Circulating myostatin in type 2 diabetes subjects: relationship with bone metabolism and fractures

R Reyes-García[1,2], A García-Martín[1,3], B García-Fontana[1], S Morales-Santana[1,4],Pedro Rozas-Moreno[1,5], M Muñoz-Torres[1]

[1]Bone Metabolic Unit (RETICEF), Endocrinology Division, Hospital Universitario San Cecilio, Granada (Spain).
[2]Endocrinology. Hospital General Universitario Rafael Mendez, Lorca, Murcia, Spain.
[3]Endocrinology. Hospital Comarcal del Noroeste, Caravaca de la Cruz, Murcia, Spain.
[4]Proteomic Research Service, Fundación para la Investigación Biosanitaria de Andalucía Oriental -Alejandro Otero- (FIBAO), Granada, Spain
[5]Endocrinology. Hospital General de Ciudad Real, Ciudad Real, Spain.

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BACKGROUND AND OBJECTIVES: Myostatin (growth differentiation factor 8, GDF-8) has an important role in the regulation of muscle mass, and mice lacking the myostatin gene show a generalized increase in bone density and strength. Type 2 diabetes subjects have an increased risk of fragility fractures despite of higher bone mass. Taking into account the myostatin influence in bone strength a better understanding of myostatin actions in type 2 diabetes is of interest. Our aims were to evaluate serum myostatin concentrations in type 2 diabetes patients, and to explore its relationship with bone mineral density (BMD), bone turnover markers and fractures.

DESIGN, SETTING AND PATIENTS: Cross-sectional study including 73 patients with type 2 diabetes mellitus.

•Lumbar spine and femoral bone mineral density (BMD) were measured by dual X-Ray absorptiometry (Hologic QDR 4500). World Health Organization criteria for osteoporosis were used.

• Serum myostatin was measured using quantitative sandwich enzyme-linked immunosorbent assay (ELISA) developed by R&D systems (Minneapolis, MN, USA) according to the manufacturer's instructions. The assay sensitivity is 5,32 pg/mL and the assay range is 31,3 - 2,000 pg/mL. Intra-assay and inter-assay variability were of 5.6% and 6%, respectively.

•Bone turnover markers were measured as follows: total osteocalcin by radioimmunoassay (DiaSorin, Stillwater, Minnesota USA); bone alkaline phosphatase (BSAP) by an enzyme-linked immunosorbent assay (Tandem-R Ostase TM; Hybritech Europe, Liege, Belgium) ; serum carboxy-terminal cross-linked telopeptide of type I collagen (CTX) by enzyme immunoassay (Elecsys [beta] CrossLaps; Roche Diagnostics SL, Barcelona, Spain) and tartrate-resistant acid phosphatase 5b (TRAP5b) (Bone TRAP® Assay IDS Ltd).

RESULTS:

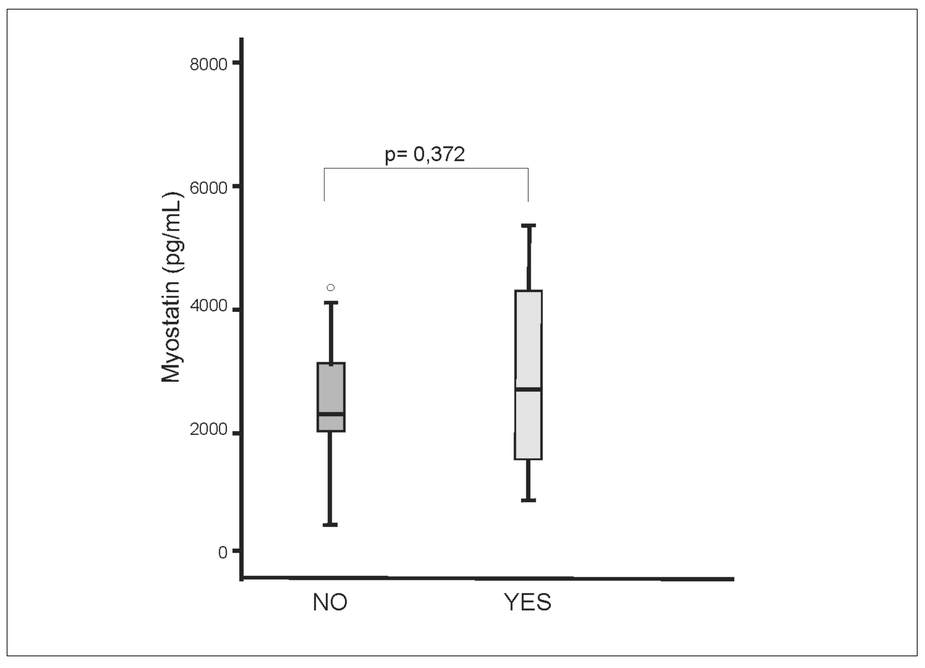
Table 1. Clinical, anthropometric and biochemical parameters of study subjects.

	Type 2 diabetes Group (n = 73)
Age (years)	56 ± 6
Male/female (n)	40/33
Medical history:	
Duration of diabetes (years)	13 ± 7
Hypertension (%)	79
Dislipidaemia (%)	95
Smoker (%)	16
Alcohol (%)	7
Sedentarism (%)	55
Clinical evaluation:	
BMI (kg/m^2)	31,3 ± 5,7
Waist circumference (cm)	106,3 ± 11,3
SBP (mm Hg)	134 ± 20
DBP (mm Hg)	79 ± 12
Serum parameters:	
FPG (mg/dL)	173 ± 60
HbA1c (%)	8,0 ± 1,9
Creatinine (mg/dl)	0,89 ± 0,19
Calcium (mg/dL)	9,7 ± 0,5
Phosphorus (mg/dL)	3,7 ± 0,6
PTH (pg/mL)	38,4 ± 18,3
25(OH)D (ng/mL)	17,6 ± 11,5
OC (ng/mL)	1,5 ± 1,3
BALP (µg/L)	14,6 ± 6,2
CTX (ng/mL)	0,209 ± 0,131
TRAP5b (UI/L)	1,4±1,0
Triglyceride (mg/dl)	169 ± 149
HDL-c (mg/dl)	49 ± 16
LDL-c (mg/dl)	97± 34
Myostatin (pg/ml)	2614,3 ± 1051,9
DXA parameters and VF:	
BMD LS (g/cm^2)	0,955 ± 0,145
BMD FN (g/cm^2)	0,818 ± 0,131
BMD TH (g/cm^2)	0,905 ± 0,144
T-score LS	-1,30 ± 1,34
T-score FN	-0,60 ± 1,03
T-score TH	- 0,62 ± 1,02
Osteoporosis (%)	24
Morphometric VF (%)	30

Table 2. Correlation coefficients (Pearson-s coefficient) between bone turnover markers and DXA parameters with serum myostatin levels.

	r	p
Lumbar spine BMD (gr/cm2)	0.074	0.132
Femoral neck BMD (gr/cm2)	0.130	0.234
Total femur BMD (gr/cm2)	0.174	0.110
OC (ng/ml)	0.080	0.098
BSAP (ug/L)	0.150	0.069
CTX (ng/dl)	0.027	0.212
TRAP (UI/L)	0.001	0.780

Figure 1. Serum myostatin levels according to the presence of vertebral fractures.



CONCLUSIONS:

1) Our data does not support an association between serum myostatin and bone parameters in type 2 diabetes. A true lack of relationship in humans may be an explanation, although a disrupted regulation of this pathway in type 2 diabetes may also take place

Conflicts of interest: none.