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Can Muscular Impairment be the "Key" for Femoral Fracture?

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Abstract

Background: Osteoporosis and osteoarthritis are the most common diseases of musculoskeletal system. Osteoporosis is characterized by low bone mass and microarchitetural deterioration of bone tissue. This disease is associated with sarcopenia and muscular impairment, while osteoarthritis seems to be independent of muscle quality.

In the elderly, sarcopenia is characterized by an histological deterioration and by an important functional impairment. The aim of the present work is to show how bone weakening is associated with muscle aging in terms of fiber atrophy and physical activity reduction, producing disability and risk of fall and fractures.

Methods: A functional evaluation of muscular performance status in twenty osteoporotic women with a femoral fracture and in twenty osteoarthritic women with a Total Hip Arthroplasty (THA) in progress was realized through the PASE test (Physical Activity Scale for the Elderly). DeXa was performed and the T-score values were considered to classify osteoporotic and osteoarthritic patients. As a part of a multiparametric model of evaluation, biopsies of vastus lateralis muscle were analyzed to find a correlation with functional index.

Results: In osteoporotic patients, the PASE test showed a low or moderate level of physical activity before occurring the fracture while osteoarthritic patients had more intensive physical performances. Hystological analysis showed that osteoporosis is characterized by a type II fiber prevalent atrophy and data correlation showed that lower scores of PASE test are associated with a lower type II fiber diameter. No correlation was found between BMD values and PASE test.

Conclusion: We demonstrated that osteoporosis is closely related to sarcopenia. Infact, bone remodeling is related to both muscle morphological and functional impairment and sarcopenia is considered one of the major responsible factors for functional limitations and motor dependency in elderly osteoporotic persons. According to our study, physical activity should be strongly recommended in osteoporotic patients at diagnosis.

Keywords: Sarcopenia; Osteoporosis; Physical activity

Introduction

Osteoporosis (OP) is a chronic progressive disease which causes a reduction in bone mineral density and in Bone Quality with a resulting imbalance in the regulation of the hormonal, cellular and metabolic system that normally governs the skeletal tissue [1-4].

This gap can lead to an increase in osteoclastic activity to the detriment of the appositive action of osteoblasts (postmenopausal osteoporosis) or to a normal osteoclasts activity together with reduced bone formation by osteoblastic cells (senile osteoporosis).

Instead, the main actor in the process of osteoarthritis's (OA) physiopathology is the cartilage. In fact, the arthritic articular cartilage is characterized by an imbalance between matrix synthesis and degradation. When the cartilage is damaged, it is replaced by a mixture of immature and disarranged collagen fibers. The subchondral bone loses its coating and is directly subjected to abnormal stress which can lead to microfractures [5] and formation of reparative sclerotic bone with a widely disorganized trabecular pattern.

The systemic tissutal "aging" is a multifactorial process related to a natural decline of physiological functions, including the decrease in bone mineral density (BMD) [6], of muscle mass and muscle strength [7]. Sarcopenia is due to an important imbalance between synthesis and deterioration of muscle proteins and cells, with a resulting poor muscular quality. This depletion strongly influence bone trophism and affects mobility and skeletal features during OP and OA.

During the last 40 years, investigators have collected considerable information demonstrating that altered loading states play a crucial role in modulating muscle fiber size as well as the contractile and metabolic phenotypes with a consequent reduction of the biomechanical stimulation on bone [8]. In particular, we know that in osteoporotic patients there is a preferential loss of type II muscle fibers (fast ones) [9]: this progressive loss of motor units leads to a rapid progressive decline of muscle power needed to perform even the simplest daily activities like rising from a chair, climbing the stairs or recovering the right position after an imbalance. This results in a reduction of bone stimulation and in an increased risk of fragility femoral fractures [10].

Muscle changes produced by the aging process can also partly encourage the development of osteoarthritis as they make the joints more susceptible to the effects of other risk factors including abnormal biomechanical stimulation, trauma, genetic alterations and comorbidities [11,12]. The differences in osteoporotic patients’ sarcopenia compared to arthritic one are highlighted at a microscopic level, in rate and type of muscle fibers’ atrophy.
The OP, as already said, is characterized by type II fibers preferential atrophy while in OA muscular atrophy appears more homogeneous in relation to fiber type of and more attenuated, although it is always connected to the functional deficit caused by the disease.

Sarcopenia in the elderly is characterized not only by an histological deterioration but also by an important functional impairment: physical inactivity or a reduction in exercise level are a part of the mechanisms that underlie sarcopenia and therefore physical activity can be seen as an important factor to reverse or modify the development of this condition [13]. Exercise is believed to be the most effective intervention proposed to improve the quality of life and functionality in older adults, improving muscular and skeletal trophism and reducing the risk of injuries [14].

The aim of our study was to show the presence and the degree of muscle atrophy in female patients with osteoporosis and osteoarthritis and to evaluate if sarcopenia, detected by morphometric analysis, is related to reduced levels of physical activity and muscular disuse in these two groups.

Materials and Method

A functional evaluation of muscle efficiency was performed in twenty osteoporotic women with a cervical femoral fracture and in twenty osteoarthritic women with a Total Hip Arthroplasty (THA) in progress using PASE test questionnaire (Physical Activity Test for the Elderly).

Personal data and case histories of patients were collected and patients were included in the two groups (OP and OA) after performing DeXA, T-score, MHarris Hip Score and after radiographic assessment by Kellgren-Lawrence scale.

In the context of a multimodal model of evaluation, we analyzed biopsies of vastus lateralis muscle performed during the surgical operation.

The patients were informed about the experimental procedures and signed an informed consent form before the study. The study was approved by the Ethical Committee of Tor Vergata University Hospital.

There was no discrepancy for age, sex and comorbidities in the two groups (women, mean age OP 76 ± 3.2 y OA 74 ± 4.1 y). We used standard statistical procedures in order to calculate means and standard deviation (SD) of age.

We calculated Pearson correlation coefficient in order to find statistically significant correlation for $p<0.05$. We performed the Student's t-test to compare statistically different data.

PASE test

A functional evaluation of their performance status was realized through the PASE test (Physical Activity Scale for the Elderly). The questionnaire assesses two main groups of activities: recreational activities carried out during free-time (reading, watching TV, walking, cycling, mild, moderate and heavy sports activities) and domestic activities (washing dishes, going to the supermarket, washing the floors, doing home repairs or gardening work, caring for someone).

Each of these actions corresponds to a set value (I) that is proportional to the "weight" that they could have in the life of each individual.

Each patient is asked how many hours in a day he/she spends in these activities (Q) for how many days per week (G). For each activity is calculated a score achieved by the operation (QXG/7) x I.

The sum of the individual scores set the patient into one of four categories related to the degree of physical activity:

- inactivity (total score <42);
- lacking physical activity (43-105);
- moderate physical activity (106-145);
- intense physical activity (>146).

We chose the PASE because it is a brief, easily scored, reliable and valid instrument for the assessment of physical activity in epidemiologic studies of older people [15].

Bone mineral density evaluation

DeXa was performed with a Lunar GE apparatus and lumbar spine (L1-L4) and femoral neck scans were analyzed to evaluate BMD (in grams per square centimetres): this evaluation is expressed as absolute values and as T-scores. For the OA group the measurements were performed on the non-dominant site, while for the OP group the measurements were performed on the limb opposite the fracture site. Each measurement was acquired with the patients laying in a supine position and after the removal of any metal object. Women with fragility hip fracture, a T-score ≤−2.5 SD, and a negative radiographic framework for hip OA were included in the OP group.

Women with a positive radiogram for hip OA and T-score ≥−2.5 SD were included in the OA group.

Morphometric analysis

Muscle biopsies were taken from the upper portion of the vastus lateralis during open surgery for hip arthroplasty.

Muscle specimen was frozen into RCL2 and histological evaluations were performed on transverse cryostat sections (7 μm thick) stained with hematoxylin–eosin, myosin-slow and Gomori trichrome. We used a a semiautomatic image analysis system (QWin Standard V3, Leica, Cambridge, UK) to obtain morphometric data. A minimum of 200 muscle fibers per biopsy have been evaluated, comparing type I and type II fibers for their relative prevalence, minimum transverse diameter, and cross-sectional area. We established as atrophic fibers those with a diameter lower than 30 μm, which is the minimum value of the normal range for women [16].

Results

Morphometric and structural subjects parameters have shown differences in the two gropus (Table 1).

Parameters	OA	OP
Age (years)	74 ± 4.1	76 ± 3.2

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Menopausal age (years)	49.8 ± 2.36	45.8 ± 2.88
HHS (points)	38 ± 7.6	Not performed
Kellgren-Lawrence Scale (degree)	4-Mar	2-Jan
T score	-0.9 ± 1.9	-2.7 ± 0.9
Pase test (score)	100 ± 20.86	62.6 ± 33
Average diameter type I fibers (µm)	30.20	33.01
Average diameter type II fibers (µm)	26.08	24.93

Table 1: Morphometric and structural subjects parameters.

In osteoporotic patients, the PASE test showed a low or moderate level of physical activity or inactivity before occurring the fracture. These findings are sustained by the old age of the patients, but they are further supported by the idea that osteoporosis is closely related to an important decrease in muscular performance, despite associated symptoms like pain are usually absent. On the contrary, osteoarthritis is characterized by a strong pain and functional limitation related to articular damage: this is the reason for the reduction in physical activity, although this impairment is not so evident (Figure 1).

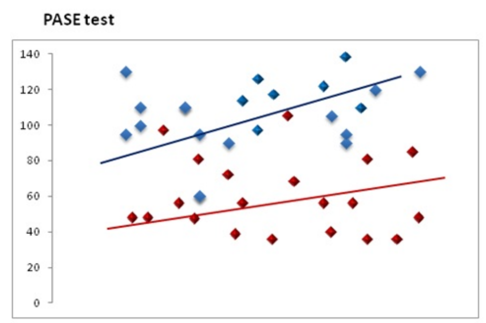

Figure 1: Trend of PASE test scores in OP and OA patients.

Our data suggest that osteoporosis is a complex disease in which a lot of factors may be associated with bone resorption and may contribute to the reduction of patients' physical skills, first of all a sarcopenic status characterized by muscular decay and fiber atrophy.

Histological analysis showed no signs of necrosis, inflammation and regeneration in muscle biopsies. The mean value of type I fibers' diameter in OP and OA was 33.01 µm (ranging between 57.13 µm to 11.27 µm) and 30.20 µm (ranging between 37.29 µm to 19.32 µm), respectively; the mean value of type II fibers' diameter in OP and OA was 24.93 µm (ranging between 32.77 µm to 15.58 µm) and 26.08 µm (ranging between 31.86 µm to 18.13 µm), respectively.

These data underline that fiber diameters in OP tend to deviation from the normal distribution toward an atrophic range. This deviation is prominent for type II fibers compared with type I fibers.

Correlation between fiber II type diameters and PASE test in OP showed that lower scores of PASE test are associated with a lower type II fiber diameter (Figure 2 and Table 2). To verify if there was a correlation we performed the Pearson product–moment correlation test ($p<0.001$).

No correlation was found in OA or referring to type II fiber diameter ($p>0.05$).

No correlation was found between BMD and PASE test ($p>0.05$), while type II fiber prevalent atrophy correlates with low BMD ($p<0.05$), suggesting that osteoporosis's severity has a central role in the pathogenesis of OP-related muscle atrophy.

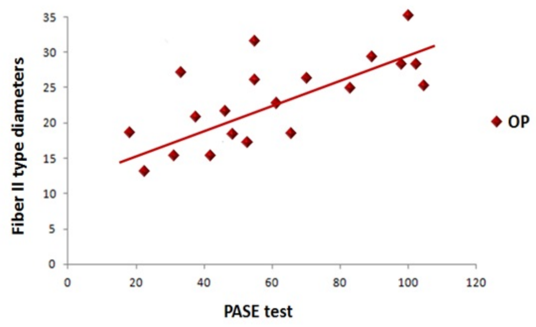

Figure 2: Correlation between fiber II type diameters and PASE test scores in OP patients.

Subgroups	Range of type I muscle fibers diameter	Range of type II muscle fibers diameters
Inactivity (<42 points)	19.32-24.73 µm	17.34- 22.46 µm
Lacking physical activity (43-105 points)	27.45-28.58 µm	22.93- 28.33 µm
Moderate physical activity (106-145 points)	26.47-31.46 µm	29.04- 30.02 µm
Intense physical activity (>146)	30.13-37.29 µm	31.86- 31.93 µm

Table 2: Subcategories of the osteoporotic patients according to PASE test scores and correlation with the average diameters of type I and type II fibers (µm) in the four groups.

Discussion

In this study, we compared from a morphological and functional point of view two of the most common skeletal disease in the elderly, osteoporosis and osteoarthritis.

We demonstrated that osteoporosis is closely related to sarcopenia: in fact, bone weakening is associated with muscle aging in terms of fiber atrophy and physical activity reduction, in a complex framework of disability and high risk of fall and fractures.

Physical impairment does not correlate with BMD measured by DeXa: this is to say that muscle functionality is not only associated with the severity of osteoporosis disease. These data confirm the idea that there is a large number of factors that influence skeletal deterioration in addition to bone remodeling, as nutritional and hormonal factors.

We selected patients that was homogeneous for age and sex so we underlined that there is no correlation between type II fiber atrophy and patients' age. This could be explained by the idea that muscle aging run faster in OP than in OA and leads to a greater state of physical impairment at the same age.

The limitation of our study is that we selected only twenty female patients. Maybe a larger sample of patients should be considered, including male individuals in order to assess the impact of physical activity according to a different genetic and hormonal substrate.

Sarcopenia is considered to be one of the major responsible factors for functional limitations and motor dependency in elderly osteoporotic persons [17].

It is important to emphasize that in OP morphological and functional alterations proceed together toward a global weakening of the musculoskeletal system.

All patients in the OP group were examined for the first time when they were admitted to the hospital because of the cervical femoral fracture and they referred important limitation in their physical daily activity before the trauma. This leads to the hypothesis that OP muscle atrophy could be enhanced by muscle disuse together with multiple factors as the decrease of circulating hormones and reduced levels of intracellular specific pathways.

On the contrary, osteoarthritis in is not linked to reduced physical activity and selective fibers' atrophy. Our data demonstrate that muscle tissue is able to maintain a good trophism during OA.

A recent study [18] reported that in the initial stage of knee osteoarthritis no accumulation of metabolic products and no alteration of muscle proteins were found, maybe because during OA muscle tissue is able to adapt itself to a new microenvironment in order to avoid injury.

Muscle impairment is typical of osteoporotic condition.

According to our study, physical activity should be strongly recommended in osteoporotic patients at diagnosis time because it could be useful to delay muscle atrophy and bone loss thanks to the biomechanical stimuli the muscle exerts on bone. In particular, multi-task and balance exercises could improve fall-related self-efficacy, gait speed and balance performance reducing the risk of falling [19].

However, it is a good clinical practice to suggest physical activity also in osteoarthritic patients. In fact, the pain could reduce their physical performance leading to obesity and mechanical overload. It is known that physical activity and changes in diet composition can reverse the inflammatory resistance, reducing progression or preventing the onset of osteoarthritis [20].

Then, exercise could be a valid instrument to improve bone and muscle quality and it could be a good strategy to reduce fracture risk and disability in the elderly population.

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