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Microstructural trabecular bone from patients with osteoporotic hip fracture or osteoarthritis: Its relationship with bone mineral density and bone remodelling markers

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ABSTRACT

Osteoporosis (OP) and osteoarthritis (OA) are the most prevalent musculoskeletal disorders in the elderly but the relationship between them is unclear. The purposes of this study are to analyze the bone turnover markers (BTM), bone mineral density (BMD) and the structural and mechanical properties of trabecular bone in patients with OP and OA, and to explore the relationship between these two diseases. We studied 12 OP patients and 13 OA patients. We analyzed BTM (β-CrossLaps and PINP), BMD and microstructural and biomechanical parameters (micro-CT). Our results were: OP group has higher levels of β-CrossLaps and lower BMD at the femoral neck. Also, OP patients have a decreased volume of trabecular bone and less trabecular number, with architecture showing prevalence of rod-like trabeculae and worse connectivity than OA patients. The biomechanical parameters were worse in OP patients. BMD was correlated with almost all the structural and biomechanical parameters. Moreover, β-CrossLaps was negatively correlated with hip BMD and with bone surface density and positively with trabecular separation. BTM, BMD and bone microstructural changes in osteoporosis are opposite to those of OA. These findings justify a less resistant bone with higher risk of fragility fractures in OP patients. These histomorphometric and biomechanical changes may be suspected by measuring of BMD and β-CrossLaps levels.

1. Introduction

Osteoporosis (OP) and osteoarthritis (OA) are the most prevalent musculoskeletal disorders in the elderly [1]. Osteoporosis is characterized by low bone mass and a deterioration of bone tissue microarchitecture leading to bone fragility, fractures (hip, spine and forearm), pain, chronic disability and premature death. Osteoarthritis is a metabolically active process that involves all joint tissues, affecting mainly to knees, hips and small hand joints leading to pain, impairment of mobility and activity limitation [2]. Both diseases affect similar populations and result in comparable functional impairments but the relationship between them is unclear. Clinical and epidemiological studies suggested that both exceptionally arise in the same patient, even some authors showed an inverse relationship between them [3,4]. Other studies, reported opposite results [5]. It has been found that the development of OA can produce deterioration of the subchondral bone microstructure [6,7] and *vice et versa*, osteoporosis can increase the severity of articular cartilage damage [8] as demonstrated in experimental models of rabbits with induced osteoporosis and osteoarthritis [9].

Bone turnover markers (BTM) are used as a measure of bone remodelling status. High bone remodelling is associated with an increased risk of fracture in OP patients [10], while a reduction of bone remodelling has been described in OA patients [3,4,11]. Previous results showed that bone mineral density (BMD) or bone mineral content (BMC) was higher in women with OA compared to controls [11]. However, it does not mean that bone strength from OA patient is higher. In fact, the association between hip OA and hip fracture remains unclear [1]. Some authors showed that in early stages of OA subchondral cancellous bone was

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significantly thicker and more plate-like, but less mechanically resistant than normal bone [12]. However, the role of the microstructural parameters is complex because they can be modified during the progression of the disease [7]. BMD is a standard parameter widely used in clinical practice to assess bone quantity and indirectly its strength; although BMD values no provide information on bone structure [13], it is a good predictor of fracture risk [14]. Micro-computed tomography (micro-CT) provides data on bone architecture in bone biopsies [15]. The potential changes in trabecular bone microarchitecture could provide evidences that explain the above mentioned inverse association between OA and OP. Studies comparing the microstructural and biomechanical bone parameters in OP and OA diseases are still uncommon and inconclusive and mostly limited to animal models [5,6,16,17]. Even more scarce are the studies showing a correlation between BMD and histomorphometric or biomechanical parameters [15] and we do not know any research about the correlation between bone turnover markers with BMD, biomechanical and histomorphometric values.

However, it may be important to know it because if this relationship is true, the measurement of serum levels of BTM may allow knowing the bone microstructure and its strength.

Therefore, the objectives of this study are to analyze the structural and mechanical properties, bone turnover and BMD in patients with OP and OA, and to explore the relation between BTM (β-CrossLaps) and BMD, microstructure and biomechanical parameters.

2. Materials and methods

2.1. Study design and patients

We designed a cross-sectional case–control study, the cases group constituted the 12 patients (4 men and 8 women) with hip osteoporotic fracture (OP group) undergoing prosthetic hip replacement (range of age 62–87 years), without radiographic signs or macroscopic signs of OA in the surgery. Control group constituted the 13 patients (6 men and 7 women) with hip osteoarthritis (OA group) but not having any osteoporotic fracture along their life, undergoing total hip arthroplasty (range of age 58–83 years). Patients with chronic kidney disease, osteomalacia, multiple myeloma, rheumatoid arthritis, secondary OP due to corticosteroids or in treatment with osteoporosis drugs were excluded.

We required 12 subjects in each group (OP and OA) in order to detect a significant standardized mean difference of 0.5 (one size average effect) with a type I error rate of 5% (alpha = 0.05) and a 90% power (1 − beta = 0.90).

Patients were included in the study in a consecutive manner (January to September 2012). In both groups, arthroplasty was done in the Orthopaedics & Traumatology Department of the "Virgen Macarena" University Hospital (Seville, Spain).

The study was approved by the Ethics Committee of our institution and written informed consent was obtained from all the participants in it. All patients included in the study acceded to donate their bone samples.

We estimated for each patient the 10-year risk of major osteoporotic fracture (clinical spine, hip, forearm, or humerus fracture) and the 10-year risk of hip fracture using the FRAX® tool, calibrated for Spain (www.shef.ac.uk/FRAX/index.htm). Although did not exist cut points to define populations at high or low risk in Spain, we tentatively use the criteria of the Scientific Advisory Council of Osteoporosis in Canada to classify the FRAX® scores as low risk (10-year risk fracture < 10%), intermediate risk (10–19%), and high risk (≥20%) of major osteoporotic fracture and low risk (<3%) or high risk (≥3%) of hip fracture.

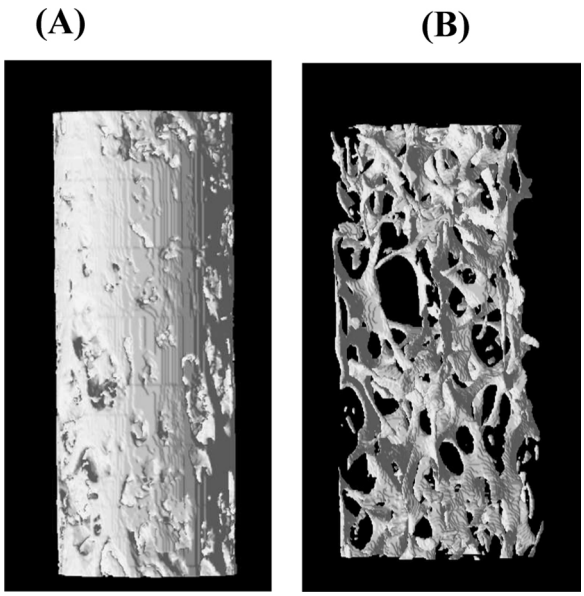

Fig. 1. Graphic representation of the extraction region of bone cores in the femoral head. 3D micro-CT models of cylindrical bone cores from a representative patient of each group. (A) OA patient, (B) OP patient.

2.2. Biochemical parameters

Fasting morning blood was obtained in the first 48 h after surgery to measure: β-CrossLaps, aminoterminal propeptide of type I procollagen (P1NP), parathyroid hormone (PTH) and 25-hydroxyvitamin D (25(OH)D).

PTH, β-CrossLaps and P1NP were analyzed by immunoassay by an autoanalyzer COBAS 601 (Roche, Spain). Interassay CV < 5.8%, <7.6% and <4.2% respectively.

25(OH)D were analyzed by direct competitive immunoassay by an autoanalyzer LIAISON (DiaSorin, Italy). Interassay CV < 5.5%. In all cases, Intra-assay CV was <5%.

2.3. Bone mineral density

Total hip and femoral neck BMD was measured at the contralateral hip by dual X-ray densitometer (Hologic-Discovery, Hologic Inc., Waltham, MA, USA). *In vivo* CV was 2.9% (femoral neck) and 2.5% (total hip).

2.4. Microstructural and biomechanical parameters

Femoral heads were stored frozen at −20 °C until processing. A cylinder of trabecular bone was extracted from each femoral head with a stainless steel trepan burr (Komet Group, Lemgo, Germany) connected to a surgical motor (INTRAsurg 300, KaVo Dental GmbH, Biberach, Germany). The ends of the cores were cut to obtain parallel surfaces, obtaining cylinders (4 mm diameter; 7–9 mm length).

The longitudinal axis of the cylinders was perpendicular to the articular surface, selecting the greater load bearing area in the femoral head [5,16,18].

The bone cores were analyzed without further preparation by micro-CT (Skyscan 1172, Bruker microCT NV, Kontich, Belgium), using an X-ray tube voltage (50 kV) and current of 200 μA and with a 0.5 mm aluminium filter. The scanning angular rotation was 185° with a rotation step of 0.4°. The image voxel size was 11.0 μm. Datasets were reconstructed using a modified Feldkamp algorithm [19] and segmented into binary images (8-bit BMP images) using adaptive local thresholding.

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