Mitochondrial DNA point mutation is associated with lower bone turnover markers

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Introduction
We previously showed that the mitochondrial DNA point mutation m.3243A>G is associated with lower BMD and altered bone structure.

The aim of this study was to assess biochemical bone turnover markers in individuals with the mutation and controls.

Background
Mitochondrial dysfunction is implicated in the human ageing process and is associated with several clinical outcomes including diabetes, myopathy, and hearing loss.

Mitochondrial dysfunction causes increased levels of reactive oxygen species and oxidative stress, which is associated with: increased apoptosis of osteoblasts and osteocytes4; increased osteoclastogenesis5; BMD negatively correlated with oxidative stress in postmenopausal women5.

Mitochondrial dysfunction could affect purinergic signalling, which is involved in parathyroid hormone signalling, osteoclast fusion and bone cell response to mechanical stimuli of the bone6.

Mitochondrial mutations cause osteoporosis in mouse models and affect both osteoblasts, osteocytes and osteoclasts7,8.

I humans mitochondrial dysfunction may be associated with subclinical disturbances in calcium metabolism, i.e. basal ganglia calcifications and hyperparathyroidism2,6.

Materials and methods
Patients:
45 subjects carrying m.3243A>G.
45 healthy controls matched with respect to sex, age, height and menopausal status.

Examinations:
• Dual-energy X-ray Absorptiometry (DXA).
• High-Resolution peripheral Quantitative Computed Tomography (HR-pQCT).
• Biochemical markers of bone turnover, i.e. CTX and P1NP.

Conclusion and perspectives
We have previously shown that carriers of the m.3243A>G mitochondrial mutation had lower bone mineral density and thinner cortical bone assessed by HR-pQCT scan and additionally decreased estimated bone strength.

In the present study we have shown that mitochondrial dysfunction is associated with lower levels of biochemical bone turnover markers. These results can possibly in part be explained by lower body mass and diabetes, however the difference in s-P1NP, but not s-CTX, remained significant after adjusting for weight and sex. Stratifying according to DM-status s-CTX and s-P1NP was significantly lower in cases with DM compared to their controls, whereas levels of bone turnover markers were the same in non-DM cases and their controls.

Further studies are needed to describe the effects of mitochondrial dysfunction on bone remodelling.

Results – Bone turnover markers

Results – DXA scan

Results – HR-pQCT scan

Results – HR-pQCT scan

Results – DXA scan

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