Aging Clin Exp Res (2013) 25 (Suppl 1):S93–S95
DOI 10.1007/s40520-013-0097-7

SHORT COMMUNICATION

# Osteoporosis and sarcopenia: the connections

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Received: 1 June 2013 / Accepted: 12 July 2013 / Published online: 18 September 2013


**Abstract** Osteoporosis and sarcopenia are the most frequent musculoskeletal disorders affecting older people. Osteoporosis is a widespread disorder affecting millions of individuals of all ethnic backgrounds worldwide, particularly among older women. It is characterized by reduced bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in the risk of fracture. Sarcopenia is considered to be one of the major factors responsible for functional limitations and motor dependency in elderly persons. In age-related muscle atrophy, a decrease in muscle fiber size and number, and a preferential loss of type II fibers have been reported. A decrease in the circulating levels of specific hormones (e.g., estrogen, testosterone, growth hormone, and insulin-like growth factor-1) has been shown to be associated with sarcopenia and this appears to play an important role in its pathogenesis.

**Keywords** Sarcopenia · Osteoporosis · Frailty syndrome

## Introduction

The increased longevity of the population is inevitably causing a rise in the incidence of chronic degenerative diseases that affect elderly people, especially those related to the musculoskeletal system. Osteoporosis and sarcopenia are essential components of frailty syndrome, a pathology that jeopardizes the health of older adults, decreasing their quality of life [1, 2]. According to Clegg [3], the condition of frailty, which is typical of older adults, can have its origin in the combination of different pathological conditions. This is why frailty syndrome is not a specific syndrome, but rather an ever-changing condition, identified by a number of elements on the basis of which Fried et al. [4, 5] conceived the idea of the frailty phenotype. Therefore, understanding the musculoskeletal system is important in the determination of frailty syndrome.

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## Muscle and bone connection

As muscles become larger and stronger during growth and in response to increased loading, bones should adapt by adding mass, size, and strength. At the age of 50–60 years, muscle mass begins to decrease by roughly 40 %, which is equal to 1 % every year. This decrease causes a reduction, which can be clinically assessed, of muscle strength and resistance. These findings are typical of sarcopenia, which features a regular decrease in bone mass, and this occurs more rapidly in women than in men [6]. It occurs because the deficit in estrogen has a negative effect on cell turnover of bones from the first year after menopause. At the age of 80 years, osteoporosis and sarcopenia have parallel progress again in a form that can be described as sarco-osteoporosis [7]. In adults, even though there is an initial reduction of muscle mass and strength, bone still receives "efficient" mechanical stimuli that maintain the basic multicellular units (BMUs) in an adapted state. In older adults, where muscle masses atrophy is no longer able to develop huge loading on the bones, the BMUs activate a "disuse pattern", which causes a loss of biomechanical

competence of the trabecular tissue [8]. According to Fielding et al. and Messier et al., this mass reduction consists of a loss of approximately 0.6 kg every 10 years after the age of 50 years old [9, 10]. Such an important mass loss changes the biomechanical properties of the muscles, causing morphological and functional changes, which represent the sarcopenic condition. After the age of 60 years, an increase in endosteal bone resorption and weak periosteal attachment leads to cortical thinning, which cause a reduction in resistance to vertical solicitation, torsion, and bending. At the same time, in trabecular bone, the high metabolic turnover leads to resorption of the horizontal trabeculae and to thinning of the vertical trabeculae [11]. The macroscopic changes of the skeletal muscles can be linked to a number of microscopic changes of single muscle fibers. In older patients, there is cellular reorganization following the loss of motor units, which is related to a reduction in the number of satellite cells and myonuclei. Over the years, denervation of single muscle fibers leads to a substantial reduction of type II fibers, which are gradually replaced by rare agglomerations of type I fibers and adipose tissue [12]. Faulkner et al. observed that, between the age of 50 and 80 years, there is a reduction in motor units by approximately 75 % [13]. Because of this adaptive stimulus, the workload lost after this denervation falls upon the surviving motor units, which are unable to cope with such an increase in functional requirements. The final result of this involution process of skeletal muscle is a loss of muscle fibers by approximately 50 % of the total amount.

With regard to bone tissue, the reduction in horizontal trabeculae and thinning of the vertical trabeculae influence bone resistance on a macroscopic level more than on a microscopic level. The origin of fractures in osteoporotic bone has to be researched at a microarchitectural level. In women after menopause, as well as in all older adults, a reduction in cross-linking among collagen fibers changes the regular spatial distribution of osteoblasts, jeopardizing the beginning of development of bone trabeculae. In such a weak tridimensional structure, lesions commonly known as micro-cracks are likely to occur, and their accumulation leads to reduced mechanical competence of bones, which leads to the osteoporotic condition.

Reduced muscle function, which is characteristic of the sarcopenic condition of older patients, is not only linked to loss of muscle mass, but also to strength, power, and resistance of muscle. Izquierdo et al. [14] and Deschenes [15] analyzed the loss of muscle function in terms of strength, power, and resistance of muscle, and showed that after the mass peak is reached by muscle, from the age of 30–80 years, the strength of muscle can be reduced by approximately 75 %, its power by 40 %, and its resistance by 65 %.

The loss of biomechanical properties of the bone appears in terms of elastic modulus, resistance, and stiffness. These three parameters, which mirror those discussed above for muscle tissue, are the actual causes of the reduced support function typical of the osteoporotic condition. Between the ages of 30 and 80 years, in cortical bone, the elastic modulus decreases by 8 %, its resistance diminishes by 11 %, and its stiffness decreases by 34 %. In cancellous bone, the elastic modulus decreases by approximately 64 %, its resistance diminishes by 68 %, and its stiffness can be reduced by up to 70 % [16].

Hormonal activity is another important aspect in the regulation of muscle trophism. Growth hormone (GH), of which the second effector is insulin-like growth factor-I (IGF-1), is one of the main regulators of muscle trophism and muscle fiber survival. A reduction in GH is the cause of types I and II fiber atrophy, which underlies the sarcopenic condition. GH reduction also causes a decrease in calcium release from the sarcoplasmic reticulum, which regulates fiber contractility. Reduced GH secretion has a negative effect on cell proliferation and on differentiation of progenitor cells at an osteoblastic level. This is associated with an increase in cellular apoptosis and with changes in mineralization of the organic matrix of the bone.

Osteoporosis-related muscle atrophy shows some similarity with other systemic conditions, such as cachexia, diabetes, and steroid myopathy, in which preferential and diffuse involvement of type II fibers has been described [17–19]. In these chronic conditions, a decrease in the levels of specific hormones causes reduced activation of the IGF-1/PI3K/Akt pathway, the major regulator of postnatal growth of muscle. This leads to impaired glucose intake, altered muscle metabolism, and muscle atrophy. IGF-1 exerts its effects through a specific receptor, IGF-1R, which is one of the most potent natural activators of the PI(3)/Akt signaling pathway. Akt, through different downstream mediators, promotes protein synthesis and retards protein degradation by regulating the expression of various atrogenes [20, 21]. In addition, IGF-1 is able to counteract the effects of myostatin, a member of the transforming growth factor-β family involved in muscle atrophy. Moreover, because IGF-1/PI3K/Akt controls glucose uptake in skeletal muscle[20], its downregulation can affect mainly glycolytic fibers (type II), whereas oxidative fibers (type I) tend to be more resistant to atrophy, because of their capacity for using other substrates than glucose to produce energy.

## Our experience

In a study published by our research group in 2012, we showed that osteoporosis is associated with preferential