

A51 BONE CELL ACTIVITY INFLUENCES BONE FRAGILITY AND FRACTURE RISK

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Background Osteoporosis is a systemic skeletal disease characterised by low bone mass, deterioration in microarchitecture, increased bone fragility and susceptibility to fracture. Besides structural properties, biological phenomena driven by differential gene expression could also contribute to the individual diversity of the structural and mechanical properties of bone that ultimately are reflected in different risks of fracture. The fracture risk assessment tool (FRAX) is an algorithm that takes into account clinical risk factors for fracture and **dual energy x-ray absorptiometry** results. It has been found to be a useful tool in risk prediction, but the structural, mechanical and biological properties of bone that it implicitly translates are unknown. The aim of this study is to evaluate the impact of bone biological parameters on bone strength and fracture risk calculated by the FRAX tool.

Methods Patients submitted to hip replacement surgery were consecutively recruited. The patients were evaluated for clinical risk factors for fracture and FRAX was calculated. Bone was collected and trabecular bone cylinders were cut in order to perform mechanical tests of compression in a universal mechanical test machine (Instron Corporation, Norwood, Massachusetts, USA) to analyse bone strength. RNA was extracted from a small trabecular bone piece and expression of genes involved in bone cell metabolism was assessed by quantitative real-time PCR.

Results Thirty-three patients aged 75±8 years were analysed. 63% referred a previous fracture, 7% had a family history of fracture and 4% had secondary osteoporosis. The average bone mineral density (BMD) was 0.7±0.1 g/cm³. The probability of a major osteoporotic fracture as calculated by FRAX was 19.4±13.0%. As expected, BMD and FRAX showed a strong negative correlation (p<0.001) and FRAX was positively associated with bone strength. Osteoprotegerin correlated positively with BMD (p<0.05) and negatively with the probability of fracture (p<0.05). On the other hand, receptor activator for nuclear factor κB ligand showed a positive correlation with the FRAX score (p<0.05) but no association with BMD or bone strength. In addition, cbfa1 and osterix, two genes involved in osteoblast differentiation, were found to be negatively correlated with the FRAX score (p<0.05). Cbfa1 was also positively

correlated with BMD ($p < 0.05$) and demonstrated a trend for a positive association with bone strength.

Conclusion These results indicate that bone cell activity influences bone strength. Moreover, we have documented for the first time that fracture risk calculated by FRAX also translates bone biological behaviour. Thus, the FRAX score has both an epidemiological and a biological basis. This can have future significant consequences for establishing a FRAX score threshold for treatment decision-making.