Injury, Int. J. Care Injured 47 S1 (2016) S21–S24

Contents lists available at ScienceDirect

Injury

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

Bone mineral density aspects in the femoral neck of hip fracture patients

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KEYWORDS

mineralization
osteoporosis
bone density
calcium
phosphorus
bone metabolism
hip fracture

ABSTRACT

Elderly people, due to neurological conditions and muscular atrophy, present a greater propensity to falls and thus are very susceptible to hip fractures. Other variables, such as osteoporosis, may also be related to the etiopathogenesis of hip fractures, although osteoporosis is in fact a concurrent disease, and merely a coadjutant cause. Nonetheless, osteoporosis can make fracture patterns more severe and interfere with osteosynthesis. Osteoporosis is the radiological image of osteopenia, a pathological concept meaning a smaller quantity of bone per unit of volume. The radiological expression of osteopenia is therefore that of bone tissue with a lower radiological density than normal. In the context of hip fractures, bone mineral density and bone architecture of the femoral neck together with protein expression profiles and cross-links of this anatomical area are of special interest which is reviewed in the current paper. Spatial variations in bone mineral density in the femoral neck were found in the literature with increased porosity from the periosteal to the endosteal region and also from the distal to the proximal part of the femoral neck. Furthermore, increased crystal size, increased cortical porosity, reduced osteocyte lacunar density and an increased Ca/P ratio associated with higher concentrations of Ca and P were described in hip fracture patients compared to control patients. Osteocalcin/collagen type 1 expression ratio and enzymatic cross-link content in high-density bone was found to be significantly lower in hip fractures compared to controls. In conclusion, further research in bone mineral density and associated parameters are of interest to deepen the understanding of osteoporotic hip fractures.

Introduction

A hip fracture immobilizes, restricts autonomy, shortens life expectancy and results in a high cost for any health care system [1–5]. Elderly people suffer more frequently from hip fractures because they have a higher propensity to falls, as a result of neurological conditions and muscular atrophy. Other variables are also related to the etiopathogenesis of hip fractures, but in recent decades the debate in this field has mainly focused on osteoporosis, to the extent that hip fractures are included within a group of "osteoporotic fractures", despite the fact that osteoporosis is a concurrent disease and only a coadjutant cause.

Anyone may suffer a hip fracture, whether or not they have osteoporosis, but, apart from pathological fractures, a traumatism is usually a necessary cause for a hip fracture to occur [6]. However, osteoporosis makes fracture patterns more severe and also interferes with osteosynthesis. Therefore, effective treatment of osteoporosis is a major issue, although the issues of pathogenesis, the outcome of treatment – particularly as concerns the prevention of fractures – and how health economic budgets must be distributed for areas such as fall avoidance, drug administration, hip fracture management and aftercare are all under discussion.

Osteoporosis is the radiological image of osteopenia, which is the understanding of less bone mass resulting in less amount of bone per unit of volume, together with bone architecture deterioration. This apparently very clear explanation of the radiology-pathology correlation may become somewhat confusing when treatment aimed at mineralizing the remaining bone structure – cortex and cancellous – is applied. Mineralization results in a radiologically denser bone but one that presents the same bone mass density (amount of mineralized osteoid substance per volume) or, in other words, a structure that is equally weak, but stiffer. Bones must be stiff enough so that they do not bend when loaded, but not so stiff as to lack the necessary flexibility to absorb energy by elastic and plastic deformation, thus decreasing the energy that can provoke tissue damage and possible bone fracture. Failure may occur if bones become deformed too much or too little, and exceed their peak stress limits [7].

The biomechanical properties of bone present many variables in relation to hip fractures. Bone strength depends on a large

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0020-1383/

number of components including, but not limited to, bone microarchitecture, geometry, cortical and trabecular porosity, and tissue mineralization density [8,9]. Also relevant are the rate of bone turnover, bone size, trabecular connectivity, molecular crosslinking, tissue maturation, microdamage burden, osteocyte density, gender, race and other factors. These properties are sometimes collectively referred to as bone quality [10]. Determining the proportional contributions made by each of these aspects is a challenge yet to be addressed [7].

In order to achieve solutions to biomechanical problems, the material and structural properties of bone that determine its strength must be quantified. Many pharmacological treatments have been proposed to reduce osteoclastic bone resorption and to increase osteoblastic bone formation and thus prevent the progression of fragility, but the main problem remains bone structure and its relation with biomechanical behaviour. A stiffer, less flexible bone is not one that is stronger and less susceptible to suffer a fracture. We have learned from engineers and architects working in earthquake-prone areas, structures must be made more flexible [11,12] in order to resist shocks, e.g. with the help of "mass dampers" [13,14]. Elasticity is known to be a property of solid bodies, one that preserves the construct from breakage but without dramatically enlarging the body mass. On the other hand, the worst combination appears to be that of a very stiff structure – such as would result from overmineralization – together with decreased body mass.

Mineralization and hip fractures

Bone quality is a very important concept with respect to hip fractures. It comprehends both bone structure and bone composition, which, in turns, includes cells, proteins and mineralization.

Bone density, microarchitecture and mineral composition in hip fracture patients

In a study using a synchrotron radiation microcomputed tomography system coupled with a multiscale biomechanical model to determine the 3-D anatomical dependence of tissue mineral density and of the elastic constants from bone specimens taken from the lower part of the femoral neck of patients undergoing joint replacement, it was found that porosity increased in the radial direction, from the periosteum inwards, but did not vary markedly along the bone axis. Tissue mineral density was significantly higher in the periosteal region than in other bone locations and decreased from the periosteal to the endosteal region, this decrease being faster in the porous part of the samples than in the dense cortical bone. This decrease also took place from the distal to the proximal part of the femur neck. Mineral density variations in the radial direction induce weak changes in bone properties compared to constant tissue mineral density; similarly, tissue variations in the axial direction are responsible for significant variations in the elastic constants. According to the authors of this study, spatial variations in tissue mineral density should be taken into account to properly describe the spatial heterogeneity of elastic coefficients of bone tissue at the organ scale [15,16]. These parameters might be of great importance in the genesis of hip fractures.

Other research into the nano-structure, composition and micro-architecture of the superolateral femoral neck in elderly hip fracture patients versus healthy controls has shown that mineral crystals at external cortical bone surfaces of the fracture group are larger, and also have a higher mineral content and a more homogeneous mineralization profile. However, the hip fracture cases presented cortical porosity values that were almost 35% higher but presented a significantly lower osteocyte lacunar number density compared to controls [17]. Together with increased crystal size, the shift toward higher mineralization, increased cortical porosity and reduced osteocyte lacunar density indicate that the cortical bone of the superolateral femoral neck bears distinct signs of fragility at various levels of its structural organization [18].

Higher mineral contents and greater porosity is the worst combination for bone strength in relation to fracture risk. This is borne out by previous studies that have shown hypermineralized osteocyte lacunae, relative to the total number, to be greater in patients with osteoporosis and osteoarthritis than in femur bone obtained at autopsy[19]. Osteoporosis is characterized by increased hypermineralized osteocyte lacunar number density whereas osteoarthritis presents decreased osteocyte lacunar number density and total osteocyte lacunar number density. The calcium-phosphorus ratio does not appear to differ between hypermineralized osteocyte lacunae and bone matrix in osteoporosis and osteoarthritis groups. Although the role of hypermineralized osteocyte lacunae in bone remodelling and bone biomechanical properties requires further research, these findings are very interesting in relating hypermineralization with neck fracture susceptibility [19], and extend our understanding of the bone stiffness-flexibility relation.

An earlier study compared the degree of mineralization of bone tissue in femoral neck cortex specimens between women with hip fractures and a control group and reported that bone fragility may be related to a greater degree of mineralization of bone tissue heterogeneity in osteons and interstitial tissue [18]. Another study, of the degree of bone mineralization, using quantitative microradiography calibrated with an aluminium step wedge in the femoral neck cortex of patients with hip fractures, compared to a control group, found that the degree of bone tissue mineralization was significantly lower in the osteons than in the interstitial tissue in both groups, whereas osteons and interstitial tissue were significantly greater in the hip fracture patients than in the controls. These data further support the view that bone fragility may be related to a higher degree of tissue mineralization [20].

We studied bone density and mineral composition in hip fracture versus osteoarthritic non-fracture patients undergoing total hip replacement, but the specimens were retrieved from the base of the femoral neck, because in osteoarthritis the femoral head becomes sclerotic, and this might provoke the introduction of bias when comparing hip fracture patients with osteoporosis to osteoarthritic patients. Studies for bone density and mineralization were performed by pinpoint electron beam at 40000× magnification (Fig. 1). The peak-to background ratio (P/B) method was used to measure the concentrations of calcium and phosphorus in each group of patients. Microcrystalline salt standards were used to quantify Ca and P as described in previous publications [21]. All results were calculated as weight fraction percentage of Ca and P [22]. Differences were statistically significant for Ca, P and the Ca/P ratio. These results reveal that cancellous bone obtained from patients with hip osteoarthritis is stoichiometrically similar to normal bone, which is characterized by a Ca/P molar ratio corresponding to hydroxyapatite (1.67). Therefore, this bone can be considered normal from the microanalytical standpoint. However, the cancellous bone in our hip fracture patients had an increased Ca/P ratio, associated with higher Ca and P concentrations (Fig. 2). The finding that hip fracture patients have an increased Ca/P ratio associated with altered Ca and P concentrations, whereas cancellous bone obtained from osteoarthritic patients can be considered normal from the microanalytical point of view, refuted the idea of increasing calcium intake or administering