

ARE FINITE ELEMENT ESTIMATES OF FEMUR STRENGTH ASSOCIATED WITH FRACTURE? THREE CLINICAL STUDIES

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Introduction

Patient specific modelling of bone segments through Computed Tomography (CT) based Finite Element (FE) models has become an established procedure in computational bone biomechanics research. The long-term aim is translational, i.e. to bring these models to clinical practice. Prerequisites are a thorough in-vitro validation against experimental measurements, and the assessment of in-vivo models performance in clinical studies.

This study will focus on osteoporotic fractures of the proximal femur. In this context, an acceptable in-vitro validation for the prediction of strains and failure load has been reached by several studies, with a surprisingly broad difference in methods. A concern for the clinical translation of several of the proposed methods is their complexity, and the use of internal best fitting to identify model parameters. The first clinical applications of FE estimates of bone strength to classify patients at risk of fracture have been recently published [1,2,3,4]. They report notable discrepancies in results, which warrant further investigation.

In past few years, we developed a simple patient-specific FE modelling procedure [5], fully based on parameters and relationships published in independent studies. This procedure was validated for bone strains, and obtained consistent results in the prediction of failure load and location through linear analyses using a simple maximum principal strain criterion [6].

This work presents the clinical application of this FE model, to classify osteoporotic fractures in three case-control studies of different design: a retrospective and a prospective study on proximal femur fracture, and a retrospective study on prevalent osteoporotic fractures.

Methods

Femur Retrospective Study: 22 women with low trauma proximal femur fractures and 33 controls were enrolled at Rizzoli Institute, Bologna. All patients were osteopenic or osteoporotic. They received full-femur CT (in acute condition for fractured cases) and DXA.

Femur Prospective Study: 21 women and 13 men on which proximal femur fractures were prospectively observed, as well as 45 (women) and 26 (men) age-matched controls were selected from the AGES-Reykjavik Study. For each individual, baseline proximal femur CT scans and DXA-simulated areal bone mineral density (aBMD) from CT were available.

Prevalent Fractures Study: 35 women with a prevalent osteoporotic fracture at any relevant site (e.g. radius, vertebrae) and 40 aBMD-matched controls were enrolled at INSERM Lyon. They were imaged with proximal femur CT scan, and DXA.

FE-analyses: the FE models were generated from CT [5]. Bone strength was defined as the load inducing on the femoral neck surface a $\epsilon_{\max} > \epsilon_{\text{lim}}$ (asymmetric maximum principal strain criterion, 0.73% tensile, 1.04% compressive limit, nodal results averaged over 3 mm around each node to avoid local effects; this procedure yielded a $R^2=0.90$ against experimental failure load on 14 femora). Bone strength was evaluated in a broad range of plausible quasi-axial (stance) and sideways-fall (fall) loading directions to mimic the in-vivo variability of hip reactions and accidental conditions. The whole femur is required to identify load directions. The procedure was adapted when only proximal femur was available. The minimum strength among all stance (FE_s) and fall configurations (FE_f) was retained for patient classification.

Statistics: we tested the ability of FE-strength (FE_s and FE_f) and aBMD to: i) discriminate groups of fractures from controls; ii) individually classify cases at risk through logistic regressions to derive Odds (OR) or Hazard ratio (HR) and Area under ROC Curve (AUC).

Results

Femur Retrospective Study: both FE_s and FE_f showed higher group differences (33%, $p < 0.001$, vs. 12% for aBMD, $p=0.01$) and better classified fractures (AUC=0.88 vs. 0.71 for aBMD). FE_s and FE_f remained associated with fracture in age- and aBMD-adjusted models.

Femur Prospective Study: a sensitivity study revealed that only FE_s was robust to load identification on proximal femur geometry. FE_f was discarded. In women, FE_s showed slightly higher group differences (19%, $p < 0.001$, vs. 15% for aBMD, $p=0.004$), a higher classification of fracture cases (AUC=0.78 vs. 0.72 for aBMD), and FE_s HR kept significance when adjusting for aBMD. In the small men cohort, FEs showed non-significant differences and HR, while aBMD could discriminate groups and classify fractures (AUC=0.76).

Prevalent Fractures Study: fractures and controls did not differ for aBMD, by design. FE_s was 5% lower in fracture cases but the differences were not significant.

Discussion

The results indicated that a simple, linear patient-specific FE model can add complementary value to the standard of care (aBMD) in elderly osteopenic or osteoporotic women, i.e. the population at the highest risk of fracture. Our results are in agreement with [4]. The few results available in men suggest a gender difference in FE predictive ability, but with opposite sign than in [3]. This points to the need of better understanding risk factors other than bone strength (e.g. fall risk) and/or refine bone constitutive modelling. We confirmed that site-specificity is important, since femur models could predict femur fractures, but not prevalent fractures; the aBMD-matched design of that study was very challenging, but our results are not in contrast with [2]. Finally, the good performance of the minimum strength in multiple loading conditions highlighted that a wider consideration of loading conditions (thus, of the whole femoral anatomy) can improve FE model performance.

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