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ORIGINAL ARTICLE

Femoral cortical index: an indicator of poor bone quality in patient with hip fracture

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Abstract

Background Osteoporosis is a common disease in elderly, characterized by poor bone quality as a result of alterations affecting trabecular bone. However, recent studies have described also an important role of alterations of cortical bone in the physiopathology of osteoporosis. Although dual-energy X-ray absorptiometry (DXA) is a valid method to assess bone mineral density, in the presence of comorbidities real bone fragility is unable to be evaluated. The number of hip fractures is rising, especially in people over 85 years old.

Aims The aim is to evaluate an alternative method so that it can indicate fracture risk, independent of bone mineral density (BMD). Femoral cortical index (FCI) assesses cortical bone stock using femur X-ray.

Methods A retrospective study has been conducted on 152 patients with hip fragility fractures. FCI has been calculated on fractured femur and on the opposite side. The presence of comorbidities, osteoporosis risk factors, vitamin D levels, and BMD have been analyzed for each patient.

Results Average values of FCI have been 0.42 for fractured femurs and 0.48 at the opposite side with a statistically significant difference ($p = 0.002$). Patients with severe hypovitaminosis D had a minor FCI compared to those with moderate deficiency (0.41 vs. 0.46, $p < 0.011$). 42 patients (27.6 %) with osteopenic or normal BMD have presented low values of FCI.

Discussion and conclusion A significant correlation among low values of FCI, comorbidities, severe hypovitaminosis D. and BMD in patients with hip fractures has been found. FCI could be a useful tool to evaluate bone fragility and to predict fracture risk even in the normal and osteopenic BMD patients.

Keywords Fragility fracture · Bone quality · Cortical thickness · Bone mineral density · Hip fracture · Comorbidity

Introduction

The progressive aging of population leads inevitably to an increase of age-related diseases, as osteoporosis, whose care should be taken as an absolute health and social priority [1]. Osteoporosis is a major public health problem worldwide, largely due to morbidity and mortality, associated with osteoporotic fractures. Osteoporosis affects 5 million people in Italy, of which 80 % includes women in post-menopausal age [2]. Particularly, it is estimated that, among people aged 50 years and above, 1 out of 3 women and 1 out of 8 men are affected by osteoporosis [3]. Fragility fractures represent a dramatic epilog in the natural history of osteoporosis. Hip, vertebrae, wrist, and proximal humerus are the most common sites of fragility fracture. Hip fractures are the worst catastrophic complications of osteoporosis because they represent a high risk for functional decline and mortality, and are also a demonstration of a hidden fragility. Moreover, 30 % of patients with hip fracture are estimated to become permanently disabled, while 40 % of them loose the ability to walk independently, and 80 % are unable to perform everyday life activities after fracture has occurred.

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Every year in Italy, 130,000 fragility fractures occur, as assessed through national hospitalizations database (SDO), but these data are not complete because only hospitalized patients are included.

The number of estimated hip fragility fractures was 93,169 in 2009 with an overall incidence rate of 77.8 per 10,000 inhabitants [4]. In the analysis of 5-year-range groups, a total of 275,302 femoral neck fractures in people over 65 years old during the last three years (2007–2009) has been reported. In patients aged ≥85 years, hip fracture progressively has increased over the three-year period, from 35,472 in 2007 to 39,244 in 2009. In the latter year, people aged ≥85 represented more than 40 % of total hospitalizations due to femoral neck fractures, although they accounted for 2.5 % of the overall Italian population.

Osteoporosis is characterized by an impairment of both bone density and bone quality, leading to a reduction of biomechanical skills, with an increased risk of fragility fractures. Bone quality refers to a cortical and trabecular bone architecture, turnover, damage accumulation (e.g., micro-fractures), and its mineralization. For decades, the main view shows that trabecular bone loss is an important measure of fragility. Indeed, cortical bone loss during aging is about 70 % and about 50 % of it is lost by intracortical remodeling in the inner third of the cortex which constitutes a much smaller volume than the outer two-thirds. Cortical bone strength depends on bone geometry, bone density, and on the position and the direction of applied loads. Long bones are tubular structures, loaded mainly in bending [5]. Bone biomechanics studies have demonstrated that fractures of predominantly trabecular sites, such as vertebral and femur fractures, have propagated from defects in cortical bone [6]. As trabecular bone is lost, the thin shell of cortical bone bears the load. Consequently, trabecular thinning and loss of trabeculae connection, and cortical thinning and porosity play an important role in bone fragility. Recently, Zebaze has explored the occurrence of porosity in cortical bone and has found large pores far from the endocortical surface [7]. He explained that these pores could not arise from the endocortical surface by endocortical resorption, dissolving the cortex 'outwards', producing cortical thinning from the marrow outwards [8]. He recognized that the mechanism was intracortical remodeling, thinning cortex from inside, especially intracortical remodeling upon Haversian canals cross the inner part of the cortex. Zebaze has studied cross-sectional areas using high-resolution peripheral CT to quantify and compare cortical and trabecular bone loss from adult women distal radius, and measured porosity using scanning electron microscopy.

Several authors have studied effects of typical elderly diseases, such as diabetes, chronic kidney disease, and ischemic miocardic disease on cortical bone. Recent studies have suggested that in type 2 diabetes, trabecular bone mass and structure are undamaged and perhaps even enhanced, whereas cortical compartment is mainly compromised [9]. Increased cortical porosity in particular has been detected at the level of radius in female diabetics who have been fractured, as measured by intracortical pore volume fraction via high-resolution peripheral quantitative computed tomography (HR-pQCT) [10]. Although endosteal cortical remnants can be mistakenly interpreted as trabeculae, true increases in cortical porosity could be an important cause of increased fracture risk in type 2 diabetes, because it reduces bone strength and is undetectable by dual-energy X-ray absorptiometry (DXA) [11]. Similar results were found by Nickolas in patients with chronic kidney disease, associated with significant cortical loss, related to hyperparathyroidism and higher serum concentrations of bone turnover markers [12]. Chronic kidney disease patients with fracture have lower cortical and trabecular volumetric bone mineral density, thinner cortices, and abnormal trabecular microarchitecture of distal radius and tibia [13]. Owing to the critical role of cortical bone in the axial load-bearing capacity of long bones, decreases in cortical density and cortical thickness, and increases in cortical porosity are considered as surrogate markers for cortical bone loss.

Several authors have proposed that changes in plain radiographs could be used to predict bone quality in proximal femur. Singh has quantified the degree of osteoporosis by observing trabecular pattern of the proximal femur in plain anteroposterior radiograph [14]. Dorr has classified bone quality as A, B, or C, and has based the findings in both AP and lateral radiographs [15]. Assessed parameters included thickness of cortices, shape of medullary canal, and width of canal at diaphyseal part. These parameters were descriptive and could not be accurately measured. Other indices that involve measurement of morphological changes over proximal femur in the AP radiograph have been described [16]. One of these is cortical index that allows us to study cortical architectural characteristics, and could reflect morphological changes associated with osteoporosis [17]. Femoral cortical index (FCI) can be calculated using the ratio between the thickness of the cortical bone and the diameter of the femoral shaft 10 cm distal to the center of the small trochanter in an AP view X-Ray of the femur (Fig. 1).

The aim of our study is to evaluate the possible association among low values of FCI, risk factors, comorbidities, and serum 25-hydroxyvitamin D levels in patients with hip fracture.
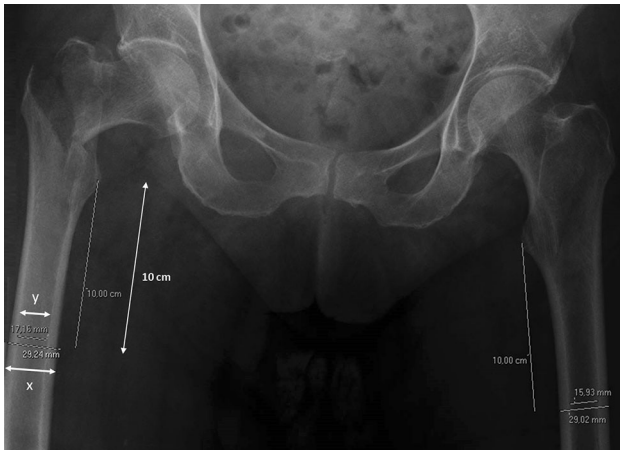
Fig. 1 FCI is calculated using diameter of the shaft (x) and the internal diameter of medullary canal (y). FCI is obtained through the ratio between thickness of cortical bone (x–y) and diameter of femoral shaft (x) measured 10 cm distal to the center of the small trochanter in an AP view X-Ray of the pelvis, on fractured femur and on the opposite side

Materials and methods

We have conducted a retrospective study on 152 consecutive patients (45 men and 107 women) surgically treated for hip fractures from October 2013 to January 2015. Average age was 79.4 years (range 51–106 years). Inclusion criteria were a fragility fracture of femur, absence of primary and secondary tumor lesions, and the ability to walk before falling. Among these patients, 70 of them showed medial fractures treated with hip prosthesis and 82 patients showed lateral fractures treated with reduction and fixation with intramedullary nail. Radiogrammetric measurements were performed on fractured femur in the pelvis AP view of routine clinical digitalized radiographs executed in the Emergency Department. We have excluded all patients with bone cortical alterations on the level of the measurement, such as dysplasia, Perthes disease, epiphysiolysis, and consequences of previous fractures [17]. We have excluded also patients with neurological diseases that could impair deambulation or functionality of the lower limbs. We calculated also FCI on the opposite side except in hip arthroplasty or an intramidullary nail patients. For each patient, we analyzed the presence of comorbidities (diabetes, hypertension, CKD, rheumatoid arthritis), previous fragility fractures, body mass index (BMI), osteoporosis risk factors (cigarettes smoking, early menopause, corticosteroid treatment, family history of hip fragility fractures), and blood levels of vitamin D, usually evaluated in our patients with fragility fractures. Conditions of "deficiency" and "insufficiency" of vitamin D are defined by following ranges of 25(OH)D levels: less than 20 and 20–30 ng/ml, respectively [18]. The diameter of the shaft (x) and the internal diameter of the medullar canal (y) were measured 10 cm distal from

the center of the small trochanter, using an image processing software (Carestream Solutions Version 11.0) (Fig. 1). The FCI was calculated using the following formula: FCI = $(x–y)/x$. The average of two measurements made by two different investigators has been calculated for each femur. Lumbar spine and nonfractured femur bone mineral density (BMD) were also evaluated few days after surgery by iDXA (Lunar, GE Healthcare, Diegem, Belgium). DXA examination was performed to estimate a possible condition of osteoporosis, according to WHO criteria; lumbar spine (L1–L4) and femoral (neck and total) scans were performed [19]. Patients were discharged with adequate anti-osteoporotic therapy and integration of calcium and vitamin D, regardless of value of DXA examination and cortical index, since the presence of proximal femur fracture for a low-energy trauma is an index of bone fragility [20]. The anti-osteoporotic therapy was adapted to patient and to individual factors.

Differences among data were analyzed, and their significance was evaluated by Student's t test. In general, P values less than 0.05 were considered statistically significant.

Results

Average values of cortical index were 0.42 (range 0.18–0.58) at fractured femur and 0.48 at the opposite side (range 0.25–0.66) with a statistically significant difference ($p = 0.002$) (Table 1). At fractured side, an average value of 0.45 was found in men (range 0.21–0.58) and 0.40 in women (range 0.18–0.52); significant differences in mean cortical thickness were found between female and male ($p = 0.032$). No significant differences in FCI were seen between patients 75 years of age or below and those above 75 years ($p > 0.05$).

Patients with severe hypovitaminosis D (serum concentration < 12 ng/ml) had a minor FCI compared to those with a moderate deficiency (0.41 vs. 0.46, $p = 0.011$) [21].

In patients with osteoporosis risk factors, average values of cortical index were 0.41 (range 0.18–0.56); these values are lower than those in patients without risk factors (0.45, range 0.24–0.58) but without a statistically significant difference ($p = 0.578$).

In Table 2, there are the most frequent comorbidities found in patients selected for the study. We divided patients into two groups according to the number of their comorbidities: in the first group, including patients with at most one comorbity ($n = 43$), values of FCI were 0.51 (range 0.23–0.58); in the second group, including patients with 2 or more comorbidities ($n = 109$), values of FCI were 0.42 (range 0.18–0.50), with a statistically significant difference ($p = 0.012$).

Table 1 FCI and BMD mean values and standard deviation (SD) in different groups and their significance

FCI values ± SD—group of patients			
Femur	Fractured: 0.42 ± 0.11	Contralateral: 0.48 ± 0.09	$p = 0.002$
Sex	Men: 0.45 ± 0.10	Women: 0.40 ± 0.11	$p = 0.032$
Age	Under 75: 0.48 ± 0.16	Over 75: 0.44 ± 0.13	$p > 0.05$
Hypovitaminosis D	Severe: 0.41 ± 0.08	Moderate: 0.46 ± 0.10	$p = 0.011$
Risk factors	Positive: 0.41 ± 0.16	Negative: 0.45 ± 0.12	$p = 0.578$
Comorbidities	<2: 0.51 ± 0.11	>2: 0.42 ± 0.10	$p = 0.012$
T-score and BMD values ± SD—group of patients			
Age	Under 75: −1.7 ± 0.9	Over 75: −2.1 ± 1.2	$p > 0.05$
Sex (on spine BMD)	Men: −1.2 ± 0.7 (BMD mean value: 1.056)	Women: −1.8 ± 0.9 (BMD mean value: 0.973)	$p > 0.05$
Sex (on femur BMD)	Men: −1.8 ± 0.4 (BMD mean value: 0.998)	Women: −2.3 ± 0.7 (BMD mean value: 0.864)	$p = 0.034$

Table 2 The most frequent comorbidities found in selected patients (number and percentage)

	n°	%
Hypertension	95	62.5
Type 2 diabetes	51	33.6
Chronic kidney disease	18	11.8
Thyroid disease	15	9.9
Rheumatoid arthritis	14	9.2
Chronic obstructive pulmonary disease	14	9.2
Depression	8	5.3
Parkinson's disease	5	3.3
Inflammatory bowel diseases	4	2.6
Others	21	13.8

Average densitometric values of the lumbar spine were −1.2 and −2.1 at the femoral neck, respectively. No significant differences in the BMD were seen between patients aged 75 years or below and those above 75 years ($p > 0.05$). Male patients showed a significantly higher femoral neck BMD than female (−1.8 vs. −2.6, $p = 0.034$), while no significant differences in BMD were found for the lumbar spine ($p > 0.05$). According to WHO criteria, we identified 64 patients with BMD values indicative of osteoporosis, 77 with BMD values indicative of osteopenia, and 11 patients with normal BMD. Low values of FCI were found in 37 patients (57.8 %) in the osteoporotic group, in 40 patients (51.9 %) in the osteopenic group, and in 2 patients (18.2 %) in the group with normal BMD.

Discussion

FCI was initially proposed for the selection of cemented vs cementless fixation of femoral component in total hip arthroplasty. Dorr used femoral shape and cortical thickness to choose a cemented or cementless prosthetic implant [22]. Although such indices describe the morphology of the proximal femur, they were also linked to hip bone quality. Lower FCI values have been associated with aging and osteoporosis. It is well known that with osteoporosis advancement, widening of the endosteal diameter and thinning of the cortices over the diaphyseal region of the long bones can be observed in plain radiograph [23]. Ahlborg et al. had been following 112 women who were premenopausal at baseline for 18 years [24]. They reported that BMD decreased by 1.7 % per year and the endosteal diameter increased by 0.9 % per year after menopause. They also mentioned the cortical bone thinning, but the latter was not actually measured. The BMD loss showed significant correlation with expansion of the medullary canal. DXA, according to the World Health Organization, is still the gold standard method for measurement of BMD at the lumbar spine and proximal femur, but it cannot discriminate cortical and cancellous bone in terms of structure. In elderly subjects, structural changes such as vascular calcifications, scoliosis, and degenerative arthritis in the posterior elements of the spine may falsely increase BMD at the spine and therefore limit its utility [25]. Thus, in these subjects, osteoporosis may be underestimated if assessed by lumbar spine BMD. For this reason, diagnosis of osteoporosis and assessment of fracture risk in elderly should be based on hip BMD and not on spine BMD. Furthermore, in the presence of some comorbidities, BMD values do not reflect the real fracture risk. In fact, an increased risk of osteoporotic fracture in type 2 diabetes has been repeatedly demonstrated and this was independent of BMD [26]. Cortical porosity observed in type 2 diabetes patients provides a potential explanation for the inability of DXA to detect elevated fracture risk in these patients presenting higher BMD levels. Moreover, hypertension has been postulated as a risk factor for fracture, but association between hypertension and fracture is independent of BMD [27].

Therefore, a method that can provide information about the architecture of the bone and thus on its strength, regardless of bone density, could be very useful. Cortical index is a valid and economic technique that, through a simple X-ray, allows to evaluate the structure of some specific bone segments at high risk of fracture. Genant created a method to assess the vertebral compression fracture, through evaluation of the height of the vertebral body measured at the anterior, middle, and posterior levels. In the same way, the cortical index gives us the way to evaluate the structure of femoral bone quantifying the effect of the osteoporosis on the cortical bone.

In our study, fractured femur showed lower FCI values compared to the healthy contralateral femur. Therefore, a lower FCI in the fractured femur than the contralateral may be a spy of a bone fragility. This is even more important in women, in which values of FCI of the fractured femur are significantly lower than in men. In fractured patients, there is a rotation of the femur due to the action of the extrarotator muscles and some studies have shown that in radiographic images, changes of the canal width of the femur are present only in its proximal part and not in the distal and diaphyseal ones [28, 29].

Cortical index is a valid tool for evaluation in all conditions that determine an alteration of bone quality, such as comorbidities, risk factors, and in particular hypovitaminosis D. The latter condition is particularly common in Italian population, affecting between 50 and 90 % of elderly [30]. A recent article showed how in older men, higher levels of endogenous 25(OH)D may increase whole-bone strength by increasing femoral volumetric BMD and cortical volume [31]. It would be very interesting to assess effects of vitamin D supplementation and of antiosteoporotic therapy on cortical index rather than BMD over time.

Moreover, we found lower values of cortical index of fractured femur (below the average of 0.42) in 42 patients who had an osteopenic or normal BMD. Therefore, cortical index is an index of bone fragility even in those patients in whom BMD is not osteoporotic. It might therefore be useful to associate evaluation of cortical index with densitometry for a better evaluation of patients at risk of fragility fracture.

Conclusions

Different standard techniques such as DXA or quantitative computed tomography are used to assess BMD as a measure for bone quantity. A 10 % loss of bone mass doubles the risk of a vertebral fracture or results in 2.5 times higher risk of hip fracture [32]. Even though BMD is a widely accepted parameter for assessing bone composition, other factors not captured by densitometry contribute to bone quality as well. The structure and micro-architecture of bone contribute significantly to its mechanical competence. Previous studies have shown that cortical index of various bone sites such as humerus, radius, metacarpals, and femur is an effective predictor in assessing osteoporotic changes in bone. FCI represents an easy, valid, and economic tool to assess the bone quality of the proximal femur on the basis of plain hip X-rays. In our opinion, it is important to prescribe therapy for osteoporosis in all patients with femoral fragility fracture, even if they have not critical densitometric values. In fact, the presence of a fragility fracture represents the major risk factor for a subsequent fracture, with rates increasing 2 to 5 times [33]. A very low BMD is an indicator of an high risk of fragility fracture and could represent a condition of impending fracture, suggesting a potential role of preventive femoroplasty [34]. This minimally invasive technique could be more suitable in case of very low FCI values, where a very small cortical thickness could represent an even higher risk of fracture.

Valuing the treatment of postmenopausal patients without history of fractures, it is necessary to perform a careful assessment of fracture risk, which may use clinical-anamnestic and densitometric data and even the estimate of cortical index. Research in drug development is focusing on new and more "physiological" approach to balance bone remodeling. The efficacy of some antiresorptive drugs was proved in the prevention of vertebral and non-vertebral fractures and is related to the ability of the drug to penetrate in cortical and trabecular bone [35]. Recently, data from several clinical studies, confirm that antiosteoporotic drugs improve fracture outcomes, also in rich cortical bone skeletal sites.

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