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BONE QUALITY: HOW DO WE ASSESS IT?

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Bone strength is determined by a number of inter-related variables which include bone mineral density, bone geometry and bone quality. The latter consists of bone turnover, bone microarchitecture, the degree of mineralisation of bone, microdamage and its repair, and the composition of bone mineral and matrix. Of these, bone turnover is the most important and is a major determinant of other components of bone quality. Whilst bone mineral density (BMD) is a strong predictor of bone strength and hence fracture risk in the untreated state, therapeutically induced changes in BMD explain only a small proportion of the associated reduction in fracture, indicating that changes in bone quality may be more important in this context.

The importance of the components of bone quality is evident from disease states in man, some of which are associated with increased fracture risk despite increased bone mineral density and even bone size. Thus increased bone fragility is seen at both extremes of mineralization, in the conditions of osteomalacia and osteopetrosis respectively. In bone exposed to supra-therapeutic doses of sodium fluoride, mineralisation of osteoid may be defective and the composition of hydroxyapatite is altered due to substitution of fluoride for the hydroxyl group; these changes are associated with reduced biomechanical strength of bone and increased fracture risk at appendicular skeletal sites. Multiple abnormalities of bone quality are seen in Paget's disease, including an abnormal bone matrix with a mosaic of lamellar and woven bone, abnormal mineralisation and alterations of bone microarchitecture. Osteogenesis imperfecta provides an example of a condition in which the primary defect is a relatively subtle alteration in type 1 collagen synthesis, with secondary changes in mineralisation. Finally, several lines of evidence support the contention that high bone turnover is an independent determinant of bone strength and fracture risk. However, whether the converse is true, i.e. that low bone turnover per se is associated with changes in bone fragility remains to be established.

Assessment of bone quality in clinical practice is currently limited to measurement of biochemical markers of bone turnover. Whilst these have utility in clinical trials, their value in individual patients is limited by the high biovariability of markers and their measurement variance. Moreover, biochemical markers of resorption and formation reflect whole body bone turnover and may not be sensitive to regional changes, particularly where these predominantly affect cancellous bone.

A number of non-invasive techniques are emerging that may lead to improvements in the assessment of bone quality in clinical studies. These include high resolution peripheral quantitative computed tomography (pQCT) and high-resolution magnetic resonance imaging (MRI); in addition, assessment of regional osteoblastic activity using ^{18}F -fluoride positron emission tomography provides a potential means by which regional bone turnover could be assessed in both the axial and appendicular skeleton. Currently, however, bone biopsy remains the most powerful tool for studying bone quality in clinical studies and its use should be more actively encouraged, particularly in the context of the effects of pharmacological interventions on bone.