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ASSOCIATION BETWEEN SERUM LEVELS OF PPARY AND VERTEBRAL FRACTURES IN TYPE 2 DIABETES MELLITUS PATIENTS.

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a risk factor for the development of fractures. Several studies have shown an inverse relationship between osteoblastogenesis and adipogenesis through a competition model between these processes. PPARy acts as regulator of adipogenesis and its increased expression is associated to decreased osteoblastogenesis.

The treatment of insulin resistance with glitazones, one of the ligands of PPARy, reduces bone mineral density increasing risk of fractures. This suggests an additional role of PPARy in the regulation of bone metabolism.

Considering this, it is of interest to know the endogenous expression of serum PPARy in patients with DMT2 without treatment with glitazones presenting osteoporosis and vertebral fractures, assessing if T2DM patients have higher levels of PPARy inhibiting bone mineralization and increasing adipogenesis and bone fragility.

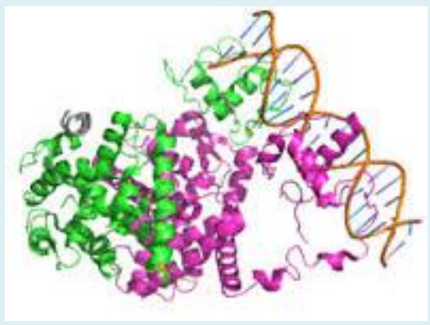

Figure 1: 3D structure of PPARy

PATIENTS AND METHODS

- A cross-sectional study was performed including 75 T2DM patients divided in 2 groups according to the presence / absence of osteoporosis and morphometric vertebral fractures
- The following variables were analyzed:
  - Anthropometric and biochemical parameters
  - Calciotropic hormones
  - Bone turnover markers (MRO)
  - Lumbar, hip and femoral neck bone mineral density (BMD) by dual X-ray absorptiometry (Hologic QDR 4500). The criteria of the World Health Organization for the diagnosis of osteoporosis were used.
  - Prevalence of vertebral fractures (VF)
  - Circulating levels of PPARy by commercial ELISA kit (Cusabio)

RESULTS

Table 1. Characteristics of the study population. The data of continuous variables are shown as mean ± SD. Data categorical variables are represented as percentages.

	DMT2 (n = 75)
Men/women (n)	43/35
Age (years)	57.8 ± 6.4
Body mass index (kg/m^2)	31.2 ± 5.6
Waist circumference (cm)	105.9 ± 11.5
Fasting plasma glucose (mg/dL)	173.3 ± 62.8
HbA1c (%)	8.0 ± 1.9
Triglyceride (mg/dL)	164.9 ± 145
High-density lipoprotein (mg/dL)	50.1 ± 17.1
Low-density lipoprotein (mg/dL)	97.03 ± 33.9
Creatinin (mg/dL)	0.9 ± 0.2
Homocysteine (mmol/L)	10.4 ± 4.7
Calcium (mg/dL)	9.6 ± 0.5
Phosphorus (mg/dL)	3.7 ± 0.58
PTHi (pg/mL)	38.4 ± 18.2
25(OH) D (ng/mL)	17.8 ± 11.1
PPARG (pg/mL)	569.8 ± 72.5
DXA parameters and fractures:	
BMD LS (g/cm2)	0.79 ± 0.75
BMD FN (g/cm2)	0.35 ± 0.56
BMD TH (g/cm2)	0.33 ± 0.53
Osteoporosis (%)	22.4
Morphometric VF (%)	27.7

Figure 1. Serum PPARy levels as presence / absence of osteoporosis

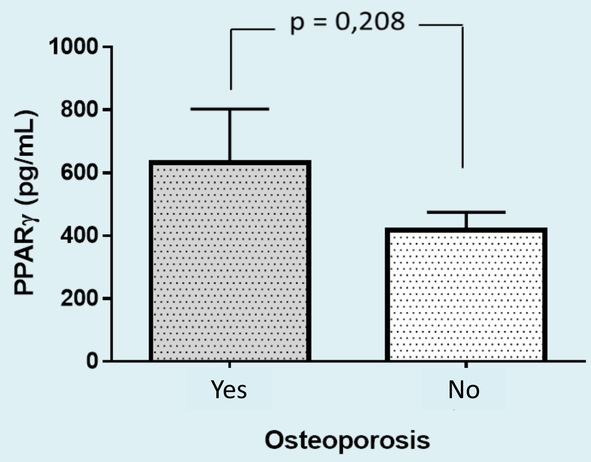

Figure 2. Serum PPARy levels as presence / absence of vertebral fractures

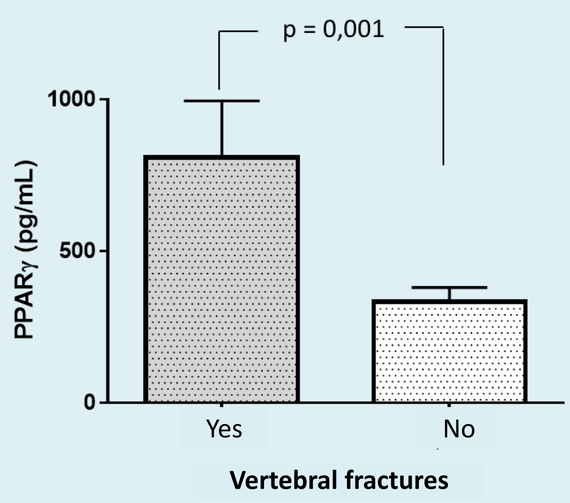

Table 2. Correlation coefficients (Pearson) between PPARy, BMD and MRO.

DMO	r/p	MRO	r/p
BMD lumbar spine (g/cm^2)	-0,102/0,410	BSAP (µg/L)	-0,067/0,575
BMD femoral neck (g/cm^2)	-0,085/0,482	CTX (ng/mL)	0,099/0,397
BMD total hip (g/cm^2)	-0,058/0,631	TRAP5b (UI/L)	0,106/0,369

Table 3. Factors independently associated with the presence of morphometric fractures in patients with T2DM. Independent variables included in the model: Serum levels of PPARy, age, sex, physical inactivity, family history of fracture, vitamin D levels and HbA1c levels.

Fracturas vertebrales	OR	95%CI	P
PPARY	1.002	1.00-1.004	0.018

CONCLUSIONS

- No significant differences of serum PPARy concentrations were observed according to the presence / absence of osteoporosis (p = 0.208). Neither, correlation between PPARy levels, MRO nor BMD values was observed (p> 0.05).
- However, circulating levels of PPARy were significantly higher in the T2DM group with VF compared to patients without VF (p = 0.001).
- The logistic regression model including risk factors of VF, showed that only PPARy levels were independently associated with the presence of morphometric VF indicating an increase of 2% in fracture risk per pg / mL of increased PPARy.
- These results suggest that this receptor might be involved in bone fragility in type 2 diabetes mellitus.

ACKNOWLEDGMENT
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