ORIGINAL ARTICLE

Appendicular Lean Mass Does Not Mediate the Significant Association Between Vitamin D Status and Functional Outcome in Hip-Fracture Women

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ABSTRACT. Di Monaco M, Castiglioni C, Vallero F, Di Monaco R, Tappero R. Appendicular lean mass does not mediate the significant association between vitamin D status and functional outcome in hip-fracture women. Arch Phys Med Rehabil 2011;92:271-6.

Objective: To investigate whether muscle mass mediates the significant association between vitamin D status and functional recovery after hip fracture in women.

Design: Observational study.

Setting: Rehabilitation hospital in Italy.

Participants: We investigated white women (N=280) of 305 who were consecutively admitted to a rehabilitation hospital because of their first fracture of the hip.

Interventions: Not applicable.

Main Outcome Measures: To assess muscle mass, we measured appendicular lean mass (aLM) by dual-energy x-ray absorptiometry (DXA), 21.2±6.2 (mean ± SD) days after hip fracture occurrence in the 280 women. On the same day, we assessed serum levels of 25-hydroxyvitamin D and parathyroid hormone (PTH). Ability to function in activities of daily living was evaluated by the Barthel Index both before and after acute inpatient rehabilitation.

Results: After adjustment for 8 confounders, including age, cognitive impairment, pressure ulcers, neurologic impairment, infections, fracture type, Barthel Index score at admission to rehabilitation, and aLM/height^2 (aLM/ht^2), 25-hydroxyvitamin D levels were significantly associated both with Barthel Index scores after rehabilitation (P=.003) and their changes during rehabilitation (P=.008). Similar results were obtained when the 25-hydroxyvitamin D/PTH ratio was substituted for 25-hydroxyvitamin D levels. Conversely, aLM/ht^2 was not significantly correlated with Barthel Index scores and their changes during rehabilitation. Furthermore, we found no significant associations between either 25-hydroxyvitamin D levels or the 25-hydroxyvitamin D/PTH ratio and aLM/ht^2.

Conclusions: The significant association between 25-hydroxyvitamin D levels (and 25-hydroxyvitamin D/PTH ratio) and the ability to function in women with hip fractures was not mediated by aLM assessed by DXA.

Key Words: Activities of daily living; Hip fractures; Parathyroid hormone; Rehabilitation; Vitamin D.

LOW LEVELS OF 25-hydroxyvitamin D were significantly associated with the occurrence of hip fractures in prospective studies.[1-3] Three recent meta-analyses showed the effectiveness of vitamin D supplements for hip fracture prevention, either when doses of more than 400IU/d of the vitamin were administered alone[4] or when a combination of calcium and vitamin D was supplied,[5,6] although controversies still exist on fracture reduction as a result of vitamin-D supplementation in community dwellers.[7] The administration of both calcium and vitamin D is recommended worldwide to reduce the risk of fracture,[8,9] but substantial proportions of older people are still affected by vitamin D deficiency,[10,11] and very low serum levels of 25-hydroxyvitamin D are common among disabled people[12,13] and at the time of hospitalization for a fracture of the hip.[14-16]

Survivors of hip fracture are at high risk of permanent disability. Up to 25% of them may require long-term nursing home care, and only 40% fully regain their prefracture level of independence.[8] Notably, vitamin D deficiency was shown to affect independence in activities of daily living, lower extremity function, and risk of falling after hip fracture,[14,15] apart from influencing the risk of fracture. Secondary hyperparathyroidism resulting from vitamin D deficiency was suggested to contribute to generate postfracture disability.[17]

One possible explanation of the effects exerted by vitamin D deficiency and PTH excess on functional recovery after a fracture of the hip rests on the reduction of MM. A loss of MM was associated with disability in the elderly,[18-22] and people with hip fractures are commonly affected by sarcopenia (ie, the clinical condition of having abnormally low levels of MM).[23] Skeletal muscles require vitamin D for structural maintenance and optimal function, with deficiency causing loss of MM, an atrophy of type II muscle fibers, and muscle weakness.[24-27]

We hypothesized that vitamin D and PTH status may affect the ability of women with hip fractures to function by altering their MM levels. To assess this hypothesis we studied the

List of Abbreviations

aLM	appendicular lean mass
aLM/ht^2	aLM divided by height squared
BMI	body mass index
DXA	dual-energy x-ray absorptiometry
LM	lean mass
MM	muscle mass
PTH	parathyroid hormone

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relationship between vitamin D status, PTH levels, MM, and functional recovery in one sample of older women with a recent hip fracture.

METHODS

Participants

We evaluated 305 white women consecutively admitted to our physical medicine and rehabilitation division during a 22-month period because of their first hip fracture. The mean ± SD value of time between fracture occurrence and admission to the rehabilitation hospital was 13.4±5.2 days. We focused on white women because few nonwhite elderly women live in Italy. Twenty-five women were excluded from the study: 14 had hip fractures from either major trauma or cancer affecting bone, 4 had hip or knee arthroplasties that could alter the assessment of body composition, and 7 could not undergo body composition assessment because of refusal, death, or acute diseases. The final study sample included 280 women who gave their informed consent to participate in the study. Of these 280 women, 102 were also included in a recently published cross-sectional study on the prevalence of sarcopenia and its association with osteoporosis in women with a hip fracture.[23] All the fractures were either spontaneous or caused by minimal trauma (trauma equal to or less than a fall from the standing position). The study protocol was approved by the regional committee for scientific research (Regione Piemonte).

Outcome Measures

We used DXA (QDR 4500W[a]) to measure whole and regional body composition. We followed the protocol for DXA total body scan as described by the manufacturer. aLM was calculated as the sum of 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,[28,29] we performed a preliminary comparison between LM assessed at fractured legs and at contralateral legs. At paired *t* test, LM assessed at fractured legs (5514±1326g; mean ± SD) was significantly higher than LM assessed at unfractured legs (5010±882g) in the 280 women (difference between sides, 503g; 95% confidence interval, 385–622g; $P<.001$). To avoid LM overestimation at fractured legs, we corrected aLM by substituting LM in the unfractured leg for LM in the fractured leg: corrected aLM = (LM in unfractured leg × 2) + LM in arms, as previously described.[23,29]

LM cannot be interpreted without some indexing to body size. At a minimum, 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 8 women who could not keep the standing position were measured supine. We accounted for body size by dividing corrected aLM by height squared (aLM/ht^2), as previously reported in 2 epidemiologic studies[30,31] focusing on the prevalence of sarcopenia. These 2 studies[30,31] supplied normative data for aLM/ht^2.

A blood sample was collected on the day of DXA scan, 21.2±6.2 (mean ± SD) days after fracture occurrence, while patients were fasting. In each woman, we evaluated 25-hydroxyvitamin D levels by an immunoenzymatic assay[b] (coefficient of variation intra-assay, <8%; interassay, <10%), and intact PTH by 2-site chemiluminescent enzyme-labeled immunometric assay[c] (coefficient of variation intra-assay, 5.7%; interassay, 8.8%). Normal values for 25-hydroxyvitamin D were above 30ng/mL; vitamin D deficiency was diagnosed when 25-hydroxyvitamin D levels were below 12ng/mL, whereas values between 12 and 30ng/mL defined vitamin D insufficiency. Hyperparathyroidism was diagnosed when PTH levels exceeded 80pg/mL. We did not record information on vitamin D supplementation and treatment with medications for osteoporosis before fracture occurrence. None of the women received medications for osteoporosis, vitamin D, or calcium supplementation during the time interval between fracture occurrence and 25-hydroxyvitamin D assessment.

Functional evaluation, both at rehabilitation admission and at discharge from the rehabilitation hospital, was assessed by skilled physiatrists with the use of the Barthel Index (original version unchanged). The functional index assesses basic activities of daily living; its score ranges from 0 (total dependence) to 100 (total independence). The physiatrists were not aware of the results of both body composition and laboratory assessments at the time of Barthel Index score evaluation.

Data Analysis

We investigated bivariate linear correlations between the potential predictors (ie, 25-hydroxyvitamin D, PTH, 25-hydroxyvitamin D/PTH ratio, and aLM/ht^2), Barthel Index scores assessed after rehabilitation, and their changes during rehabilitation by using a Spearman rank test. Furthermore, we took into account the role of 11 potential confounders: age, BMI, hip fracture type (cervical or trochanteric), surgical procedure type (arthroplasty or internal fixation), cognitive impairment (Mini-Mental State Examination score, <24/30), pressure ulcers (stage 2 or higher according to the classification from the National Pressure Ulcer Advisory Panel), neurologic impairment (impairment found at clinical examination caused by neurologic diseases, ie, Parkinson disease, stroke with hemiplegia, paraparesis, monoparesis, tetraparesis, or cerebellar syndrome), infections (all the infections needing antibiotic treatment during the length of stay), comorbidities (all the prevalent diseases judged clinically relevant during the length of stay), number of medications in use, and Barthel Index score at admission to inpatient rehabilitation.

Descriptive statistics for the 280 women are shown in table 1. We had no missing data. BMI was evaluated both as individual values and after categorization in 4 classes, in agreement

Table 1: Characteristics of the 280 Women Included in the Study

Age (y)	79.7±7.4
BMI (kg/m^2)	22.5±4.4
Hip fracture type: trochanteric/cervical	57/43
Surgical procedure type: arthroplasty/internal fixation	55/45
Cognitive impairment	21
Pressure ulcers	28
Neurologic impairment	14
Infections	51
No. of concomitant diseases	2.7±1.6
No. of medications in use	3.6±2.1
Barthel Index score at admission to inpatient rehabilitation	45 (35–55)
Barthel Index score at discharge from inpatient rehabilitation	90 (75–95)
25-Hydroxyvitamin D (ng/mL)	8.9 (4.3–15.5)
PTH (pg/mL)	46 (30–74.5)
Corrected aLM (g)	13,315±2573
Corrected aLM/ht^2 (g/m^2)	5389±1025

NOTE. Values are mean ± SD, percentages, or median (interquartile range).