Bone 80 (2015) 126–130

Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Osteoporosis and sarcopenia in older age

M.H. Edwards [a], E.M. Dennison [a,b], A. Aihie Sayer [a], R. Fielding [c], C. Cooper [a,d,e,*]

[a] MRC Lifecourse Epidemiology Unit, University of Southampton, UK
[b] Victoria University, Wellington, New Zealand
[c] Nutrition, Exercise Physiology and Sarcopenia Laboratory, Jean Mayer Human Nutrition Research Center on Aging at Tufts University, Boston, MA, USA
[d] NIHR Musculoskeletal Biomedical Research Unit, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Science, University of Oxford, Oxford OX3 5UG, UK
[e] NIHR Nutrition Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Trust, Southampton General Hospital, Southampton SO16 6YD, UK

ARTICLE INFO

Article history:
Received 9 January 2015
Revised 19 March 2015
Accepted 7 April 2015
Available online 14 April 2015

Keywords:
Osteoporosis
Sarcopenia
Bone
Muscle
Epidemiology
Definition

ABSTRACT

Osteoporosis and sarcopenia are common in older age and associated with significant morbidity and mortality. Consequently, they are both attended by a considerable socioeconomic burden. Osteoporosis was defined by the World Health Organisation (WHO) in 1994 as a bone mineral density of less than 2.5 standard deviations below the sex-specific young adult mean and this characterisation has been adopted globally. Subsequently, a further step forward was taken when bone mineral density was incorporated into fracture risk prediction algorithms, such as the Fracture Risk Assessment Tool (FRAX®) also developed by the WHO. In contrast, for sarcopenia there have been several diagnostic criteria suggested, initially relating to low muscle mass alone and more recently low muscle mass and muscle function. However, none of these have been universally accepted. This has led to difficulties in accurately delineating the burden of disease, exploring geographic differences, and recruiting appropriate subjects to clinical trials. There is also uncertainty about how improvement in sarcopenia should be measured in pharmaceutical trials. Reasons for these difficulties include the number of facets of muscle health available, e.g. mass, strength, function, and performance, and the various clinical outcomes to which sarcopenia can be related such as falls, fracture, disability and premature mortality. It is imperative that a universal definition of sarcopenia is reached soon to facilitate greater progress in research into this debilitating condition.

This article is part of a Special Issue entitled "Muscle Bone Interactions".

Introduction

Osteoporosis and sarcopenia are common diseases that predominantly affect older individuals [1,2]. They are both associated with significant morbidity and can therefore lead to considerable health and social costs [3,4]. Specially, sarcopenia is associated with increased rates of disability, poor mobility, frailty, and hospitalisation [5,6] and it has been estimated that, in the United States, sarcopenia resulted in additional healthcare costs of over $18 billion in 2001 [4]. Furthermore, in common with hip and vertebral fracture fractures, a decline in muscle health has also been shown to predict future mortality from middle-age into later life [7]. Given current secular trends in population demographics with greater longevity, the burden of both osteoporosis and sarcopenia may continue to increase.

In addition to the similar population in which they occur, there is also growing evidence of a link between the two conditions. Studies have shown associations between bone and muscle health by dual energy X-ray absorptiometry (DXA) and more recently using cross-sectional imaging techniques [8,9]. DXA studies have focussed on relationships between facets of muscle health and either bone mass or density and have tended to show positive relationships [10–12]. The use of peripheral quantitative computed tomography (pQCT) has additionally shown bone size and strength to be associated with muscle size, and to a lesser extent, muscle strength. Relationships of muscle with cortical and trabecular volumetric bone mineral density (vBMD) have been less consistent [8,9].

There are several potential explanations for these interrelationships (Fig. 1). The mechanostat hypothesis describes the action of muscle contraction providing a direct mechanical stimulus to bone which promotes osteogenesis [13]. Hormones, such as growth hormone, can have positive effects on the growth of muscle and bone [14,15]. Furthermore, exercise and levels of activity clearly augment both of these components of the musculoskeletal system. There are also likely to be common genetic and developmental components to muscle and bone health [16,17].

Despite their similarities and interrelationships, study into these diseases is at very different stages of evolution, with research into osteoporosis considerably ahead. This review describes the progress

* Corresponding author at: MRC Lifecourse Epidemiology Unit, Southampton General Hospital, Tremona Road, Southampton, SO16 6YD, UK. Fax: +44 23 8070 4021.
E-mail address: cc@mrc.soton.ac.uk (C. Cooper).

http://dx.doi.org/10.1016/j.bone.2015.04.016
8756-3282/

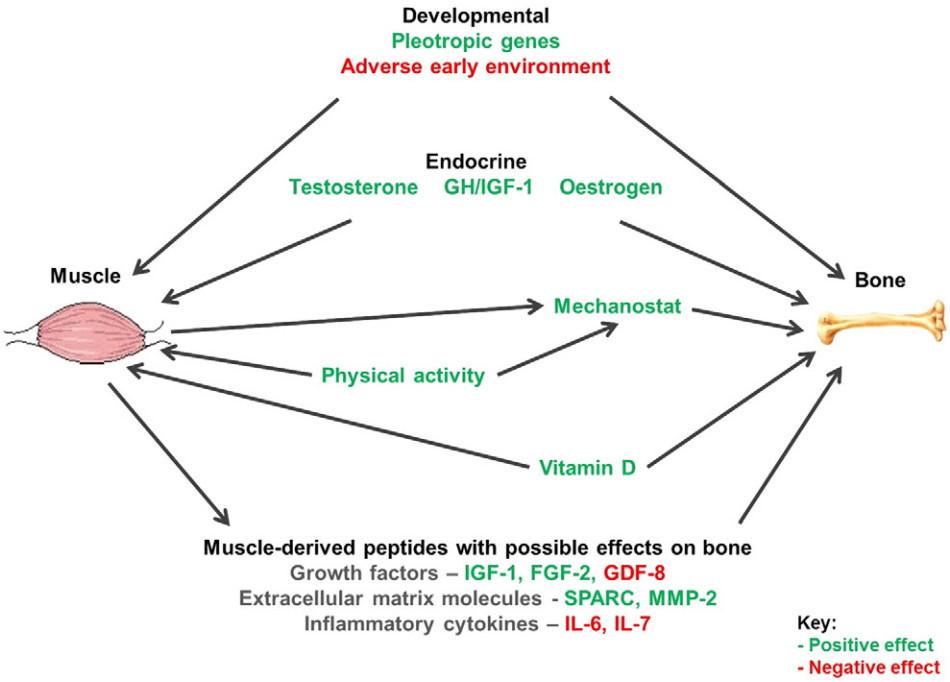

Fig. 1. Interrelationships between muscle and bone.

that has been made in defining these conditions and explores the reasons for the discrepancy in progress made.

The history of osteoporosis

Osteoporosis is a skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture [18]. The term literally means "porous bone" and was first introduced in France and Germany when it described a histological diagnosis. We now know this to represent bone tissue which is normally mineralised but reduced in quantity. This abnormality is the mechanism through which bones become weaker, increasing the risk of fractures occurring.

A significant leap forward was made with the development of non-invasive techniques able to assess bone mineral density (BMD) in vivo. Up to that point, attempts had been made to quantify bone health purely using plain radiographs, such as assessments of cortical morphometry [19]. Single photon absorptiometry was introduced in the 1960s and was subsequently replaced by dual photon absorptiometry. Both relied on radionuclide sources [20] and took over 15 min to complete (per site). The radionuclide decayed and consequently had a finite lifespan, needing to be changed at regular intervals. Around 25 years ago, the radionuclide source was superseded by an X-ray source and DXA scanners were born with faster scanning times and greater spatial resolution. This technique allows measurement of areal bone mineral density (aBMD) primarily at the hip and lumbar spine.

In 1994, the next step change in the definition of osteoporosis occurred, when a working group of the World Health Organisation (WHO) used bone density measurements by DXA to provide a practical definition of osteoporosis as an aBMD of less than 2.5 standard deviations (SD) below the young normal mean [21]. As earlier definitions had incorporated fracture, in order to provide comparability, the subset of women with osteoporosis who had also suffered one or more fragility fractures were deemed to have severe (established) osteoporosis. Osteopenia was defined as an aBMD level between 1 and 2.5 SD below the young normal mean.

This definition has been adopted throughout the world and has allowed great strides forward within this disease area. Prevalence was compared between different geographical locations and this led to hypotheses regarding likely aetiology. Study participants could be more easily selected and beneficial effects on bone could be quantified facilitating research into pharmaceutical agents to treat osteoporosis. This has led to the licensing of several medications with good evidence for efficacy in fracture risk reduction.

Overall within a population, higher aBMD is associated with greater bone strength. Specifically, it has been shown that there is an almost doubling of fracture risk for every one standard deviation reduction in aBMD [22]. However, these measures alone do not explain all of the variance in fracture risk. This is partly related to the inability to measure cortical and trabecular bone separately, and to take into consideration the bone's material quality or structural geometry [23,24]. Recent studies have shown some additional fracture discrimination using cross-sectional imaging techniques but the incremental gains tend to be relatively small [25,26]. These techniques may however allow better understanding of the specific pathogenesis of osteoporosis at the structural level. In contrast, a considerable improvement in fracture prediction has been achieved with the development of fracture risk prediction algorithms, such as the Fracture Risk Assessment Tool (FRAX®).

FRAX® uses clinically available risk factors, with or without aBMD, to determine an individual's risk of major osteoporotic fracture and hip fracture in the next 10 years [27]. As this is more accurate than using aBMD alone, it allows better targeting of treatments to those at greatest risk with positive effects on the ratio of risk to benefit. Therefore, we are now at a point where we can evaluate whether or not to treat an individual and have several effective therapies to do so, with more in the pipeline.

The history of sarcopenia

The term sarcopenia was first coined in 1989 by Irwin Rosenberg who used it to pertain to the loss of muscle mass with age [28,29]. It has since become apparent that muscle function, in addition to muscle mass, is necessary to describe sarcopenia and so the definition has undergone an evolution to reflect this. Although muscle mass would intuitively be thought to be the central factor, it is only weakly associated with function and disability. It does, however, relate to low muscle strength which is strongly associated with these clinical outcomes [30]. Furthermore, although both muscle mass and muscle function