Biochemical bone markers of bone turnover in diabetes patients -a meta-analysis.

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Background

Diabetes is a common disease with multiple potential complications including an increased risk of fractures.

The increased fracture risk is not entirely explained by bone mineral density measurements, thus biochemical bone markers may be of importance.

Aim

To study existing literature on biochemical markers of bone turnover in diabetes patients compared to controls and conduct a meta-analysis on the findings determining whether bone markers differ among diabetes patients.

Methods

- A systematic literature search was conducted using: Pubmed, Embase, Cinahl and Svemed+
- Search terms included: "Diabetes mellitus", "Diabetes mellitus type 1", "Insulin dependent diabetes mellitus", "Diabetes mellitus type 2", "Non insulin dependent diabetes mellitus", "Bone", "Bone and Bones", "Bone diseases", "Bone turnover".
- Eligibility criteria: Examination of biochemical bone turnover among diabetes patients and controls. Study design: Cross-sectional, cohorte, case-control and randomised controlled trial. Studies must not assess the effect of different medications on bone markers.
- Search results: 1,188 records with no duplicates were screened by title and abstract and 75 records were assessed by full text for inclusion. After screening, 22 records fulfilled the criteria for the meta-analysis.
- Data analysis: Revman and Stata 8 was used in the data analysis. I^2 determined heterogeneity and Random Effects Model was used in the pooled analysis.

Results

From the pooled data in the meta-analysis:
- Diabetes patients had lower: Osteocalcin (p<0.01), CTX (p<0.01), and 25-hydroxy vitamin D.
- Diabetes patients had higher : Alkaline phosphatase (p<0.01).
- Following markers were not different among diabetes patients: Bone specific alkaline phosphatase ,deoxypyridinoline, NTX, and C1CP, PTH, and serum calcium.
- In a metaregression analysis age, BMI, and gender determined the osteocalcin levels.
- All markers displayed very high heterogeneity by I^2 statistics. No publication bias was present (analyses by funnel plot).

Pooled analysis				
Biochemical marker	Number of populations in the analysis	I^2	Pooled estimate (95% CI)	P
Vitamin 25 OHD (ng/ml)	**12**	**97 %**	**-11.14 (-20.13;-2.15)**	**0.02**
Calcium (mg/dl)	13	85 %	-0.01 (-0.05;0.02)	0.54
PTH (pg/dl)	20	95 %	-1.03 (-4.47;2.41)	0.56
Alkaline Phosphatase (U/L)	**9**	**100 %**	**16.37 (12.47;20.27)**	**<0.0001**
Bone specifik alkaline phosphatase (U/L)	7	100 %	-0.82 (-3.34;1.71)	0.53
Osteocalcin (ng/ml)	**27**	**100 %**	**-1.15 (-1.78;-0.52)**	**0.0003**
CICP (ng/ml)	3	84 %	-12.68 (-52.8;27.43)	0.54
CTX (ng/ml)	**11**	**95%**	**-0.14 (-0.22;-0.05)**	**0.002**
U-NTX (nM/mM crea)	6	99 %	15.44 (-0.74;31.62)	0.06
Deoxypyridinoline (nM/mM crea)	7	95 %	-0.01 (-0.175;0.173)	0.99

Metaregression analysis			
Variable	Calcium	PTH	Osteocalcin
Diabetes (type 1/2)	-0.02 (-0.53, 0.49)	-	-
Age (years)	0.01 (-0.01, 0.010)	0.44 (-7.45, 8.34)	**0.37 (0.25, 0.49)**
Gender (male vs. Female)	-0.34 (-0.77, 0.09)	28.20 (-85.49, 141.89)	**38.73 (33.36, 44.11)**
HbA1c (%)	-0.02 (-0.13, 0.10)	3.03 (-10.04, 16.08)	-1.33 (-3.06, 0.41)
BMI (kg/m^2)	0.01 (-0.02, 0.03)	-.16 (-13.17, 12.84)	**-0.82 (-1.23, -0.40)**
Diabetes duration (years)	-	-2.84 (-12.63, 6.95)	-

Values are regression coefficients (95 % CI). Bold indicates significance (P<0.05).

Conclusion

We found a dissociative pattern of biochemical bone markers of formation and resorption in diabetes patients.

We speculate that this may be due to glycation of bone markers and altered configuration of these, thus disrupting the measurements. This could imply that biochemical markers of bone turnover are less reliable in patients with diabetes.