Association of CT-based Finite Element Estimates of Femur Strength with Fracture Status in Three Clinical Studies on Post-menopausal Women

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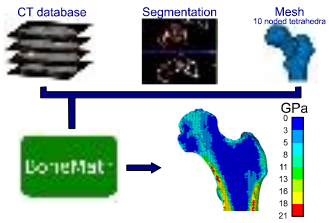
Background and objective

Bone strength estimates from Computed Tomography-based Finite Element models have been recently proposed to classify osteoporotic fractures, with promising but inhomogeneous results among published studies [1,2,3,4].
A comparison among existing studies is not easy since they rely on different methodologies and different study design, which can influence the results, although to an unknown extent.
We recently developed a CT-based FE model that correlates well with femur strength in-vitro (R2=0.9, 14 femurs) [5,6].

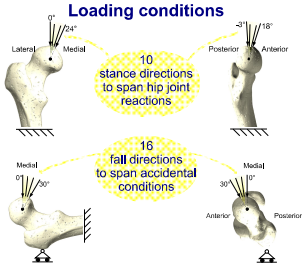
The present study aimed to verify if and to what extent our FE model is associated with osteoporotic fractures in three differently designed case-controls studies in post-menopausal women: a retrospective and a prospective study on proximal femur fracture, and a retrospective study on prevalent osteoporotic fractures. The same association was sought for aBMD, and results compared.

Modelling

From CT to FE model



Loading conditions



Why multiple loading conditions?

- Loads acting on the proximal femur show a high variability both in physiological [7] and accidental [8] conditions
- A-priori selecting a single direction may fail in identifying specific weak features of the femur

Femur strength definition

- Linear model
- Maximum principal strain criterion
  Limit strain= 0.73% tension, 1.04% compression
- Minimum strength concept
  FEstance = minimum strength among all stance loading conditions
  FEfall = minimum strength among all fall loading conditions

Clinical studies

Prevalent fractures

Project: VPHOP
Clinical centre: INSERM Lyon, France
Study design: Case-control study on prevalent fractures with an aBMD-matched control group (p=0.4)
Imaging: DXA and QCT
Fracture group: Low trauma fractures at wrist (n=19), vertebra (n=8), femur (n=1), wrist + vertebra (n=7)
Control group: No history of low trauma fractures
Matched for age, height, weight, AND aBMD

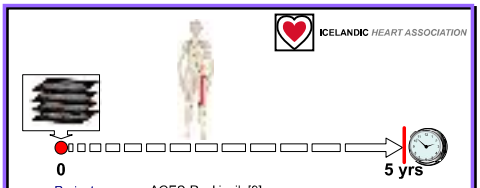
	Cases n=35	Controls n=40	
	Mean (SD)		p=value
Age (years)	73.0 (5.6)	71.6 (6.8)	0.21
Height (cm)	156 (4.9)	158 (6.0)	0.10
Weight (kg)	63 (8.0)	60 (9.0)	0.09

Retrospective

Project: Emilia-Romagna Region-University
Clinical centre: Istituto Ortopedico Rizzoli, Bologna, Italy
Study design: Case-control study; fractures enrolled in acute conditions
All patients osteopenic or osteoporotic, > 60 yrs
Imaging: DXA and QCT within one week after fracture
Fracture group: Low-trauma proximal femur fracture
Control group: No history of low trauma fractures
Matched for height, weight, but NOT age

	Cases n=22	Controls n=33	
	Mean (SD)		p=value
Age (years)	80 (6.2)	69 (6.2)	<0.0001
Height (cm)	160 (5.5)	158 (5.7)	0.400
Weight (kg)	62 (10.1)	61 (7.0)	0.904

Prospective

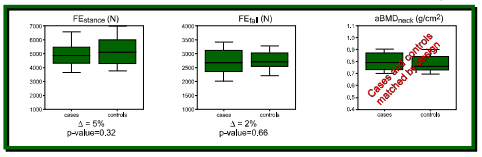


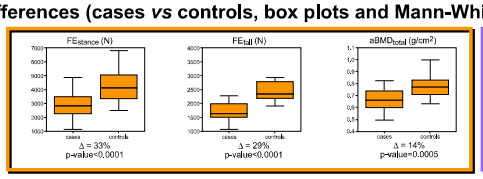
Project: AGES-Reykjavik [9]
Clinical centre: Icelandic Heart Association, Kopavogur, Iceland
Study design: Nested case-control study from a longitudinal prospective study of incident hip fracture
Imaging: QCT at baseline; aBMD simulated from QCT
Fracture group: Proximal femur fractures during 5 year follow-up
Control group: No fractures during 5 year follow-up
Matched for age, height, but NOT weight

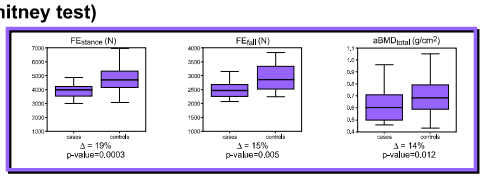
	Cases n=21	Controls n=45	
	Mean (SD)		p=value
Age (years)	79.3 (4.5)	78.3 (4.6)	0.433
Height (cm)	159.2 (5.5)	160.2 (5.2)	0.591
Weight (kg)	61.8 (10.0)	70.9 (15.8)	0.023

Results

Group differences (cases *vs* controls, box plots and Mann-Whitney test)







Fracture classification (Odds or Hazard Ratios and Area Under Curve)

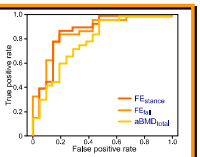
Variables	OR[a] (95% CI)	AUC
Unadjusted models		
FE_{stance}	1.3 (0.8-2.0)	0.57
FE_{fall}	1.1 (0.7-1.8)	0.53
$aBMD_{neck}$	Cases and controls matched by design	

[a]Odds ratio per SD decrease for all variables

Proximal femur FE-strength, though slightly lower in fracture cases (5%) was not significantly associated with prevalent fractures at other skeletal sites

Variables	OR[a] (95% CI)	AUC
Unadjusted models		
FE_{stance}	9.6 (3.0-31.3)	0.87
FE_{fall}	9.5 (2.9-31.2)	0.88
$aBMD_{total}$	3.6 (1.6-8.2)	0.79

[a]Odds ratio per SD decrease for all variables

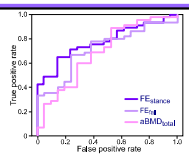


Variables	OR[a] (95% CI)	AUC
Age-adjusted models		
FE_{fall}	8.2 (1.9-35.8)	0.95
$aBMD_{total}$	1.5 (0.6-3.9)	0.90
Age and aBMD-adjusted models		
FE_{fall}	10.5 (1.8-61.3)	0.95

[a]Odds ratio per SD decrease for all variables

Variables	HR[a] (95% CI)	AUC
Unadjusted models		
FE_{stance}	3.2 (1.6-6.4)	0.78
FE_{fall}	2.6 (1.2-3.5)	0.72
$aBMD_{total}$	2.0 (1.1-3.6)	0.69

[a]Hazard ratio per SD decrease for all variables



Variables	HR[a] (95% CI)	AUC
Weight-adjusted models		
FE_{fall}	2.6 (1.3-6.2)	0.78
$aBMD_{total}$	1.8 (0.9-3.2)	0.73
Weight and aBMD-adjusted models		
FE_{stance}	2.6 (1.2-5.6)	0.79

[a]Hazard ratio per SD decrease for all variables

In retrospective and prospective studies FE-strength classified fractures better than aBMD, and remained associated with fracture in models adjusted for the unbalanced variables.

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Conclusions

In postmenopausal women, i.e. the population at the highest risk of bone fracture, our simple FE model was highly associated with proximal femur fracture.

FE-strength estimates from multiple loading conditions add important information to aBMD in classifying proximal femur fractures.

Site-specific use of proximal femur FE models seems crucial, since they are associated with femur fractures, but not with prevalent osteoporotic fracures at other skeletal sites.

References

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Conflict of interest

None to declare