all the patients included in this study.

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