The Association between Metabolic Syndrome, Bone Mineral Density, Hip Bone Geometry and Fracture Risk: The Rotterdam Study

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Objectives

1. We examined whether metabolic syndrome (MS) was associated with femoral neck bone mineral density (FN-BMD), hip bone geometry (HBG) parameters and osteoporosis in females and males using a cross-sectional design.
2. We aimed to determine whether MS predicts FN-BMD, and incident fractures using a longitudinal design.
3. We examined whether these associations were independent of body mass index.

Background

Different factors have been associated with osteoporosis including abdominal obesity, hypertension, dyslipidemia and abnormal glucose metabolism, which are considered components of metabolic syndrome (MS). However, whether MS is associated with bone health remains unclear. Furthermore, recently, a new cluster of criteria for diagnosis of MS had been presented, but has not been adequately studied in relation to bone.

Methods

Data of 2040 women and 1510 men participants in the third visit (1997-1999) of the Rotterdam Study (RSI-3), a prospective population based cohort, were available (mean follow-up 6.7 years).

» MS was defined according to the new criteria announced by a joint scientific statement from the International Diabetes Federation (IDF), the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI), World Heart Federation, International Atherosclerosis Society and International Association for the Study of Obesity.

» HBG parameters were measured at the third round visit whereas FN-BMD was assessed at the third round and 5 years later.

» Multivariable (linear and logistic) regression models were used to examine the cross-sectional association of MS with FN-BMD, HBG and osteoporosis.

» Cox proportional hazard models were used to study the association of MS with fracture risk.

» All associations were corrected for age, height, smoking status, physical activity, alcohol intake, fallings in the last 12 months, use of diuretics drugs, use of hormone replacement therapy, use of corticosteroids drugs, use of drugs for bone and other musculoskeletal diseases, Dutch Healthy Diet Index and body mass index.

» All analyses were conducted separately for men and women because of gender differences in MS and bone parameters.

» To correct for multiple testing, a two-tailed *P* value of 0.025 or less was considered as statistically significant.

Results

The association of MS with FN-BMD, hip bone geometry parameters and osteoporosis.

» Individuals with MS had lower bone width (β= -0.054, *P*=0.003), lower cortical buckling ratio (β= -0.81, *P*=0.003) and lower odds of having osteoporosis (odds ratio=0.56, *P*=0.007) in women but not in men. No association was found for other HBG parameters in either gender.

» MS was associated with higher FN-BMD only in women (β= 0.028, *P*=0.001).

The association between MS and incident fracture risk.

» No association was observed between MS with fracture risk.

Conclusions

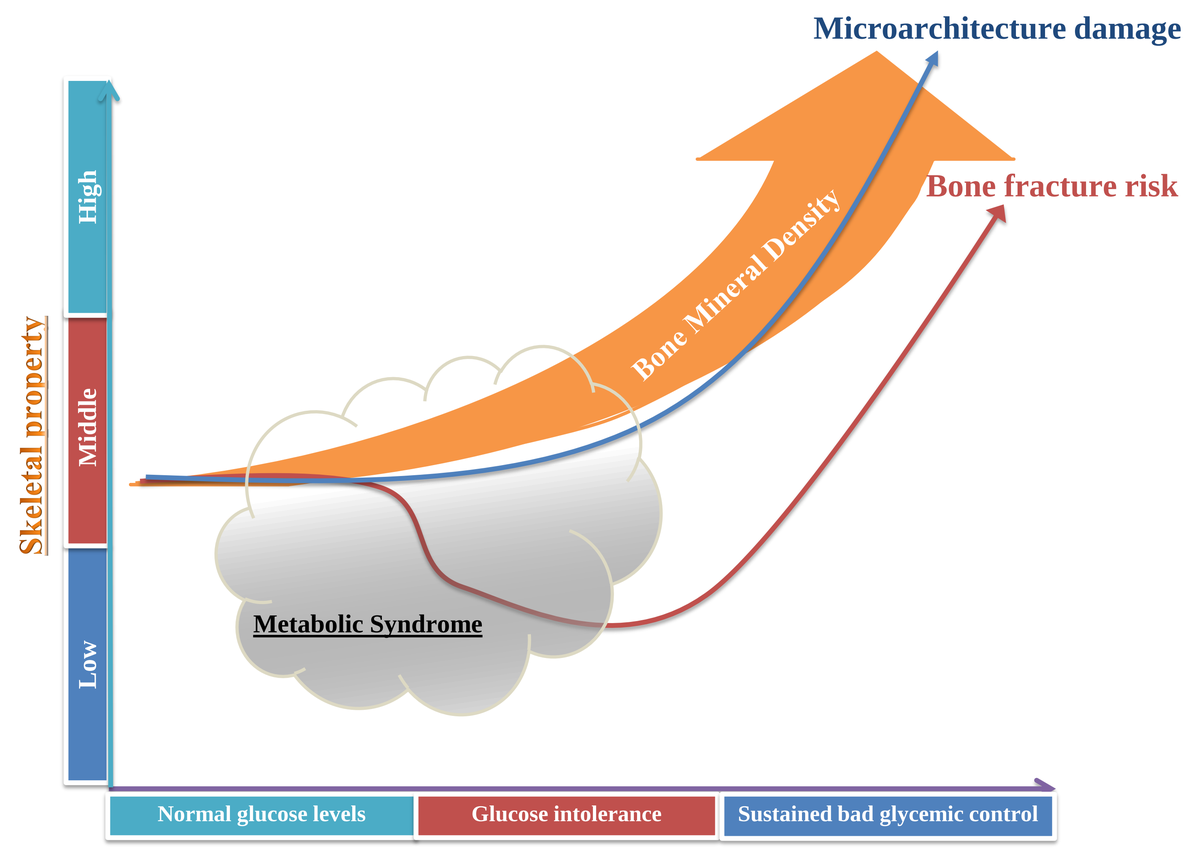
1. Females with MS, have significantly higher BMD, narrower bone at the hip, and increased bone instability (lower buckling ratio), lower odds of having osteoporosis than non-MS individuals, which was independent of BMI.
2. In males, the positive association of MS with BMD and hip bone geometry were masked by BMI.
3. There was no association between MS and the risk of fracture in either gender
4. Our results highlight the importance of maintaining glycemic control in individuals with MS to pervert skeletal complications and preserve bone health.

Table 1 The association of individually components of metabolic syndrome with bone mineral density

Women			Men		
Metabolic syndrome component (Yes vs. No)	**FN-BMD**	**P-value**	**Metabolic syndrome component (Yes vs. No)**	**FN-BMD**	**P-value**
Waist Circumference: β, 95% CI	-0.013 (-0.029; 0.002)	0.098	Waist Circumference: β, 95% CI[1]	-0.030 (-0.05; -0.01)	0.004
Triglyceride: β , 95% CI	0.005 (-0.009; 0.019)	0.47	Triglyceride: β , 95% CI[2]	0.004 (-0.01; 0.02)	0.66
HDL-cholesterol: β , 95% CI	0.013 (0.001; 0.027)	0.01	HDL-cholesterol: β , 95% CI[3]	-0.010 (-0.028; 0.008)	0.29
Glucose :β , 95% CI	0.016 (0.004; 0.028)	0.01	Glucose :β , 95% CI[4]	0.022 (0.007; 0.0037)	0.004
Blood pressure: β , 95% CI	0.003 (-0.010; 0.016)	0.64	HTA: β , 95% CI[5]	-0.014 (-0.032; 0.004)	0.13

In the analyses of MS components, the glucose component (unrelated to diabetes status) was positively associated with FN-BMD in both genders (β= 0.016, P=0.01 for women and β= 0.022, P=0.004 for men). In women, HDL-cholesterol was positively associated with FN-BMD ((β= 0.013, P=0.01) In men, waist circumference was inversely associated with FN-BMD (β= -0.03, P=0.004).

Figure 1 Level of glycemic derangement, bone architecture and fracture risk.



The Cartoon depicting the differences in bone mineral density, fracture risk and changes in bone microarchitecture across the stages of glucose derangement. Metabolic syndrome and diabetes mellitus individuals have higher BMD but do not experience yet an increase in fracture risk. With sustained bad glycemic control, the damage of bone microarchitecture represented by accumulation of microcracks and cortical porosity becomes a possibility which may explain the bone fragility and fracture susceptibility despite the observed increase in BMD. Drawing is not to scale.

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