

INCREASED OSTEOCLAST ACTIVITY IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES MELLITUS (T1DM) INDICATED BY HIGHER LEVELS OF OSTEOPROTEGERIN AND S-RANKL MAY PREDISPOSE TO LOWER BONE MASS

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Background: Several bone metabolic pathways seem to be disrupted in patients with type 1 diabetes mellitus (T1DM), leading to reduced bone mass.

Objective and hypotheses: Our aim was to study bone metabolism markers in children and adolescents with T1DM and their correlation with Bone Mineral Density (BMD).

Methods: We evaluated 40 patients (mean±SD age 13.04±3.53 years, mean±SD T1DM duration 5.15±3.33years) and 40 healthy age- and gender-matched controls (mean±SD age 12.99±3.3years). Osteoprotegerin (OPG), Receptor Activator of Nuclear factor-KappaB Ligand(s-RANKL), Osteocalcin, C-telopeptide crosslinks-CTX, electrolytes, PTH, total 25(OH)D were measured. Total body (TB) and lumbar spine (LS) BMD were evaluated with dual energy X-ray absorptiometry (DXA)

Results: Patients had significantly higher levels of OPG, s-RANKL and ALP but lower levels of PTH and magnesium. (Table 1.)

Patients and controls had comparable 25(OH)vitD levels, while one third of both groups had low 25(OH)vitD levels (<20ng/ml), (Table 2.)

25(OH)D	<20 ng/ml	≥20ng/dl	total
patients	13(32.5%)	27(67.5%)	40(100%)
controls	11(28.21%)	28(71.79%)	39(100%)
total	24(30.38%)	55(69.62%)	79(100%)

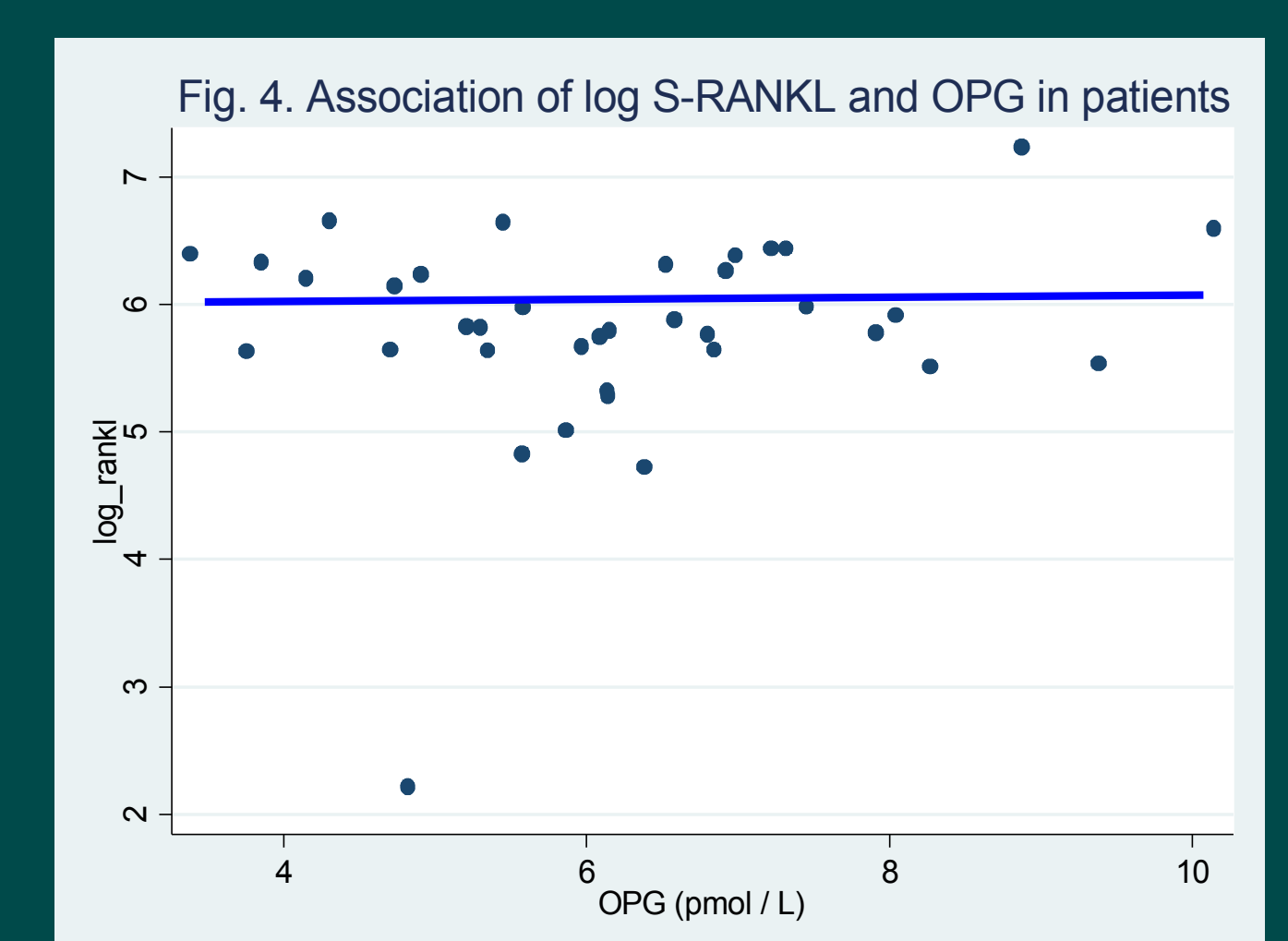
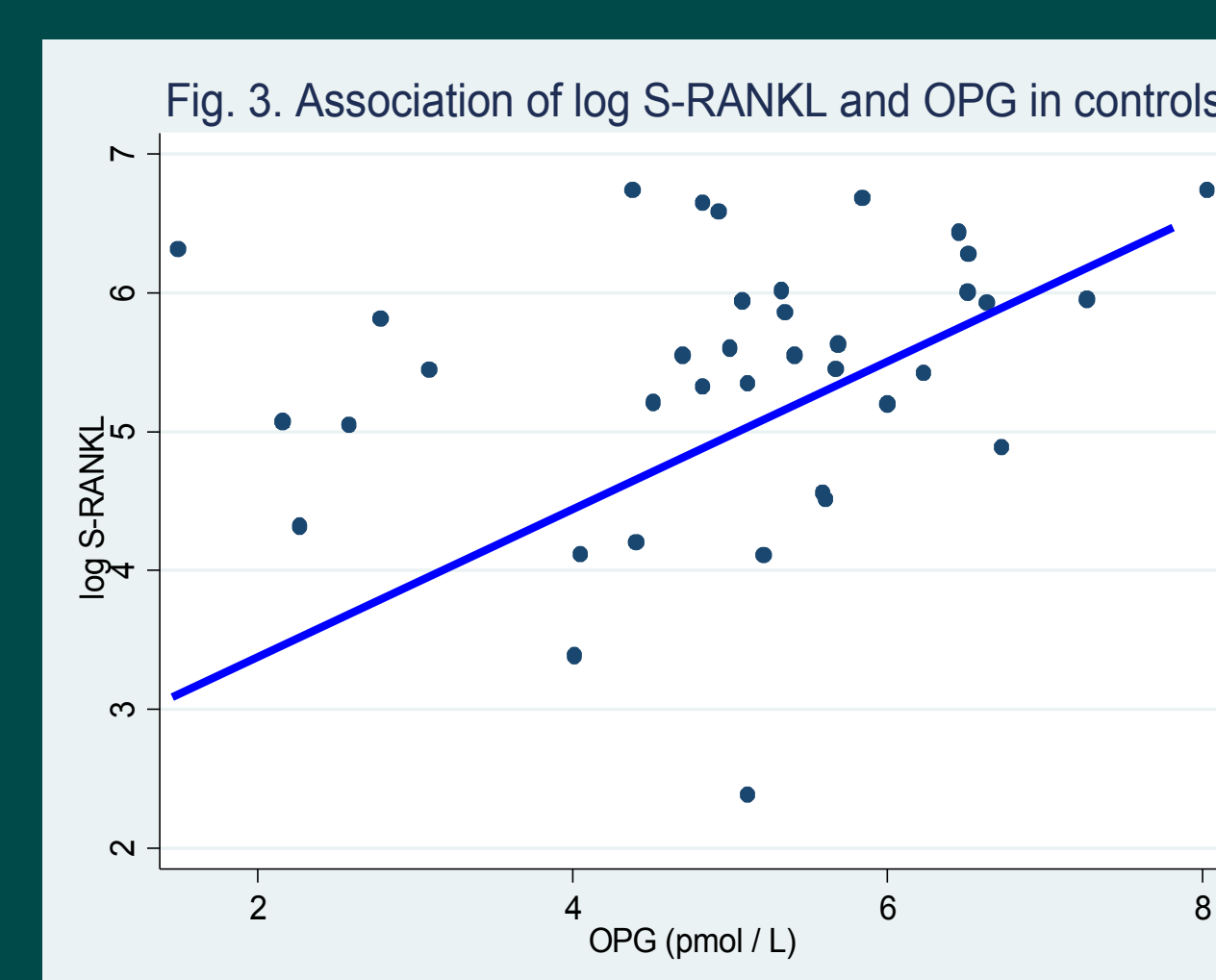
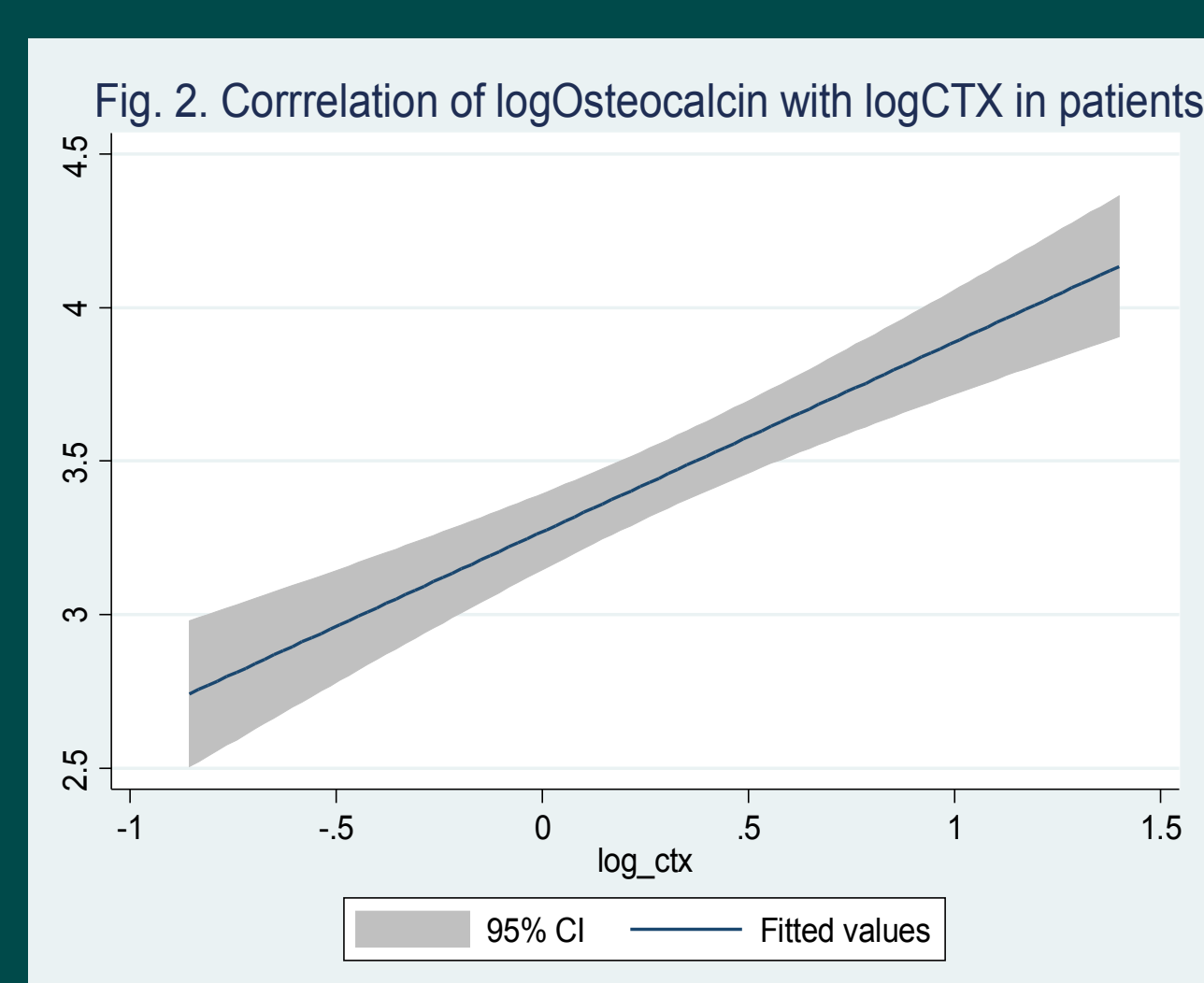
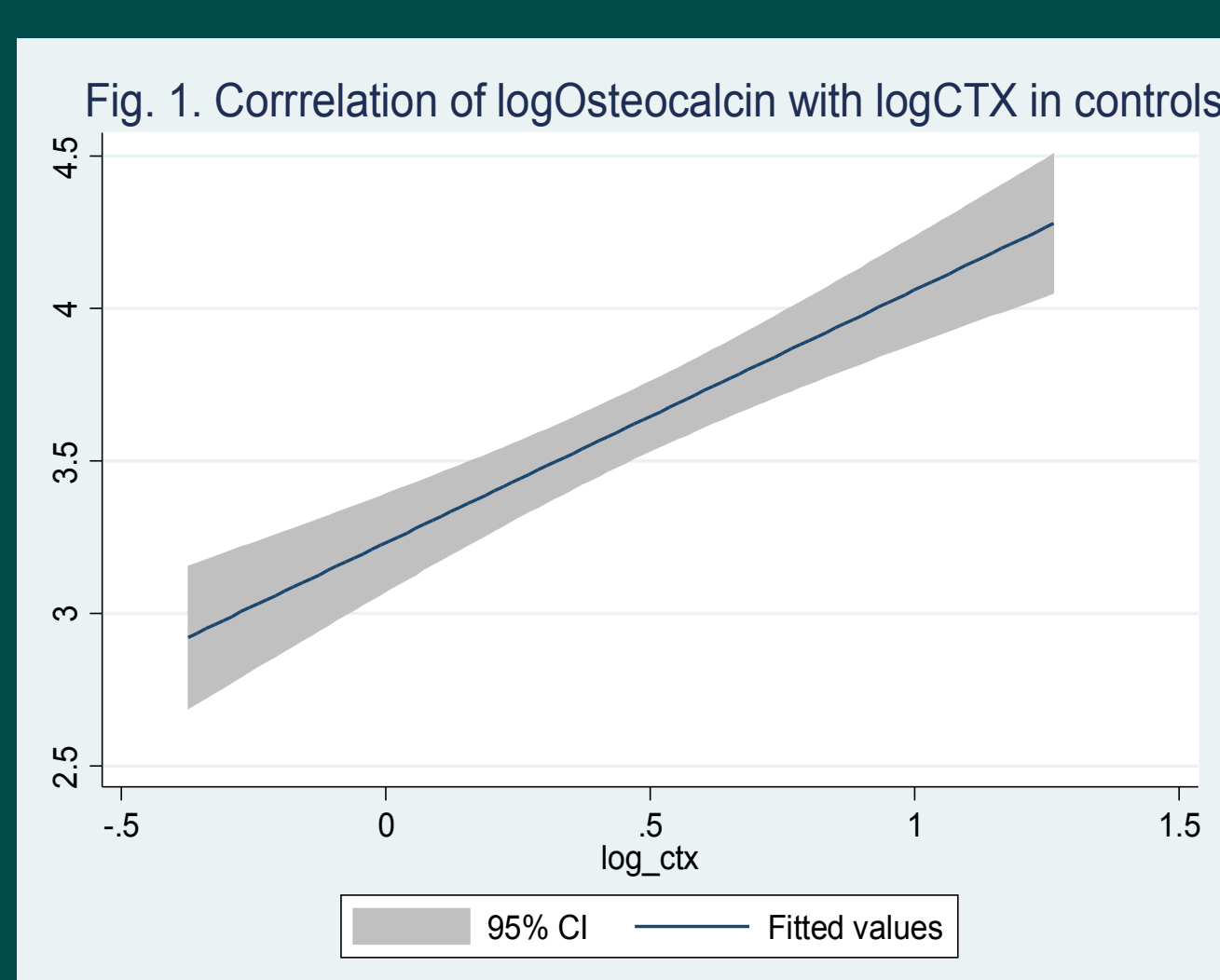
one-sided Fischer's exact test p=0.43

Table 1. Variable comparison between patients and controls

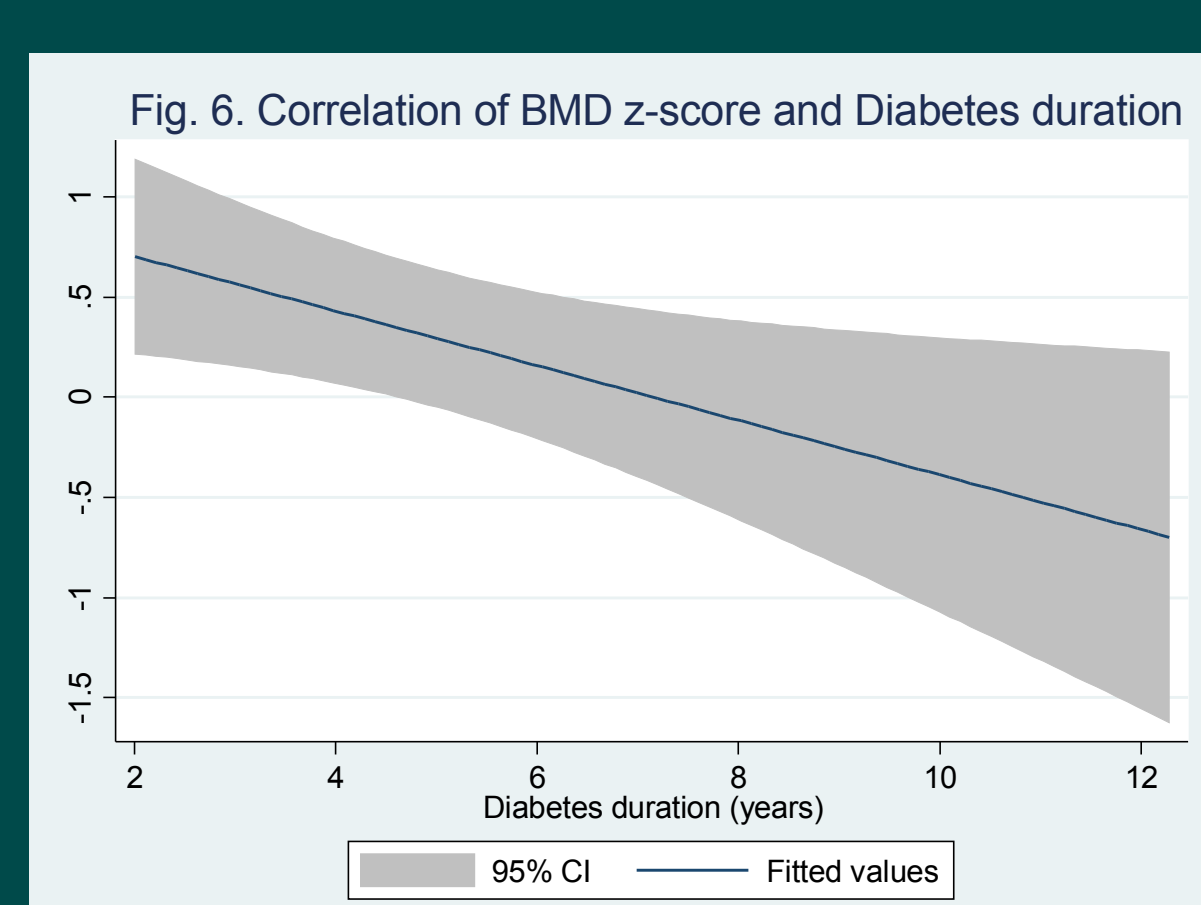
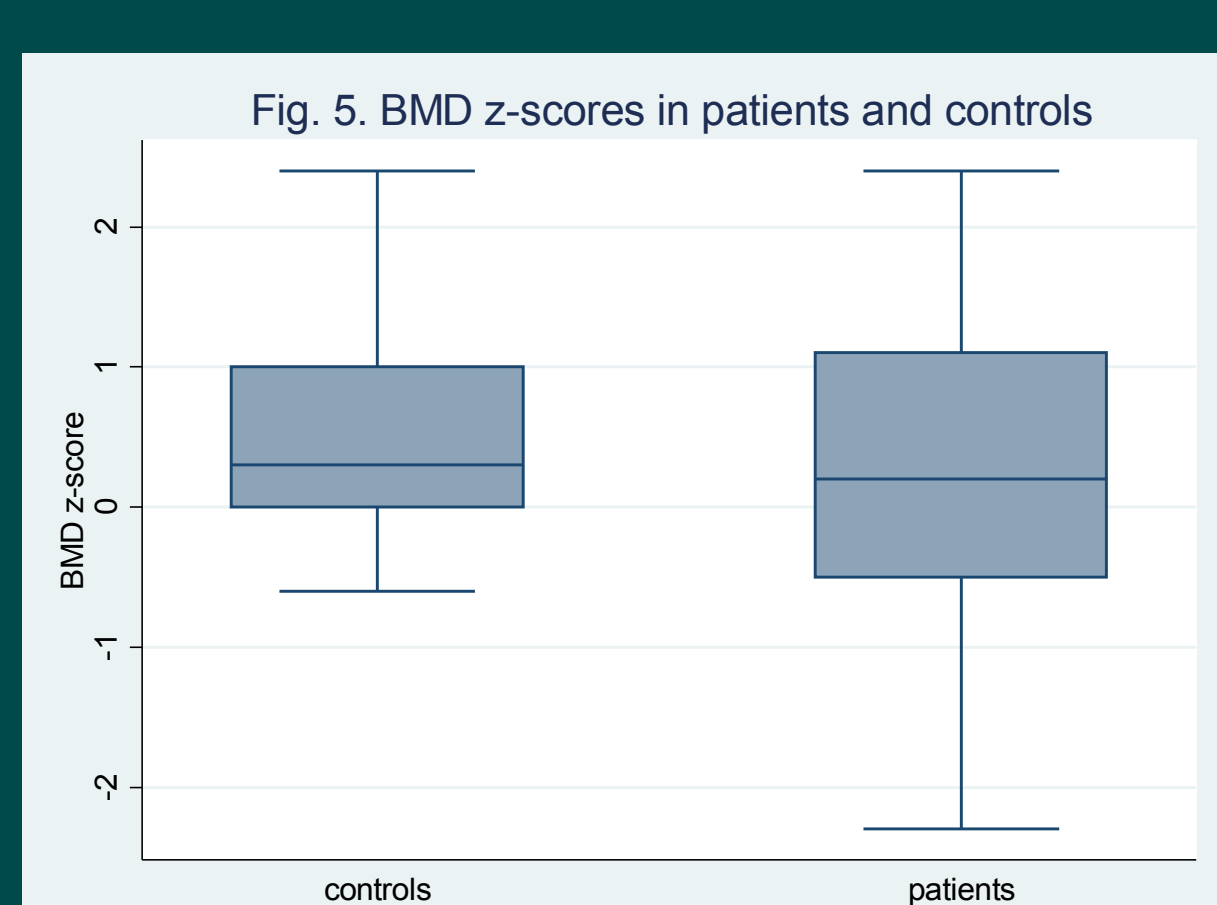
mean±SD	controls	patients	p-value*
logCTX	0.45±0.46	0.29±0.62	0.10
logOsteocalcin	3.6±0.51	3.45±0.5	0.09
OPG (pmol/L)	5.01±1.5	6.15±1.56	<0.001
logS-RANKL	5.51±0.84	5.97±0.63	0.004
logPTH	3.43±0.33	3.25±0.52	0.036
25(OH)D (ng/ml)	23.8±6.93	24.0±8.28	0.45
Ca (mg/dl)	9.82±0.35	9.77±0.33	0.29
P (mg/dl)	4.37±0.51	4.45±0.64	0.27
Mg (mg/dl)	2.03±0.12	1.88±0.12	<0.001
√ALP	12.61±3.24	14.07±4.13	0.05
BMD (gr/cm)	1.041±0.15	1.03±0.17	0.46
BMD z-score	0.513±0.80	0.308±1.05	0.17

*One-sided Student T-test

Osteocalcin was highly correlated with CTX in both groups ($r=0.75$, $p<0.001$), indicating coupling of bone resorption and formation. (Fig. 1. and Fig. 2.). OPG and s-RANKL were associated in controls ($R^2=0.15$, $p=0.021$) but not in patients ($R^2=0.006$, $p=0.64$), possibly indicating an osteoclastic disorder (Fig. 3 and Fig. 4.) Bone formation was not significantly affected.



BMD had greater variance in patients (Fig. 5). Longer T1DM duration was associated with lower BMD Z-scores (TB-BMD $r=-0.41$, $p=0.009$, LS-BMD $r=-0.34$, $p=0.043$) (Fig. 6.)



Conclusion: RANKL/OPG axis seems to be significantly activated in patients with T1DM. These changes could indicate abnormal osteoclast function and could be associated with the lower bone mass, found in patients with longer disease duration.