PREVALENCE OF CONCOMITANT BONE AND MUSCLE WASTING IN ELDERLY WOMEN FROM THE SARCOPHAGE COHORT: PRELIMINARY RESULTS

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Abstract: *Background:* Recent studies suggest that bone and muscle wasting are closely interconnected. *Objective:* The aim was of this study is to assess the prevalence of osteoporosis in a population of women diagnosed with sarcopenia. *Participants, setting and design:* We analyzed cross-sectional data of women, aged 65 years and above, for whom bone mineral density was available at the time of inclusion in the SarcoPhAge (Sarcopenia and Physical impairment with advancing Age) cohort, an ongoing prospective study with the aim to assess consequences of sarcopenia. *Measurements:* Muscle strength was evaluated with a hydraulic hand-dynamometer, appendicular lean mass and bone mineral density by Dual-Energy X-Ray Absorptiometry and physical performance by the Short Physical Performance Battery test (SPPB). Sarcopenia was diagnosed according to the European Working Group on Sarcopenia in Older People definition, i.e. a low muscle mass plus either low muscle strength or low physical performance. A bone mineral density T-score equal to or below -2.5SD at the lumbar spine, at the total hip or at the femoral neck was used to define osteoporosis (World Health Organization definition). *Results:* A total of 126 women aged 74.38±6.32 years were included. Among them, 26 were assessed with sarcopenia (20.6%) and 34 (27.0%) with osteoporosis. There were more osteoporotic women among sarcopenic subjects (46.1%) than among non-sarcopenic subjects (22.0%) (p-value=0.011). A significant lower appendicular lean mass index was observed in osteoporotic women (p-value=0.025). We also observed, in osteoporotic subjects, a lower muscle strength (p-value=0.023). Numerical values of bone mineral density were lower in the sarcopenic population but the differences did not reach the level of statistical significance. *Conclusion:* Our study demonstrated that muscle mass and strength are lower in patients with osteoporosis. Prospective changes in bone and muscle mass will be investigated during the follow-up of our cohort.

Key words: Osteoporosis; sarcopenia; muscle-bone unit; bone mineral density; lean mass .

Introduction

The aging process has an impact on the body composition of individuals. With ageing, a wasting of bone and muscle is observed. Regarding bone health, a reduction in bone mineral density (BMD) and a deterioration of bone microarchitecture are observed. The World Health Organization (WHO) has identified thresholds (1) at which the decline in bone density is considered as pathological and is then called "osteoporosis". Concerning muscle health, a progressive decline in the size and number of muscle fibres is also observed throughout the life. According to the European Working Group on Sarcopenia in Older People (EWGSOP) (2), this loss of skeletal muscle mass is considered abnormal from a pre-defined threshold and, when combined with the impairment of other criteria (i.e. loss of muscle strength and/or loss of physical function), constitutes the geriatric syndrome called "sarcopenia".

The awareness of clinical significance of osteoporosis and sarcopenia, being both major components of frailty in the elderly, is constantly increasing. They represent a serious public health burden and extensive social costs (3, 4). The two states generate a greater exposure to morbidity events, i.e. injurious falls and fractures, reduced ambulatory capacity, physical disability, hospitalization, loss of independence, ultimately mortality and impaired quality of life (5).

There may be common pathways regarding bone and muscle wasting (6). Indeed, there is now growing evidence of positive relationships between bone and muscle metabolism which may be considered as a "muscle-bone unit" (7). Several mechanisms can explain these interrelationships as endocrine (7), genetic (8), developmental (9) factors but also as biological and mechanical effects. Consequently, the two tissues seem to have a shared pathogenesis and dysfunctions of this "muscle-bone unit" may lead to a particular pathology, affecting both structures and for which the term "sarco-osteopenia" has been proposed (10).

Previous studies have disclosed that a decline in muscle mass is related to decline in bone mass but results among studies are not homogenous (11-13).

Our objective was to assess the prevalence of osteoporosis in a population of elderly women diagnosed with sarcopenia, as a part of the SarcoPhAge (Sarcopenia and Physical impairment

1

with advancing Age) study (14).

Methods

Subjects

The SarcoPhAge study is an ongoing prospective cohort following community-dwelling elderly subjects and developed in 2013, in Liège, Belgium. The objective of this study is to assess health and functional consequences of sarcopenia. The recruitment of subjects who volunteered to participate took place at the end of physiotherapist, rheumatology and geriatric consultations but also by means of press advertisement. The baseline data of the 534 subjects have recently been published (14). For this ancillary study, looking at the prevalence of osteoporosis in patients with or without sarcopenia, our population consisted of women aged 65 years and older and for whom BMD values were available at the time of inclusion in the SarcoPhAge cohort (between June 2013 and June 2014). Finally, 126 Caucasian women were included in this analysis. Nevertheless, it should be noted that this subgroup of 126 women is not representative of all individuals included in our cohort. Indeed, even if the mean age did not differ between the group of 126 women and the rest of the cohort (74.3±6.32 years versus 73.5±6.12 years, p-value=0.641), we observed that the body mass index (BMI) was significantly lower among women on which this analysis was carried out, compared to individuals of the SarcoPhAge cohort (respectively, 25.3±4.14 kg/m² versus 26.9±1.37 kg/m², p-value = 0.040).

Ethics statement

The study protocol received the approval of the Ethics Committee of the University Teaching Hospital of Liège under the reference 2012-277. All participants were informed about the aims of our study and gave their written consent.

Parameters investigated

Clinical characteristics

Medical history, data regarding current alcohol and tobacco consumption were collected. Weight was recorded to the nearest 0.1 kg, using a digital scale with subjects slightly clothed. Height was measured without shoes, to the nearest 0.1cm. Body mass Index (BMI) was determined as weight (kg) divided by height squared (m²). We also used the Mini-Mental State Examination (MMSE) (15) to assess the cognitive function. Physical performance and risk of falls have also been measured using the Time Up and Go (TUG) test (16).

Diagnosis of sarcopenia

A diagnosis of sarcopenia was established on the basis of the criteria proposed by the EWGSOP (2) and thus involved three different investigations:
- Evaluation of muscle mass: an analysis of body composition was performed by means of Dual Energy X-ray Absorptiometry (DEXA) (Hologic Discovery A, USA) using the APEX software v3.1. The device was daily calibrated with a spine phantom in accordance with manufacturer's instructions. For this evaluation, all women wore very light cotton clothing without any buttons and they had to remove their jewellery and other metal objects. Appendicular skeletal muscle mass (ASM) was calculated as the sum of both arms and legs skeletal muscle mass. By dividing this ASM by the height squared, we obtained a skeletal muscle mass index (SMI). To define a weak SMI in women, we used the cut-off of 5.50 kg/m², threshold defined by Baumgartner et al. (17) and also proposed by the EWGSOP (2).
- Evaluation of hand grip strength: muscle strength was measured by using a hydraulic hand-dynamometer (Saehan Corporation, MSD Europe Bvba, Belgium), calibrate at the beginning of the research for 10, 40 and 90kg. Subjects had to squeeze the device as hard as possible 3 times with each hand, dominant and non-dominant. For our analysis, we used the highest results of the six measurements (18). In women, the proposed cut-off of 20kg is used to diagnose sarcopenia (2).
- Evaluation of physical performance: an assessment of physical performance was conducted through the Short Physical Performance Battery (SPPB) test (/12 points) (19). This evaluation consisted of three parts: balance, 4-meter gait speed and chair stand tests. A maximum of four points was attributed for each test. As recommended, the threshold of 8 points or less out of a maximum 12 points is employed for the diagnosis of sarcopenia (22).

In conclusion, using the cut-off limits proposed by the EWGSOP (2), women with a low SMI (<5.50kg/m²) plus either a low muscle strength (<20kg) or a low physical performance (SPPB <8 points) were considered sarcopenic.

Diagnosis of osteoporosis

BMD measurements were performed at three sites: lumbar spine (L2-L4), total hip and femoral neck. We carried out this evaluation using a DEXA device (Hologic QDR Delphi (S/N) 70249). A T-score equal to or below –2.5 standard deviation (SD) at the lumbar spine or at the hip (i.e. total hip or femoral neck) was used to define osteoporosis (1).

Statistical analysis

All statistical analyses were performed by means of the software Statistica 12. Continuous and normally distributed variables were reported as mean ± SD. Normality of the different data was tested using the Shapiro-Wilk test. Regarding qualitative variables, results were expressed in terms of absolute (N) and relative frequency (%). Characteristics differences between two groups of patients were tested by Student's t test for continuous and normally distributed parameters and by the Chi-square test for qualitative data. The

Chi-square test for independence was also applied to compare the prevalence of osteoporosis in women with or without sarcopenia. Pearson's correlations were used to analyse the relationship between SMI, grip strength, SPPB test and the three BMD values. All values of p <0.05 were considered as statistically significant.

Results

A total of 126 women aged 74.3±6.32 years with BMD assessments at baseline were included. The mean BMI was 25.3±4.14 kg/m² and MMSE mean results amounted to 27.5±2.67 points. The majority of our population had two or more comorbidities. Characteristics of the study population are summarized in Table 1.

Table 1
Summary of participant characteristics

Variables	N	%	Mean	SD
Age (years)	106		74.3	6.32
Weight (kg)	106		62.1	10.6
Height (cm)	106		156.8	6.69
BMI (kg/m²)	106		25.3	4.14
Current smoking				
Yes	11	8.73		
Current alcohol consumption				
Yes	55	43.6		
Two or more co-morbidities				
Yes	115	91.3		
MMSE (/30 points)	106		27.5	2.67
TUG (s)	106		12.0	5.74
SMI (kg/m²)	106		5.88	0.79
Muscle strength (kg)	106		20.9	6.50
SPPB (/12 points)	106		8.78	2.79
Lumbar spine BMD (g/cm²)	106		0.958	0.189
Total hip BMD (g/cm²)	106		0.779	0.118
Femoral neck BMD (g/cm²)	106		0.674	0.103

BMI: Body Mass Index; MMSE: Mini Mental State Examination; TUG: Timed Up and Go test; SMI: Skeletal Muscle Index; SPPB: Short Physical Performance Battery; BMD: Bone mineral density

Among women included in our study, 26 (20.6%) were diagnosed with sarcopenia, on the basis of the EWGSOP algorithm (2). According to the OMS definition (1), we diagnosed 34 (27.0%) women with osteoporosis. There were significantly more osteoporotic women among sarcopenic subjects (46.1%) than among non-sarcopenic subjects (22.0%) (p-value=0.011). In our sample, 12 women (9.52%) were diagnosed both sarcopenic and osteoporotic.

Comparisons of clinical characteristics between osteoporotic and non-osteoporotic women are developed in Table 2.

The osteoporotic group showed a significant lower SMI compared with the non-osteoporotic group (p-value=0.025). We also observed, in osteoporotic women, a significantly lower muscle strength (p-value=0.023) and a significantly lower physical performance (p-value=0.014). The physical performance, evaluated using the TUG test, was not significantly lower among women with osteoporosis. Moreover, results to the TUG test were significantly worse in the osteoporotic population (p-value<0.001).

When looking at the differences in baseline characteristics between sarcopenic and non-sarcopenic elderly women from our sample, we found that numerical values of BMD were lower in the sarcopenic versus non-sarcopenic populations but the differences are not statistically significant (p-value=0.522 for the lumbar spine, p-value=0.055 for the total hip and p-value=0.052 for the femoral neck; Table 3). Compared with non-sarcopenic subjects, we also observe that sarcopenic subjects had significant lower performance as assessed by the TUG test (p-value=0.049).

At last, we found that SMI is the only component of the definition of sarcopenia positively and significantly correlated with lumbar spine, total hip and femoral neck BMD (Table 4).

Figure 1
Criteria of eligibility for the present ancillary study
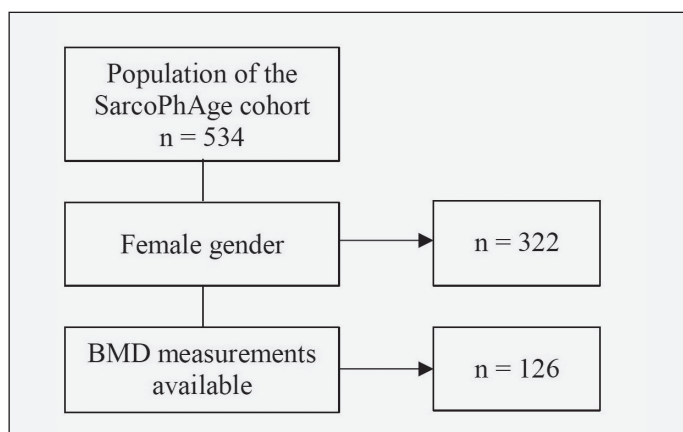
Discussion

The aim of this preliminary study was to investigate the prevalence of concomitant bone and muscle wasting in 106 elderly women aged over 65 years included in the SarcoPhAge study. This present analysis showed that osteoporosis more prevalent in elderly women presenting sarcopenia (46.1% versus 22.0%). Furthermore, we highlighted that muscle mass and muscle strength (i.e. two of the three components impaired in sarcopenia) were lower in elderly women presenting osteoporosis. This may suggest dysfunctions of a "muscle-bone unit", affecting both structures. Previous works have also

BONE AND MUSCLE WASTING: SARCOPHAGE STUDY

Table 2
Comparisons of clinical characteristics between osteoporotic and non-osteoporotic women

Variables	Osteoporotic women (n = 34)			Non-osteoporotic women (n=92)			P-value
	n	%	Mean ± SD	n	%	Mean ± SD	
Age (years)	34		75.6±6.18	92		73.9±6.33	0.164
Weight (kg)	34		57.0±9.40	92		64.0±10.4	<0.001
Height (cm)	34		154.5±7.63	92		157.6±6.14	0.019
BMI (kg/m²)	34		23.9±4.13	92		25.8±4.06	0.025
Current smoking							
Yes	3	8.82		8	8.69		0.982
Current alcohol consumption							
Yes	11	32.3		44	47.8		0.120
Two or more co-morbidities							
Yes	31	91.2		84	91.3		0.739
MMSE (/30 points)	34		26.8±3.07	92		27.7±2.48	0.121
TUG (s)	34		16.0±8.62	92		10.7±3.31	<0.001
SMI (kg/m²)	34		5.62±0.79	92		5.98±0.78	0.025
Muscle strength (kg)	34		18.7±6.61	92		21.7±6.31	0.023
SPPB (/12 points)	34		8.03±3.11	92		9.05±2.62	0.067

BMI: Body Mass Index; MMSE: Mini Mental State Examination; TUG: Timed Up and Go test; SMI: Skeletal Muscle Index; SPPB: Short Physical Performance Battery; BMD: Bone mineral density

Table 3
Comparisons of clinical characteristics between sarcopenic and non-sarcopenic women

Variables	Sarcopenic women (n = 26)			Non-sarcopenic women (n=100)			P-value
	n	%	Mean ± SD	n	%	Mean ± SD	
Age (years)	26		76.2±6.27	100		73.6±6.14	0.056
Weight (kg)	26		56.3±7.40	100		63.7±10.9	0.001
Height (cm)	26		156.6±6.76	100		156.8±6.75	0.931
BMI (kg/m²)	26		22.9±2.29	100		25.9±4.32	<0.001
Current smoking							
Yes	5	19.2		8	8.00		0.093
Current alcohol consumption							
Yes	11	42.3		42	42.0		0.977
Two or more co-morbidities							
Yes	25	96.1		90	90.0		0.322
MMSE (/30 points)	26		27.2±2.53	100		27.5±2.72	0.613
TUG (s)	26		13.7±5.60	100		10.1±5.84	0.049
Lumbar spine BMD (g/cm²)	26		0.937±0.196	100		0.964±0.189	0.522
Total hip BMD (g/cm²)	26		0.740±0.113	100		0.790±0.119	0.055
Femoral neck BMD (g/cm²)	26		0.638±0.121	100		0.682±0.095	0.052

BMI: Body Mass Index; MMSE: Mini Mental State Examination; TUG: Timed Up and Go test; SMI: Skeletal Muscle Index; SPPB: Short Physical Performance Battery; BMD: Bone mineral density

Table 4
Correlations between estimated variables

	Lumbar spine BMD	Total hip BMD	Femoral neck BMD
SMI	0.243*	0.331*	0.283*
Grip strength	0.172*	0.129*	0.181*
SPPB	0.039*	0.009*	0.082*

* P-value <0.05; SMI: Skeletal Muscle Index; SPPB: Short Physical Performance Battery; BMD: Bone mineral density

reported a relationship between sarcopenia and osteoporosis (11, 20, 21). These studies suggested that sarcopenia is significantly associated with osteoporosis but the magnitude of the relationship varies greatly from one study to another. This can be explained by the lack of uniformity in this type of analysis, particularly as regards the study population (e.g. differences in age, gender or racial group). But above all, the problem lies in the difficulty to define sarcopenia and tools used to assess it (22). The cut-points proposed by the EWGSOP (2) are currently quite consensual in Europe but, up to now, a universally and widely accepted way to define and diagnose sarcopenia does not exist (23). Moreover, two recent studies (24, 25) demonstrated that the prevalence of sarcopenia is device-dependent (e.g. whether it be diagnosed with DEXA or bio-electrical impedance analysis) and varies depending on definition and cut-offs employed. Undoubtedly, this could generate wide differences in the amount of observed prevalence of sarcopenia in the osteoporotic subjects.

Some population-based studies have also reported a positive correlation between lean body mass and BMD values (11, 26-28), some even suggesting that muscle mass is associated with BMD. These correlations may advocate that there is a simultaneous loss of muscle and bone mass which can lead to an increased risk of fractures and other morbid outcomes. Our study also showed that values of both tissues are positively correlated (according to the site where BMD is measured, coefficients varied between r=0.243 and r=0.331, p-value<0.05). However, these correlations remain weak, as highlighted by the results of the research of Miyakoshi et al., in 2012 (r=0.197 between SMI and lumbar spine BMD, r=0.274 between SMI and total hip BMD) (11). Hong et al., in 2015, also demonstrated the weakness of correlation between SMI and BMD in elderly women (29). However, some studies suggest that there is no significant correlation between lean and bone mass (12, 30). These discrepancies could probably be explained by numerous factors which can strongly influence observed relationships between lean mass and BMD such as the age, the gender, the racial group and the selection process of volunteers.

Strengths and limitations of our study should be addressed. The diagnosis of sarcopenia was performed according to EWGSOP definition (2) and this thus involved a complete investigation of the three impaired parameters in sarcopenia (i.e. muscle mass, muscle strength and physical performance),

and not only using the SMI. However, the moderate number of women included in our study, and therefore the lack of statistical power, do not allow us to drawn definitive conclusion regarding the relationship between osteoporosis and sarcopenia. Furthermore, the data presented are limited by the cross-sectional design of our analysis and must be interpreted with care. The results of our study could also be limited by external validity. Indeed, our sample, composed of voluntary subjects, is not fully representative of the overall population nor of the female elderly population. Moreover, we did not take into account a great variety of risk factors related to both pathologies such as physical activity level, nutrition status and vitamin D deficiency. However, the follow-up data of the SarcoPhAge cohort, for which more bone health assessments (i.e. BMD values, Trabecular Bone Score (TBS), Fracture Risk Assessment (FRAX), biochemical markers) are currently collected, will allow us to gather all these factors.

In conclusion, this preliminary study showed an association between sarcopenia and osteoporosis in a population of women of 65 and above. Prospective changes in age-related bone and muscle wasting will be investigated during the follow-up of the SarcoPhAge cohort.

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