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The atherogenic index of plasma is related to a degraded bone microarchitecture assessed by the trabecular bone score in postmenopausal women: The Camargo Cohort Study

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Highlights

- The atherogenic index of plasma (AIP) is significantly and inversely related to trabecular bone score.
- AIP values > 0.11 are independently related to a degraded bone microarchitecture as measured by trabecular bone score.
- The AIP might be a useful tool in the overall assessment of bone metabolism in postmenopausal women.

Abstract

Objective: To assess the association between the atherogenic index of plasma (AIP) and the trabecular bone score (TBS) in postmenopausal women. Furthermore, to analyze its relationship with bone mineral density (BMD), and serum concentrations of 25OHD, PTH, and bone turnover markers.

Study design: Cross-sectional study nested in a population-based cohort of 1,367 postmenopausal women aged 44-94 years. Participants were classified according to TBS values (<1.230, between 1.230-1.310 and >1.310) and regarding a widely accepted cut-off point of ≥0.11 for AIP. We analyzed TBS, BMD, serum levels of 25OHD, PTH, P1NP, CTX, and clinical covariates. A multivariate analysis was performed to assess the adjusted association between AIP and TBS.

Results: The mean age of participants was 63±10 years. Women with TBS values <1.230 were older, had greater BMI, greater prevalence of fractures after the age of 40 years, more years since menopause, higher values of AIP, and significantly lower levels of HDL-C, serum phosphate, and 25OHD. AIP values ≥0.11 were not associated with the presence of densitometric osteoporosis (OR=0.83, 95%CI 0.58-1.18; p=0.30) but, in multivariate analysis, AIP values ≥0.11 were related to a degraded microarchitecture after controlling for age, BMI, smoking, diabetes status, ischemic heart disease, statin use, GFR, a fragility fracture at over 40 years of age and lumbar osteoporosis by DXA, with an adjusted OR=1.61 (95%CI 1.06-2.46; p=0.009).

Conclusions: AIP is significantly and independently associated with a degraded bone microarchitecture as measured by TBS. In this sense, AIP might be a useful tool in the overall assessment of bone metabolism in postmenopausal women.

Keywords: atherogenic index of plasma, TBS, BMD, osteoporosis; postmenopausal women

1. INTRODUCTION

The interplay between lipid and bone metabolism is an active field of research, due to the growing evidence for a biological linkage between two of the leading public health problems; osteoporosis and atherosclerosis [1]. Several studies have mainly addressed the relationship between some

conventional lipid parameters and bone mineral density (BMD) and bone turnover markers, although results have been inconsistent and even contradictory [2].

Atherogenic dyslipidemia, that is, the combined occurrence of high fasting blood concentrations of triglycerides (TG) and low levels of high-density lipoprotein cholesterol (HDL-C), is frequent in patients with metabolic disorders such as diabetes and metabolic syndrome [3]. Comprehensive lipid ratios are considered to be better predictors for coronary artery disease than single lipid parameters. [4]. In this sense, the atherogenic index of plasma (AIP) defined as the base 10 logarithm of the ratio of the molar concentration of TG to HDL-C [5] has shown a good correlation with smaller LDL-C particles and also with increased fractional esterification rate for cholesterol in plasma, and represents a strong and independent predictor factor for coronary disease [6-8]. Noteworthy, AIP has also been associated with raised serum C-reactive protein levels, suggesting a lipid-driven immune-inflammatory link [3,9].

Bone quality is not well captured by bone densitometry (DXA), and new techniques have been emerged in the last years to provide us with additional skeletal information, especially on bone microarchitecture. Thus, the trabecular bone score (TBS) is a simple and reproducible procedure based on an algorithm that assesses the pixel-gray level and spatial variations in DXA lumbar spine images [10]. It provides an indirect estimation of bone microarchitecture independent of BMD and clinical risk factors and has shown a good correlation with bone micro-computed tomography and histomorphometric parameters, as well as a good predictive value for fragility fractures [11,12].

Taking into account the above considerations, the present study aimed to assess the potential association between AIP and TBS values. Besides, we intend to analyze the relationship of this atherogenic index with BMD, and serum concentrations of intact PTH, 25OHD, and bone turnover markers.

2. SUBJECTS AND METHODS

2.1. Study design and participants

We have performed a cross-sectional study nested in a population-based cohort. The study population included Caucasian postmenopausal women participating in the Camargo Cohort Study whose full details have been previously published [13,14]. Briefly, the cohort was set up between February 2006 and February 2011 with postmenopausal women and men aged 50 years and older attending a primary care center in Northern Spain for their regular health examination or for medical reasons, whichever happened first. In the current study, we have included those postmenopausal women whose baseline assessment did not reveal the presence of diseases or treatments known to affect bone metabolism, such as primary hyperparathyroidism, hyperthyroidism, serum creatinine >1.7 mg/dl (151 μmol/L), or were not taking bisphosphonates, estrogen, raloxifene, strontium ranelate, teriparatide, L-thyroxin, anticonvulsants or glucocorticoids in the previous year.

2.2 Data collection and working definitions

At the baseline visit, subjects were interviewed by investigators using a structured questionnaire which included age, years since menopause, body mass index (BMI), waist circumference, personal history of fractures in adulthood (>40 years), history of osteoporotic fractures among first-degree relatives, tobacco use, consumption of dairy products, alcohol use (g/day), physical exercise, chronic disorders including cardiovascular diseases and present or past consumption of medications. BMI was defined as the weight (kg) divided by squared height (m^2). Dairy calcium consumption was assessed by a food frequency questionnaire [15]. Current alcohol consumption was defined as >20 g of alcohol per day. Subjects with fasting glucose ≥ 126 mg/dl (7 mmol/L) or using regular antidiabetic medications were defined as diabetic ones. Previous non-vertebral fractures unrelated to major trauma were self-reported and later confirmed by examination of medical or radiological reports.

The study was approved by the Local Ethics Committee (Comité Ético de Investigación Clínica de Cantabria-IDIVAL. Internal Code 2014.155), and all patients gave written informed consent.

2.3. Biochemical tests

Blood samples were obtained from an antecubital vein in the morning after a requested 12-hour overnight fast. Routine biochemical parameters and a complete lipid profile including total cholesterol, LDL-C, HDL-C, TG were obtained. These baseline parameters were measured using standard methods (ADVIA 2400 Chemistry System autoanalyzer; Siemens, Germany). AIP was

calculated as the base 10 logarithm of the molar concentrations of TG to HDL-C. The glomerular filtration rate (GFR) was estimated according to the formula CKD-EPI and expressed in ml/min/1.73 m². Serum concentrations of 25-hydroxyvitamin D (25OHD), intact parathyroid hormone (PTH), aminoterminal propeptide of type I collagen (PINP), and C-terminal telopeptide of type I collagen (CTX) were determined by a fully automated Roche electrochemiluminescence system (Elecsys 2010, Roche Diagnostics, GmbH, Mannheim, Germany). The detection limit of serum 25OHD was 4 ng/ml, its intraassay coefficient of variation (CV) was 5%, and its interassay CV 7.5%. Regarding intact PTH, the detection limit was 6 pg/ml, and the intraassay and interassay CV were 3.4% and 5.9%, respectively. The PINP limit of detection was 5 ng/ml, and its intraassay and interassay CV were 3.9% and 4.1%, respectively. Intraassay and interassay CV for CTX were 4.2% and 4.7% and the detection limit was 0.01 ng/ml.

2.4. BMD measurements

All subjects underwent BMD testing by DXA (Hologic QDR 4500, Bedford, MA, USA) at the lumbar spine (LS), femoral neck (FN), and total hip (TH). In vivo precision was 0.4-1.5% at the different measurement sites. Quality control was performed according to the usual standards. Osteoporosis was defined as a T score ≤ -2.5 following the WHO classification [16].

2.5. Trabecular Bone Score

Spine TBS measurements were performed with the TBS software (TBS iNsight® version 2.1, Medimaps, Mérignac, France) on the DXA lumbar spine images. TBS was calculated assessing the same vertebrae at which the LS-BMD had been measured [13]. As a rule, the measurement of BMD in LS was performed in L1-L4, except for those cases in which the vertebral morphology advised its exclusion. A TBS value <1.230 was considered as a degraded microarchitecture. This value corresponds to the high-risk threshold obtained from an extensive meta-analysis of 14 population-based cohorts [11].

2.6. Statistical analysis

All continuous variables were tested for normality. Results were expressed as numbers (percentage), mean ± standard deviation (SD), or median and interquartile range (IQR), as appropriate. Student's t-test or Mann-Whitney U-test was used to determine the differences between groups for continuous variables and χ^2-test for categorical variables. Spearman's rank correlation coefficients were calculated to assess the relationship between AIP and demographic, laboratory parameters, and DXA and TBS values. The patients were divided into three groups

according to the TBS values (< 1.230, between 1.230-1.310 and > 1.310). A cut-off point for AIP >0.11, based on previously published data, has been considered for the analysis [4,18]. To further assess the potential association between AIP and TBS values consistent with degraded microarchitecture (TBS <1.230), multiple logistic regression analysis adjusted for confounder variables was used. The strength of the association between the study parameters and TBS was evaluated via the odds ratio (OR) and 95% confidence interval (CI). Finally, ROC curve analysis has been performed to test the performance of the regression model. All *p*-values were two-tailed and < 0.05 were considered to be statistically significant in all the calculations.

3. RESULTS

3.1 Baseline characteristics

We included 1367 postmenopausal women from the Camargo cohort. The mean age of participants was 63±10 (range, 44-92 years). The median (IQR) years since menopause was 11 (4-21). Some 262 women were on statins (19.2%). There was an inverse correlation between waist circumference and TBS values (r=-0.348; p<0.0001). TBS values consistent with degraded bone microarchitecture (<1.230) were present in 198 participants (14.5%) and 298 (21.9%) subjects showed values indicating partially degraded microarchitecture (1.230-1.310). Normal TBS values (>1.310) were observed in 871 (63.7%) women. Table 2 shows the baseline characteristics of the study population according to the TBS results. Women with TBS values <1.230 were older, had greater BMI, more years since menopause, and greater prevalence of personal history of fragility fractures over 40 years, diabetes mellitus, and ischemic heart disease than those with normal TBS values.

Table 1 summarizes the main baseline lipid and bone metabolism parameters according to the TBS values. Women with a degraded bone microarchitecture (TBS<1.230) had higher serum glucose, TG, and C-reactive protein levels than women with normal TBS results. Besides, HDL-C, serum phosphate, and 25OHD were significantly lower, and intact PTH levels were higher in women with TBS values <1.230 compared with those with normal TBS.

Figure 1 represents the AIP values according to the TBS groups. Women with the most degraded bone microarchitecture have the highest AIP values.

3.2. Association between AIP and other variables

The correlations between AIP and several epidemiological and laboratory parameters are shown in Table 3. In the overall sample, AIP is significantly and positively related to age, BMI, active smoking, LDL-C, triglycerides, non-HDL-C, fasting glucose, and C-reactive protein levels, and negatively to HDL-C and GFR. Regarding bone metabolism parameters, AIP is directly related to serum PTH levels, and inversely to 25OHD and bone turnover markers concentrations. The associations between AIP and serum PTH, 25OHD levels, and BMD were canceled once adjusting for age and BMI, whilst significant correlations with bone turnover markers were maintained. AIP values >0.11 were not associated with the presence of densitometric osteoporosis (OR 0.83 95%CI, 0.58-1.18; p=0.30).

3.3. AIP and TBS values

As shown in Table 2, AIP is inversely and significantly related to TBS values. After controlling for age, BMI, statin use, and active smoking this relationship persisted significant (r=-0.066; p=0.015).

The results of stepwise multiple logistic regression analysis of the parameters with potential association with TBS values <1.230, adjusted for age, BMI, smoking, diabetes status, statin use, ischemic heart disease, GFR, previous fragility fracture, and lumbar densitometric osteoporosis are shown in Table 4. AIP values > 0.11 were independently related to a degraded microarchitecture (adjusted OR 1.61, 95%CI, 1.06-2.46; p=0.009). Further adjustment for waist circumference, years since menopause, fasting glucose, calciotropic hormones, bone turnover markers, or serum C-reactive protein levels did not change these results.

Figure 2 shows the ROC curve for the regression model. The area under the curve is 0.84 (95% CI, 0.82-0.87; *p*<0.0001).

4. DISCUSSION

In the present study, AIP was negatively correlated to TBS values. We have found that an AIP >0.11 is associated with a degraded bone microarchitecture measured by this technique. This relationship is independent of age, BMI, smoking, statin use, a history of diabetes, ischemic heart disease and fragility fractures, GFR, and the presence of lumbar osteoporosis measured by DXA.

It has been suggested that dyslipidemia may influence bone quality rather than BMD, and therefore, in this context, it could be important to assess the TBS as well as BMD. Thus, according to our data, AIP might be useful not only to detect patients at high risk for metabolic (obesity, diabetes, or

metabolic syndrome) or cardiovascular complications (high blood pressure, cardiovascular events) but also to alert the clinicians to the presence of an impaired trabecular microarchitecture.

Osteoporosis and atherosclerosis share classical cardiovascular risk factors and pathophysiological pathways. Lipid profile has been linked to bone metabolism in several studies, with different results. Recently, Mishra et al. [20], carried out a study on 1494 Caucasian participants from the Cardiovascular Risk in Young Finns Study Cohort to assess the relationship between the serum lipidome and subclinical surrogate markers of atherosclerosis (carotid intima-media thickness) and osteoporosis (peripheral quantitative computed tomography bone parameters). They found that all the 37 statistically significant lipid species related to subclinical markers of both atherosclerosis and osteoporosis were triacylglycerols. This is an important issue since triglyceride-rich lipoproteins can deposit in the arterial wall intima and be taken up by macrophages to convert into foam cells leading to atherosclerotic plaque development. Besides, some studies have shown the presence of a lower triglyceride metabolism in patients with osteoporosis compared with those with osteoarthritis or healthy controls [21],

It is well-known that postmenopausal women exhibit a less favorable bone and lipid profile than before menopause, and that this period is related to central adiposity, increased insulin resistance, and higher blood pressure values [22]. Wu et al. [23], suggested that AIP might be a strong and independent marker for coronary artery disease risk in postmenopausal women. Higher values of AIP are a surrogate for small and dense LDL-C particles. These modified lipoproteins are more prone to convert in oxidized LDL-C leading to the formation of foam cells, increasing lipid peroxidation, activating reactive oxygen species, inducing endothelial dysfunction, and, therefore, initiating the atherosclerotic process [24]. Besides, oxidized-LDL has been suggested as the link between bone metabolism and atherosclerosis. It promotes atherosclerosis by stimulating the adhesion of monocytes into the endothelial cells and its transformation in foam cells, as well as enhance the migration and proliferation of smooth muscle cells and the development of the fibrous lining in the atherosclerotic plaque. Furthermore, oxidized-LDL has been implicated in the inhibition of differentiation of bone marrow cells to osteoblasts and its transformation into adipocytes [25,26]

Ando et al. [25], in a retrospective case-control study found that middle-aged and elderly Japanese women with elevated concentrations of triglycerides had impaired bone resorption and an increased risk for sustaining fragility fractures. Our data are consistent with these findings since serum triglycerides and AIP were inversely related to both PINP and CTX levels. These results

support the hypothesis that bone fragility in patients with higher plasma triglycerides and AIP, depends on a deterioration in bone quality rather than on bone mass reduction.

Regarding the association between atherogenic indexes and BMD, Chuang et al. [28], analyzed the potential relationship between some of these lipid ratios and lumbar and hip BMD in 3249 Taiwanese adults (71% males and 43% vegetarians) with a mean age of 58 years. Although they did not analyze the AIP, they found that the TG/HDL-C ratio was related to BMD after adjusting by confounders, mainly in non-obese participants (except for lumbar BMD in non-obese women).

The relationship between lipid metabolism and bone quality, measured by TBS, has been scarcely explored. A study on 56 young individuals found that TBS was inversely related to insulin resistance, and visceral adiposity, intrahepatic lipids, and saturated lipids in bone marrow adipose tissue quantified by magnetic resonance imaging, suggesting that these parameters might be related to bone quality instead of BMD [29]. Panahi et al. [30], explored the associations between the lipid profile and the TBS values in a population-based study of elderly Iranian subjects. In contrast to our data, they did not find any significant relationship between any of the conventional lipid parameters in women, although HDL-C was negatively correlated with the TBS in men. Nevertheless, the AIP was not assessed.

Finally, data on the relationship between serum 25OHD and AIP are limited. Wang et al. [31], analyzed the association between AIP and serum 25OHD in 829 men and 646 women aged 24-64 years (mean age, 38 years) studied in a single institution. The authors found a significant negative correlation between serum 25OHD and AIP in the group of men, but they did not find any significant association in women. The differences with our study probably rely on the age and BMI of both populations. Nevertheless, when adjusting for age and BMI, this association is also canceled in our study, suggesting that the relationship AIP-25OHD is highly dependent on these factors.

Our study has several limitations. Firstly, the inherent limitations of a case-control study regarding causality. Secondly, as an observational study, it may be subject to some bias due to the possible existence of confounders. However, to try to avoid this issue, adjustment for multiple potential confounding factors has been carried out. Finally, we did not collect specific data on protein and macro and micronutrient intake. Nevertheless, a recent study carried out in our region (Cantabria, Northern Spain) has shown a greater consumption of fish, oil, dairy products, pastries, cookies and cereals, and fresh fruits compared to the Spanish average. However, the intake of soft drinks and soda, fresh vegetables, and bread is slightly lower. Our region also occupies the first national

position in the consumption of fish and food of high nutritional value and high protein content. In 2016, the mean energy intake of the Cantabria population was 2038 kcal and the consumption of proteins, carbohydrates, lipids, and dietary fiber was 74.7 (79.7) g, 207,3 (220.6) g, 94,8 (94.8) g, and 15.8 (16.6) g, respectively (in parentheses, each average data in Spain) [32].

In conclusion, AIP is significantly and independently associated with a degraded bone microarchitecture measured by TBS. Therefore, clinicians might consider this index in the overall assessment of bone metabolism. Further studies are needed to confirm these results and continue to deepen the knowledge of the underlying links between lipid and bone metabolism.

Contributors

José L. Hernández participated in the conception and design of the study, analysis, and interpretation of the data, and wrote the paper.

José M. Olmos participated in the conception, design, and analysis, and interpretation of the data, and the revision of the paper.

Emilio Pariente participated in the analysis and interpretation of the data, and the revision of the paper.

Carmen Ramos participated in the analysis and interpretation of the data, and the revision of the paper.

Josefina Martínez performed the laboratory analysis and participated in the interpretation of the data, and the revision of the paper.

Daniel Nan participated in the analysis and interpretation of the data, and the revision of the paper.

All authors read and approved the final version of the manuscript.

Conflict of interest

The authors declare that they have no conflict of interest regarding this paper.

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Ethical approval

The study was approved by the Local Ethics Committee (Comité Ético de Investigación Clínica de Cantabria-IDIVAL. Internal Code 2014.155), and all patients gave written informed consent.

Conflict of Interest

José L. Hernández, José M. Olmos, Emilio Pariente,Carmen Ramos, Josefina Martínez, and Daniel Nan declare that they have no conflict of interest regarding this paper.

Provenance and peer review

This article was not commissioned and was externally peer reviewed.

Research data (data sharing and collaboration)

There are no linked research data sets for this paper. Some or all of the data sets generated and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request..

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TABLES

Table 1. Baseline characteristics of the study population according to TBS values.

Variable	TBS group <1.230 N=198	1.230-1.310 N=298	>1.310 N=871	p[1]	p[2]
Age, *yrs., mean±SD*	68.5±10.1	65.8±9.7	60.0±9.0	0.005	0.0001
BMI, *Kg/m², mean±SD*	30.7±3.6	28.3±3.8	27.0±3.7	0.0001	0.0001
Waist circumference, *cm, mean±SD*	102.4±10.5	95.9±11.5	91.1±11.5	0.0001	0.0001
Years since menopause*, median (IQR)*	21 (12-28)	15 (8-24)	8 (3-16)	0.0001	0.0001
Family history of fractures, *%*	13.6	18.8	17.8	0.13	0.16
Fragility fracture > 40 yrs., *%*	28.3	18.5	10.6	0.01	0.0001
Current smoking, *%*	13.1	11.4	15.2	0.57	0.47
Current alcohol, *%*	10.1	12.8	13.2	0.39	0.24
Dairy calcium, *mg/day, median (IQR)*	650 (450-800)	600 (450-800)	700 (450-900)	0.72	0.08
Statin use, *%*	23.7	20.1	17.8	0.34	0.06
Diabetes mellitus, *%*	19.2	13.8	7.5	0.051	0.0001
Ischemic heart disease, *%*	6.1	2.0	3.3	0.02	0.07
Cerebrovascular disease, *%*	3.0	3.0	1.8	0.99	0.29

p[1]: TBS <1.230 vs. TBS 1.230-1.310; p[2]: TBS <1.210 vs TBS >1.310.

Table 2. Laboratory parameters according to TBS values.

Variable	TBS group			p[1]	p[2]
	<1.230 N=198	1.230-1.310 N=298	>1.310 N=871		
Glucose, *mg/dl, mean±SD*	104±28	96±23	92±16	0.0001	0.0001
Cholesterol, *mg/dl, mean±SD*	220±39	227±38	227±36	0.11	0.09
LDL-C, *mg/dl, mean±SD*	140±34	144±33	143±33	0.60	0.61
HDL-C, *mg/dl, median (IQR)*	54 (45-66)	59 (49-70)	62 (52-74)	0.005	0.0001
TG, *mg/dl, median (IQR)*	112 (82-143)	100 (76-139)	89 (65-121)	0.07	0.0001
AIP, *median (IQR)*	-0.07 (-0.26-0.11)	-0.11 (-0.30-0.07)	-0.21 (-0.38-[-0.02])	0.06	0.0001
C-reactive protein, *mg/dl*	0.30 (0.10-0.60)	0.30 (0.10-0.50)	0.20 (0.10-0.40)	0.31	0.0001
Calcium, *mg/dl, mean±SD*	9.3±0.3	9.3±0.3	9.3±0.3	1.00	1.00
Phosphate, *mg/dl, mean±SD*	3.4±0.5	3.4±0.4	3.5±0.5	1.00	0.016
GFR, *ml/min/1.73m², mean±SD*	70±19	67±14	71±17	0.46	0.60
i-PTH, *pg/ml, median (IQR*	54.1 (44.5-68.9)	51.9 (41.8-64.3)	47.5 (37.8-59.7)	0.18	0.0001
25OHD, *ng/ml, mean±SD*	21±8	22±7	24±9	1.00	0.0001
PINP, *ng/ml, median (IQR)*	43.6 (34.6-58.9)	44.2 (33.7-57.9)	47.6 (35.8-61.7)	0.15	1.00
CTX, *ng/ml, median (IQR)*	0.341 (0.238-0.486)	0.377 (0.259-0.503)	0.392 (0.265-0.517)	0.75	0.25

p[1]: TBS <1.230 vs. TBS 1.230-1.310; p[2]: TBS <1.230 vs TBS >1.310.

Table 3. Correlation between the atherogenic index of plasma and some demographic, laboratory parameters, and DXA values in the study population.

	Overall sample N=1367	
	r	**p**
Age, *years*	0.178	0.0001
Years since menopause	0.168	0.0001
BMI, *Kg/m²*	0.341	0.0001
Waist circumpherence, *cm*	0.345	0.0001
Smoking, *yes*	0.072	0.008
Alcohol intake, *yes*	0.027	0.31
Total cholesterol, *mg/dl*	0.011	0.69
LDL-C, *mg/dl*	0.083	0.002
HDL-C, *mg/dl*	-0.760	0.0001
TG, *mg/dl*	0.925	0.0001
Non-HDL cholesterol, *mg/dl*	0.324	0.0001
Fasting glucose, *mg/dl*	0.218	0.0001
GFR, *ml/min/1.73 m²*	-0.215	0.0001
Alkaline phosphatase, *U/L*	0.031	0.25
Corrected calcium, *mg/dl*	0.023	0.43
Phosphate, *mg/dl*	-0.011	0.70
C-reactive protein, *mg/dl*	0.219	0.0001
i-PTH, *pg/ml*	0.079	0.003
25OHD, *ng/ml*	-0.090	0.001
PINP, *ng/ml*	-0.185	0.0001
CTX, *ng/ml*	-0.192	0.0001
Lumbar BMD, *g/cm²*	0.085	0.002
Femoral neck BMD, *g/cm²*	0.102	0.0001
Total hip BMD, *g/cm²*	0.146	0.0001
TBS	-0.204	0.0001
Osteoporosis (DXA), *yes*	-0.065	0.016

Table 4. Adjusted multiple logistic regression analysis showing the best set of factors associated with TBS values corresponding to degraded microarchitecture (TBS <1.230).

	B	OR (95% CI)	*p*
Age, *years*	0.064	1.07 (1.05-1.09)	0.0001
BMI, *Kg/m²*	0.284	1.33 (1.26-1.40)	0.0001
Smoking, *yes*	0.823	2.28 (1.31-3.95)	0.003
Previous fracture, *yes*	0.552	1.74 (1.15-2.62)	0.009
GFR, *ml/min/1.73 m²*	0.014	1.01 (1.003-1.03)	0.009
Lumbar osteoporosis, *yes*	1.741	5.70 (3.80-8.57)	0.0001
AIP >0.11	0.478	1.61 (1.06-2.46)	0.027

Adjusted for age, BMI, smoking, diabetes status, ischemic heart disease, statin use, GFR, history of a fragility fracture after the age of 40 years, lumbar osteoporosis diagnosed by DXA and AIP values >0.11.

BMI: Body mass index; GFR: Glomerular filtration rate (MDRD-4 formula); BMD: Bone mineral density; AIP: atherogenic index of plasma.

FIGURES

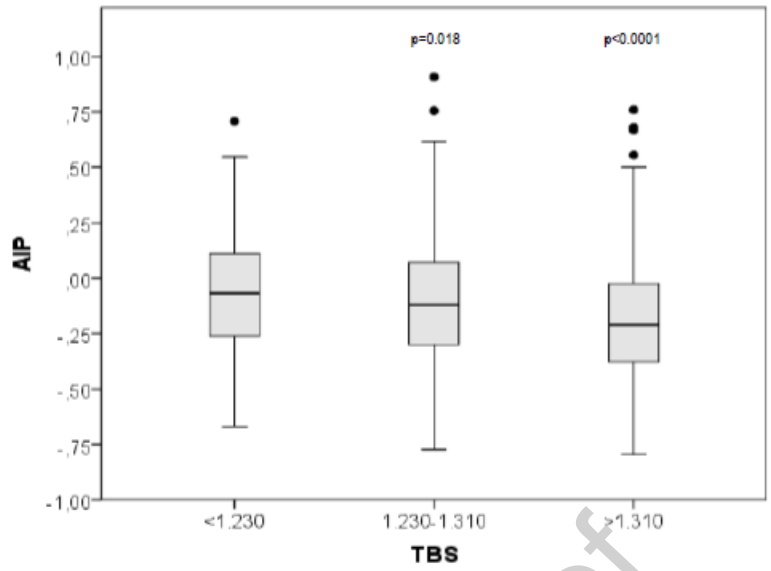

Figure 1. AIP values according to the TBS groups.

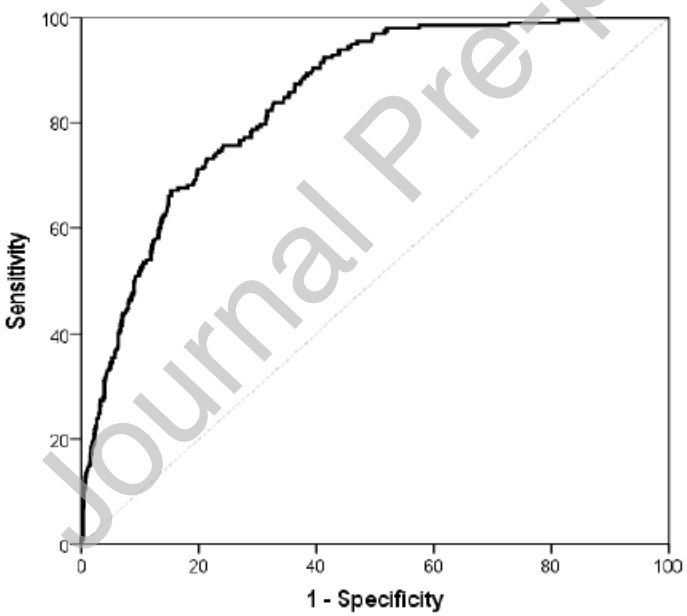

Figure 2. ROC curve for the regression model.