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Multiple loading conditions analysis can improve the association between finite element bone strength estimates and proximal femur fractures: A preliminary study in elderly women

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ABSTRACT

This is a preliminary case–control study on osteopenic/osteoporotic elderly women, testing the association of proximal femur fracture with minimum femoral strength, as derived from finite element (FE) analysis in multiple loading conditions.

Fracture cases ($n = 22$) in acute conditions were enrolled among low-trauma fractures admitted in various hospitals in the Emilia Romagna Region, Italy. Women with no history of low-trauma fractures were enrolled as controls ($n = 33$). Patients were imaged with DXA to obtain aBMD, and with a bilateral full femur CT scan. FE-strength was derived in stance and fall configurations: (i) as the minimum strength among those obtained for multiple loading conditions spanning a domain of plausible force directions, and (ii) as the strength associated to the most commonly used single loading conditions. The association of FE-strength and aBMD with fractures was tested with logistic regression models, deriving odds ratios (ORs) and area under the receiver operating characteristic curve (AUC).

FE-strength from multiple loading conditions better classified fracture cases from controls (OR per SD change = 9.6, 95% CI = 3.0–31.3, AUC = 0.87 in stance; OR = 9.5, 95% CI = 2.9–31.2, AUC = 0.88 in fall) compared to aBMD (OR = 3.6, 95% CI = 1.6–8.2, AUC = 0.79 for total femur aBMD), while FE-strength results from the most commonly used single loading conditions were similar to aBMD. Only FE-strength from multiple loading conditions remained significant in age- and aBMD-adjusted models (OR = 10.5, 95% CI = 1.8–61.3, AUC = 0.95).

In summary, we highlighted the importance of considering different loading conditions to identify bone weakness, and confirmed that femoral FE-strength estimates may add value to aBMD predictions in elderly osteopenic/osteoporotic women.

Introduction

Osteoporosis is a condition characterised by compromised bone strength predisposing to an increased risk of fracture. In the year 2000, there were an estimated 9 million osteoporotic fractures worldwide, 1.6 million of which affected the hip [1]. The risk of bone fracture is currently estimated by measuring the areal bone mineral density (aBMD) as measured by dual-energy absorptiometry (DXA). However, BMD allows only a limited evaluation of the mechanical determinants of bone fracture [2,3].

Finite element (FE) models from computed tomography (CT) data, which can better model the personalised mechanical determinants of fracture, include bone three dimensional geometry, bone tissue quantity and distribution and, finally, bone loading [4]. These models have often been proposed to overcome aBMD limitations and CT-based FE models have been extensively validated in vitro [5–10]. They consistently showed a better performance compared to BMD in the prediction of proximal femur strength in vitro [4,11]. The first in vivo applications

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of CT-based FE models of the proximal femur have recently been reported in case–control clinical studies of bone fractures. They generally confirmed the potential of CT-based FE models by showing a higher relative difference (compared to aBMD) of the average FE-derived strength between cases and controls [12,13]. Among the three studies that reported an individual classification of cases and controls based on FE-derived strength, two [13,14] could not give conclusive evidence of a clear superiority compared to BMD measurements, while the most recent and largest study [15] found a significantly higher association of fractures and FE-derived strength.

There are reasons to envisage further improvements of FE-derived strength performance. Almost all published studies focused on the simulation of a single loading condition, mimicking either the stance phase of gait or an unprotected fall to the side. Some authors [13] have already expressed the need for a wider consideration of the loading component, among bone fracture determinants. Evidence of result differences emerged in the only study where three fall loading conditions were simulated [16]. We hypothesise that the simulation of multiple loading directions, among those admissible, in order to identify the weakest structural condition of the proximal femur (the minimum strength), could improve the association of FE-derived bone strength with fracture.

The aim of the present work was to verify, in a preliminary case–control study of acute fractures in elderly women, whether the association of FE-derived bone strength with fracture status can be improved by taking into account multiple loading conditions, and how this compares with aBMD.

Materials and methods

Patients

The data were generated from the clinical arm of the project “Advanced diagnostics in osteoporosis with predictive models of the risk of fracture in elders” of the Emilia Romagna Region-University Program in Italy. All patients gave their written informed consent to the participation in the study. The clinical protocol was submitted and approved by the local ethical committee.

The performance of FE-derived strength and aBMD indicators was tested on a cohort of postmenopausal women, aged over 60. Fracture cases were enrolled among women admitted to the hospital with a diagnosis of a low-trauma acute fracture of the proximal femur. Women with no history of previous low-trauma fracture attending a routine densitometry examination formed the control group.

Fracture cases were enrolled in three clinical centres of the Emilia Romagna Region, Italy: Istituto Ortopedico Rizzoli (IOR) in Bologna (30 patients, June 2010–January 2012), Orthopaedics and Traumatology Unit of the Ravenna-Lugo-Faenza Hospitals (10 patients, November 2010–April 2012) and Locomotor Apparatus Pathology Department, University of Parma (10 patients, March 2011–December 2011). Control cases were all enrolled at the referral centre for densitometry of IOR (92 patients, June 2010–May 2011).

The exclusion criteria were: body mass index (BMI) lower than 18 or higher than 33, central nervous system disease, cancer, chronic inflammatory conditions (e.g. rheumatoid arthritis), primary hyperparathyroidism, hyperthyroidism, cardiovascular conditions, diabetes, long term cortico-steroid treatments (more than 3 months), and alcohol intake greater than three units per day. According to these criteria, 20 among the 50 fractured cases and one among the 92 controls (that had been previously subjected to a screening interview) were excluded from the study. Among the remaining 30 fractured cases, 8 patients were not included in the finite element analysis for the following reasons: i) for two patients, the CT scan was not performed; ii) for one patient, the DXA scan was not performed; iii) in three patients, the CT scan was limited to the proximal femur while a full femoral CT scan was requested to identify the loads acting on the femur for the FE analyses; and iv) in two patients, a hip prosthesis produced streak artefacts on the CT images, which could strongly influence the FE results. Among the 91 controls, CT scan was performed only on 33 patients.

A total of 55 patients (22 cases and 33 controls) were therefore analysed. Fracture cases included 10 trochanteric, 8 sub-capital, 1 medio-cervical, and 3 basi-cervical fractures according to Garden's classification. All women enrolled, with the exception of three, were osteopenic or osteoporotic according to DXA T-score (mean -2.39, SD 0.94, min 4.62, max 0.10). Mean height, weight and body mass index (BMI) were not significantly different between cases and controls (p-values 0.400, 0.904 and 0.783 respectively), while age was significantly different (p-value < 0.0001) (Table 1).

Imaging

All patients received a DXA scan (IOR: Norland XR36; Parma: Hologic QDR4500A; Faenza: Lunar Prodigy Primo) from which aBMD values (g/cm^2) in the femoral neck (aBMD$_{\text{neck}}$), total femur (aBMD$_{\text{total}}$) and trochanteric (aBMD$_{\text{troch}}$) regions of interest were calculated. The DXA scan was performed on the left femur for the controls and on the remaining intact femur for the cases.

All patients received a bilateral full femoral CT scan (IOR: Brightspeed, GE Medical Systems, USA; Parma: Somatom Emotion, Siemens, Germany; Faenza: Brilliance 6 and Brilliance 16, Philips, The Netherlands). An optimised CT scan protocol was used [17] with a slice thickness of 2 mm in the regions with high morphological and density gradients (proximal and distal epiphysis), and a thickness of 4 mm in the diaphysis. All scans were performed at 120 kVp, while tube current was constant for each patient and varied among patients between 120 and 180 mAs. Densitometric calibration was obtained at all sites with the European Spine Phantom (ESP) [18].

DXA and CT scans on fractured patients were performed within 4 days from the fracture event. Only in three cases the DXA exam was performed 30–45 days after the fracture event due to technical problems with the DXA scanner.

FE-strength calculation

The FE-strength was estimated for each patient from the CT images, with a procedure validated in the prediction of bone strains [19], bone failure characteristics [10] and bone failure load [20]. The controls' FE-strength was computed for the right and left femur (^{R}FE and ^{L}FE) and for the remaining intact femur in fracture cases. FE-strength was evaluated in multiple loading conditions, taking into account a large variability of quasi-axial (i.e. resembling the hip joint reaction force, also known as “stance”) and sideways-fall loading directions. FE-strength in stance position (FE$_{\text{stance}}$) was the minimum strength among those obtained for 12 plausible quasi-axial loading directions. Similarly, FE$_{\text{fall}}$ was the minimum strength among those obtained for 10 different sideways-fall loading directions.

To fully characterise the variability in predicted bone strength under loading conditions, and its correlation with fracture, FE-strength estimates in all loading configurations, taken singularly, were also derived. Results from the one specific “stance” and one specific “fall” conditions that are most similar to those reported in published studies were

Table 1
Descriptive statistics of the patients' cohort, divided in fracture cases and controls.

	All	Cases (n = 22)	Controls (n = 33)	p-Value
	Mean (SD) *[min, max]*	Mean (SD) *[min, max]*	Mean (SD) *[min, max]*	
Age (yr)	73 (8.3) *[61, 88]*	80 (6.2) *[69, 88]*	69 (6.2) *[61, 87]*	<0.0001
Height (cm)	159 (5.6) *[143, 172]*	160 (5.5) *[148, 170]*	158 (5.7) *[143, 172]*	0.400
Weight (kg)	61 (8.3) *[42, 82]*	62 (10.1) *[42, 82]*	61 (7) *[50, 79]*	0.904