Prevalence of sarcopenia and its association with osteoporosis in 313 older women following a hip fracture

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ABSTRACT

Changes in body composition, including a decrease in muscle and bone mass, accompany aging. Our aim was to assess the prevalence of sarcopenia and its association with osteoporosis in hip-fracture women. We performed a Dual-Energy X-Ray Absorptiometry (DXA) scan in 313 of 340 women, 20.9 ± 6.5 (mean ± S.D.) days after hip-fracture occurrence. To adjust appendicular lean mass for body size we divided it by height squared in each woman. A total of 180 of the 313 women (58%) were sarcopenic, whereas 230 (74%) were osteoporotic. After adjustment for age and interval between fracture and DXA scan we found a significant association between sarcopenia and osteoporosis (p = 0.026). For a sarcopenic woman the adjusted odds ratio (OR) for osteoporosis was 1.80 (95%CI = 1.07–3.02). Our data shows the high prevalence of sarcopenia and its significant association with osteoporosis in a large sample of hip-fracture women. Data supports a research approach on preventive and treatment strategies for osteoporosis and sarcopenia targeting both bone and muscle tissue. Furthermore, data should be considered when the economic burden of sarcopenia is estimated, given the high proportion of sarcopenic women with bone fragility.

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1. Introduction

Changes in body composition, including a decrease in both muscle and bone mass, accompany aging, as stated by several longitudinal studies (Frontera et al., 2000; Visser et al., 2003; Kanis et al., 2008a). The loss of muscle mass is thought to affect functional ability given the positive association between muscle mass and lower extremity function, and the negative association between muscle mass and risks of use of cane or walker, self-reported difficulties in activities of daily living and gait, and a history of falling (Baumgartner et al., 1998; Melton et al., 2000; Sternfeld et al., 2002; Castillo et al., 2003; Newman et al., 2003; Janssen et al., 2004a; Janssen, 2006). The loss of bone mass is a potent risk factor for fragility fractures that in turn cause loss of ability to function, dependency, and increased risk of institutionalization (Clinician's Guide, 2008; Di Monaco, 2008; Kanis et al., 2008a). Abnormally elevated muscle loss associated with qualitative changes of the muscle, resulting in loss of strength and function, characterizes sarcopenia (Baumgartner et al., 1998; Thompson, 2009). Abnormally high bone loss associated with qualitative alterations of the bone tissue resulting in bone fragility depicts osteoporosis (Clinician's Guide, 2008; Kanis et al., 2008a). The genesis of both sarcopenia and osteoporosis is multifactorial. Interestingly, several factors that play a role in the origin of osteoporosis are thought to contribute in causing sarcopenia. These putative causal factors include a decreased level of physical activity, hormonal changes (mainly low levels of sex steroids, growth hormone and insulin-like growth factor-I), a reduction in dietary protein, and catabolic stimuli from chronic inflammation (Kamel et al., 2002; Roubenoff, 2003; Evans, 2004; Kanis et al., 2008a; Pereira et al., 2009). Furthermore, a role of genetic factors in linking muscle and bone mass has been advocated (Karasis and Kiel, 2008). A common etiology may be responsible for a positive association between osteoporosis and sarcopenia, two conditions that may act together in the genesis of disability, imposing a relevant economic burden on healthcare services (Janssen et al., 2004b; Kanis et al., 2008a; Weigl et al., 2008).

Hip-fracture patients are frail subjects at high risk of disability: up to 25% of the patients who sustain a hip fracture may require long-term nursing home care and only 40% fully regain their pre-fracture level of independence (Clinician's Guide, 2008). Poor functional outcome contributes to the designation of hip fracture as a major public health problem in Western society (Kanis et al., 2008a). Osteoporosis causes bone fragility and is a well recognized major risk factor for hip fracture (Clinician's Guide, 2008; Kanis et al., 2008a). Sarcopenia increases the hazard of falling. Falls
enhance hip-fracture risk (Roubenoff and Hughes, 2000; Castillo et al., 2003) and may cause disability even after successful rehabilitation following hip-fracture occurrence (Di Monaco et al., 2009a). Prevalence of sarcopenia in hip-fracture subjects is largely unknown, and the association between sarcopenia and osteoporosis has not been defined in the patients who sustain a fracture of the hip. Our aim was to investigate the prevalence of sarcopenia and the association between sarcopenia and osteoporosis in a large sample of women who sustained a hip fracture.

2. Subjects and methods

2.1. Patients and setting

The study was performed in a city with about one-million inhabitants. We evaluated 340 white women consecutively admitted to our physical medicine and rehabilitation division because of their first hip fracture. We focused on white women because few non-white elderly women live in Italy. Seventeen of the 340 women we evaluated were excluded from our study because their hip fractures resulted from either major trauma or cancer affecting bone. The remaining 323 women sustained fractures that were either spontaneous or resulted from minimal trauma (trauma equal to or less than a fall from a standing position). Three of these 323 women were excluded from our study because they had hip or knee arthroplasties that could alter DXA assessment. The remaining 320 women were asked to undergo a DXA scan. Seven of these 320 women refused to undergo DXA assessment and were excluded from the study. The final study sample included 313 women who gave their informed consent to undergo DXA assessment. IRB approval was obtained for the study protocol.

2.2. Outcome measures

DXA (QDR 4500W, Hologic, Inc.) was used to measure whole and regional body composition. Appendicular lean mass (aLM) was calculated as the sum of lean mass (LM) in arms and legs. Because metal implants (prostheses and nails) were reported to affect the regional assessment of body composition with overestimation of LM (Madsen et al., 1999; Giangregorio and Webber, 2003), we performed a preliminary comparison between LM assessed at fractured legs and at contralateral legs. At a paired T-test, LM assessed at fractured legs (5423.4 ± 1015.4 g) was significantly higher than LM assessed at unfractured legs (4972.5 ± 872.5 g) in the 313 women (difference between sides 451.0 g; 95%CI = 393.2–508.7; p < 0.001). To avoid LM overestimation at fractured legs, we corrected aLM by substituting LM in unfractured leg for LM in fractured leg: corrected aLM = (LM in unfractured leg + 2) + LM in arms, as previously described (Di Monaco et al., 2006, 2007a).

LM cannot be interpreted without some indexing to body size: it is necessary to account for height when comparisons are performed among different subjects. Height was assessed by a standard method (with the patients standing) in the majority of the patients, whereas eleven women, who could not keep the standing position, were measured supine. We accounted for body size by dividing corrected aLM by height squared (aLM/ht²). Sarcopenia was defined according to normative data from the New Mexico Elder Health Study (Baumgartner et al., 1998) when aLM was less than two standard deviations below the mean of the young reference group. Also, we investigated time between fracture occurrence and DXA assessment, because rapid changes in body composition were observed after hip-fracture occurrence (Fox et al., 2000) and differences across the patients might be affected by the assessment time. We evaluated bone mineral density by DXA scan at the non-fractured hip. Two sites were assessed: femoral neck and total proximal femur. Osteoporosis was diagnosed when a T-score < −2.5 was found at least at one of the two femoral sites. The reference population for T-score calculation was from the Third National Health and Nutrition Examination Survey (NHANES III) (Kanis et al., 2008b).

2.3. Statistical analyses

We evaluated linear correlation between aLM/height² and BMD assessed both at femoral neck and total proximal femur by using a Pearson’s test. The association between sarcopenia and osteoporosis was investigated by a chi-square test for independence. A binary logistic regression test was used to adjust the association between sarcopenia and osteoporosis (dependent variable) for age and interval between fracture occurrence and DXA scan. The statistical package used was SPSS, version 14.

3. Results

Descriptive statistics for the 313 women are shown in Table 1. At a Pearson’s test, we found a significant positive correlation between aLM/height² and BMD assessed at both total proximal femur (r = 0.333; p < 0.001) and femoral neck (r = 0.257; p < 0.001), as shown in Fig. 1. A total of 180 of the 313 women (i.e., 58%) were sarcopenic, whereas 230 (i.e., 73%) were affected by osteoporosis, as shown in Table 2. A χ²-test for independence showed a significant association between sarcopenia and osteoporosis (p = 0.024). At a binary logistic regression, we found a significant association between sarcopenia and osteoporosis after adjustment for age and interval between fracture occurrence and DXA scan (p = 0.026), as shown in Table 3. For a sarcopenic woman the OR for osteoporosis was 1.8 (95%CI = 1.073–3.018).

4. Discussion

We show that sarcopenia was significantly associated with osteoporosis in a large sample of women following a fragility fracture of the hip. To our knowledge this result is original, because no previous reports investigated the association between sarcopenia and osteoporosis in hip-fracture survivors, who are affected by the main clinical consequence of the combination of bone fragility and falls, resulting in a very high risk of permanent disability. A similar significant association was shown in a sample of women unselected on the basis of previous fragility fractures (Walsh et al., 2006). At now, sarcopenia is thought to impose a relevant economic burden on healthcare services because it enhances the risk of physical disability in elderly subjects (Janssen et al., 2004a,b). The association between sarcopenia and osteoporosis suggests that a further increase in healthcare expenditures may be associated with sarcopenia, given relevant costs due to fragility fractures (Kanis et al., 2008a) that are suggested to be more common among sarcopenic than non-sarcopenic women. Our study actually shows that hip-fracture women with sarcopenia had a higher risk of osteoporosis than hip-fracture women without sarcopenia (adjusted OR = 1.8). Further clinical studies are

<table>
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<th>Table 1</th>
<th>Descriptives in the 313 women, mean ± S.D., or %.</th>
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<tbody>
<tr>
<td>Age, years</td>
<td>79.7 ± 7.4</td>
</tr>
<tr>
<td>Height, cm</td>
<td>157.1 ± 6.5</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>55.2 ± 11.1</td>
</tr>
<tr>
<td>Fracture type: trochanteric/cervical</td>
<td>55/45</td>
</tr>
<tr>
<td>Bone mineral density at total hip, T-score</td>
<td>-2.86 ± 1.0</td>
</tr>
<tr>
<td>Bone mineral density at femoral neck, T-score</td>
<td>-2.72 ± 0.81</td>
</tr>
<tr>
<td>Corrected appendicular lean mass, g</td>
<td>13 099 ± 2156</td>
</tr>
<tr>
<td>Corrected appendicular lean mass/height², g/m²</td>
<td>2156 ± 819.5</td>
</tr>
<tr>
<td>Interval fracture occurrence–DXA scan, days</td>
<td>20.9 ± 6.5</td>
</tr>
</tbody>
</table>
needed to confirm the association between sarcopenia and osteoporosis and to make possible a reliable estimation of the economic burden associated with sarcopenia. We did not investigate the mechanism underlying the association we describe and the cross-sectional design of our study does not prove causal inference. Several previous studies investigated the association between soft tissue body composition and bone mass. Previous results generally showed a significant positive association between both lean and fat components of soft tissue and BMD, although a definitive conclusion on causal relationships has not been driven both lean and fat components of soft tissue and BMD, although a definitive conclusion on causal relationships has not been driven (Pluijm et al., 2001; Reid, 2002; Wang et al., 2005; Di Monaco et al., 2007c), and the strict co-correlation between lean and fat mass makes difficult to distinguish the role of each component (Iannuzzi-Sucich et al., 2002; Di Monaco et al., 2007b). Irrespective of the mechanism, we support the hypothesis of an at least partly common origin of low bone and muscle mass. We emphasize a research approach on preventive strategies and treatment options for sarcopenia and osteoporosis targeting both bone and muscle tissue (Joseph et al., 2005; Hedstrom et al., 2006; Di Monaco et al., 2009b). This may be the case for lifestyle changes (i.e., increase in physical activity and optimal protein nutrition) and medications that exert anabolic actions, although type and dosage of each intervention should be specifically investigated. Age was significantly associated with osteoporosis in our sample. This is in agreement with the wider literature. Notably, the association between sarcopenia and osteoporosis was independent of age at binary logistic regression.

In our sample, the prevalence of osteoporosis (i.e., 73%) was higher than the one expected in age matched women unselected on the basis of previous fractures (Kanis et al., 2008a). This is consistent with the well known association between low BMD and high hip-fracture risk. Sarcopenia prevalence was 58% among the 313 women we investigated. In prevalence assessment, a crucial role is played by normative data. As for osteoporosis a general consensus exists on the use of reference data from NHANES III; with BMD assessment at femoral neck or total proximal femur the threshold for osteoporosis diagnosis is well established at a T-score <-2.5 (Clinician’s Guide, 2008; Kanis et al., 2008a). Conversely, normative data for sarcopenia is not universally agreed upon. We used reference data from the first large population-based study that investigated normative data for aLM (Baumgartner et al., 1998); according to the authors sarcopenia was diagnosed when aLM/ht^2 was less than two standard deviations below the mean of the young reference group. A single previous report from our group showed a similar prevalence of sarcopenia in a smaller sample of hip-fracture women (Di Monaco et al., 2006). Sarcopenia prevalence in our study seems higher than the one found in samples of older women unselected on the basis of bone fragility and fractures using the same threshold and the same reference population (Baumgartner et al., 1998; Iannuzzi-Sucich et al., 2002). This is not surprising, given frailty typical of hip-fracture women.

Our study has several limitations. We assessed both BMD and aLM by DXA. This method is the gold standard for BMD assessment (Clinician’s Guide, 2008; Kanis et al., 2008a). For LM assessment DXA has a good reported reproducibility and was validated against multislice computed tomography scans, magnetic resonance imaging, and body composition models (Albanese et al., 2003). However, DXA does not capture qualitative changes of bone and muscle that play a relevant role in the genesis of both bone fragility and impaired muscle function. We performed no other evaluations of bone and muscle quality. This limitation may be particularly important in muscle assessment, because several changes in muscle composition that occur with aging (Goodpaster et al., 2001) may play a pivotal role in impairing muscle performance irrespective of muscle mass as assessed by DXA (Visser et al., 2000; Wehren et al., 2005; Di Monaco et al., 2006; Clark and Manini, 2008). Metal implants (prostheses and nails) were reported to affect the regional assessment of body composition by DXA with overestimation of LM (Madsen et al., 1999; Giangregorio and Webber, 2003). In agreement with these reports, our patients had a significantly higher LM at fractured leg than at the contralateral leg. To avoid LM overestimation at fractured legs, we corrected aLM by substituting LM in unfractured leg for LM in fractured leg as previously described (Di Monaco et al., 2006, 2007a). We performed DXA assessment after hip fracture. The interval between fracture occurrence and DXA assessment may be a confounding variable in our study, because relevant changes in body composition, including a decrease in LM and BMD, have been shown after hip fracture. In a prospective study, the percentages of decrease in LM and femoral neck BMD were 6.4% and 2.1%, respectively, two months after fracture occurrence (Fox et al., 2000). In our study the loss of LM and BMD is expected to be lower,

Table 2
Count and expected count of women with sarcopenia and osteoporosis.

<table>
<thead>
<tr>
<th></th>
<th>With osteoporosis</th>
<th>Without osteoporosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>With sarcopenia (count)</td>
<td>141</td>
<td>39</td>
<td>180</td>
</tr>
<tr>
<td></td>
<td>(expected count)</td>
<td>132.3</td>
<td>47.7</td>
</tr>
<tr>
<td>Without sarcopenia (count)</td>
<td>89</td>
<td>44</td>
<td>133</td>
</tr>
<tr>
<td></td>
<td>(expected count)</td>
<td>97.7</td>
<td>35.3</td>
</tr>
<tr>
<td>Total</td>
<td>230</td>
<td>83</td>
<td>313</td>
</tr>
</tbody>
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because we performed DXA assessment about three weeks after fracture occurrence. A shorter time (i.e., a few days) between fracture occurrence and DXA assessment may be better to minimize the changes in BMD, but many patients cannot undergo DXA scan a few days after fracture occurrence. Anyway, to adjust our results for this potential confounder, we included it in binary logistic regression analysis as an independent variable. Our study included white women admitted to a single rehabilitation hospital in Italy, who agreed to be studied and who could be evaluated by DXA. As a consequence, data cannot be generalized to the overall population of hip-fracture patients. Finally, because our study has a cross-sectional design, data does not prove causal inference.

5. Conclusions

We show the high prevalence of sarcopenia and a significant association between sarcopenia and osteoporosis in a large sample of hip-fracture women. Data supports a research approach on preventive strategies and treatment options for sarcopenia and osteoporosis targeting both bone and muscle tissue, although cross-sectional design does not prove causal inference. Furthermore, data should be considered when the economic burden of sarcopenia is estimated, given the high proportion of bone fragility in sarcopenic women.

References