Role of pentraxin-3 in risk assessment of patients with metabolic syndrome

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Background: Inflammation plays a major role in the development of metabolic syndrome (MetS) and its progression. Recent studies have shown that pentraxin-3 (PTX-3), osteoprogerin (OPG), and tumor necrosis factor-alpha (TNF-α) are key factors in MetS pathophysiology, but evidence for endorsing their clinical use is currently unclear and insufficient. *Aim:* The study aimed to evaluate the association between the inflammatory biomarkers' levels and the severity of MetS. *Methods:* The study was observational, transversal, prospective, cohort, and analytical type. We enrolled 80 patients (M:F = 1, mean age = 55 ± 10.77 years) who met MetS criteria. The study protocol included: medical history, physical examination, 6-min walk test distance (6MWTD), biochemical tests, electrocardiogram, echocardiography, and carotid ultrasonography. We also performed plasmatic measurement of PTX-3, OPG, and TNF-α, in addition to standard biochemical tests. *Results:* Subjects with severe MetS had higher values of body mass index (BMI) and waist circumference ($p < 0.001$, $p = 0.001$). PTX-3 levels were significantly higher in patients with severe MetS ($p = 0.03$) and the values were not influenced by age or gender. OPG positively correlated with BMI ($r = 0.264$, $p = 0.018$). 6MWTD was lower in patients with severe MetS ($p = 0.005$), whereas CCA-IMT was higher in this group of patients ($p = 0.005$). In addition, the receiver operating characteristic (ROC) curve analysis for PTX-3 identified a cut-off value of 10.7 ng/dl that differentiates between mild and severe MetS [AUC 0.656; sensitivity = 47.1% (95% CI = 36.1%–62.3%); specificity = 78.9% (95% CI = 54.4%–93.9%)]. *Conclusion:* PTX-3 was correlated with the severity of MetS, with other inflammatory parameters and cardiovascular tests. CCA-IMT and 6MWTD are useful in differentiating between mild and severe MetS.

Keywords: pentraxin-3, osteoprotegerin, tumor necrosis factor-alpha, metabolic syndrome, atherosclerosis

Introduction

Metabolic syndrome (MetS) represents a cluster of risk factors, including hypertension, dyslipidemia, elevated plasma glucose, and central obesity (7, 25), with a prevalence of 20%–25% in adults (7). MetS increases cardiovascular morbidity twofold, which is a major healthcare burden.

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The pathophysiological mechanisms behind the development and progression of MetS are not fully understood. Inflammation (14) and endothelial dysfunction (18) seem to play a significant role, leading to atherosclerosis and its complications, including cardiac ischemic disease (14). MetS is characterized by a chronic low-grade inflammation that involves inner humoral and cellular immunity (17). Recent studies have shown that some inflammatory cytokines, adipokines, neuropeptides, prothrombotic, and other factors are involved in MetS pathogenesis (1, 17, 18). These mediators could be used to diagnose, monitor, or predict the severity of MetS.

Pentraxin-3 (PTX-3), like C-reactive protein (CRP), is a member of the pentraxin superfamily, which is produced by different cells in response to several inflammatory stimuli, including tumor necrosis factor-alpha (TNF-α) and interleukin-1 (16). PTX-3 is released by monocytes/macrophages and endothelial cells and, to a lesser extent, by smooth muscle cells. It is overexpressed in atherosclerotic plaques (19), suggesting that it could be a valuable biomarker of atherosclerosis. A recent study reported that the plasmatic levels of PTX-3 were higher in subjects with MetS than in those without it. PTX-3 is also strongly correlated with metabolic parameters (10, 29), so it could be considered a marker for the diagnosis of MetS.

Osteoprotegerin (OPG) is a cytokine receptor belonging to the TNF receptor superfamily. OPG modulates the progression of the calcification of atherosclerotic lesions by acting as a decoy receptor for the receptor activator of nuclear factor kappa B ligand (4). The plasmatic level of OPG is significantly higher in patients with MetS compared to those without MetS, and OPG levels are correlated with the presence of microvascular lesions (27).

TNF-α is involved in the progression of atherosclerotic plaques (3), due to an increased uptake of atherogenic lipoproteins by enhanced scavenger receptor activity (22). Current research confirms the involvement of TNF-α in the pathogenesis of MetS (3, 23).

Thus, PTX-3, OPG, and TNF-α are all connected with the inflammatory process within subclinical atherosclerosis (4, 10, 23, 27, 29) and they were investigated as possible markers of cardiovascular disorders with an inflammatory component. Their combined use in the assessment of MetS severity and subclinical atherosclerotic lesions has not yet been addressed.

The aim of this study was to assess the association between these inflammatory biomarkers, the severity of MetS, and cardiovascular risk.

Materials and Methods

Patients

The study was observational, transversal, prospective, cohort, analytical type. We enrolled 80 patients (M:F = 1, mean age = 55 ± 10.77 years) who met MetS criteria (25). The patients were evaluated in First Department of Internal Medicine of County Hospital, between March 2016 and 2017. The study protocol is in conformity with the Declaration of Helsinki and was approved by the Ethics Committee of the University of Medicine and Pharmacy. All patients were informed about the study protocol and signed the informed consent.

MetS was defined by the presence of three or more of the following criteria: waist circumference >94 cm in men/>80 cm in women; systolic blood pressure (SBP) over 130 mmHg or/and diastolic blood pressure (DBP) over 85 mmHg, or antihypertensive treatment; triglycerides >150 mg/dl; HDL cholesterol <40 mg/dl in men/<50 mg/dl in women; fasting serum glucose >100 mg/dl or confirmed diabetes mellitus (7).

The exclusion criteria were: inflammatory disorders, coronary artery disease, impaired renal function or retinopathy, females under oral contraceptives, patients undergoing treatment with vitamin K antagonists, and patients with poor echocardiographic window or those who refused to participate in the research.

The investigation protocol included: medical history, physical examination, 6-minute walk test (6MWT), biochemical tests, electrocardiography, echocardiography, and carotid ultrasonography.

Waist size, SBP, and DBP were measured on admission. Body mass index (BMI) was calculated to diagnose and grade obesity [overweight (25–29 kg/m^2) or obese ($\geq$30 kg/m^2)]. Patients who smoked at least 1 cigarette/day within the previous 2 months were considered active smokers. Impaired fasting glucose was defined by an elevated fasting plasma glucose concentration (>100 and <126 mg/dl). We recorded the history of hypertension, diabetes mellitus, dyslipidemia, and current treatment.

Biochemical analysis

Standard biochemical markers were measured in the Department of Biochemistry of County Hospital using a Beckman Coulter AU480 Chemistry Analyzer (Atlanta, GA, USA). The inflammatory markers were determined using ELISA methods with specific standardized kits: high-sensitivity CRP (hs-CRP; DIAsource Immuno Assays SA, Belgium), PTX-3 (OmniKineHuman, Assay biotech, Germany), OPG (Abbexa, USA), and TNF-α (DuoSet, R&D Systems Europe). All the aforementioned determinations were assayed according to the manufacturers' instructions.

Echocardiography

Standard echocardiography was performed on a General Electric Logiq 7 (GE Medical Systems, Tokyo, Japan) echocardiograph with a M3S 2.5–3.5 MHz active matrix phased array transducer. The following measurements were recorded: left ventricle ejection fraction, end-diastolic volume, end-systolic volume, left ventricular mass, mitral flow pulsed wave Doppler (E wave, A wave, E/A ratio, and deceleration time), tissue Doppler imaging measurements, E/E′ ratio, and left atrial volume; also in addition, pulmonary artery pressure and tricuspid annular plane systolic excursion were determined. These parameters were evaluated to exclude any ischemic impairment of the heart.

Carotid ultrasonography

Common carotid arteries (CCAs) were examined on a General Electric Logiq 7 (GE Medical Systems, Japan) device with a 7.5 MHz linear array transducer. CCA diameters were measured 10 mm proximal to the bulb, on longitudinal axis. CCA wall thickness was quantified based on the intima-media thickness (CCA-IMT), measured from the leading edges of the transition zones between lumen – intima and media – adventitia. Atherosclerotic plaques were defined as focal wall regions >1.5-mm thick that protruded into the lumen (12).

Arterial stiffness

Arterial wall stiffness was assessed by two estimates of the arterial stiffness index by M-mode ultrasonography and calculated by the formula: log(SBP/DBP)/[(Ds – Dd)/Dd], where Ds and Dd are the end-systolic and end-diastolic diameters of the CCA, respectively and SBP and DBP are the systolic and diastolic blood pressures (11). Carotid femoral pulse wave

velocity (PWV) was measured in the supine position using an automatic waveform analyzer (TensioMed Ltd., Hungary).

Statistical analysis

Statistical analysis was performed using the MedCalc Software, version 16.1.2 (Belgium). Parametric and non-parametric distribution of variables was assessed by the Kolmogorov–Smirnov test. Parametric data were expressed as mean $\pm$ standard deviation and non-parametric data were expressed as median value and interquartile ranges. Relative frequencies for categorical variables were reported as percentages. Correlations between parameters were determined by the Pearson's test for parametric data and by Spearman's test for non-parametric data. We used the χ^2 test for data analysis. The results were considered statistically significant if $p < 0.05$.

Results

The demographic and clinical data

Demographic and clinical data are presented in Table I.

To establish the severity of MetS, the patients were divided in two groups: the first group included the patients with minimally three components of MetS and they were considered having the mild form of MetS, whereas the second group included patients with the severe form of MetS presenting four or five diagnostic criteria. Nineteen patients (23.75%) had mild MetS, whereas 61 patients (76.25%) presented severe MetS. The severity of MetS was not correlated with the patients' gender ($p > 0.05$).

There was no correlation between anthropometric parameters and patients' age or gender ($p > 0.05$).

More patients with severe MetS were smokers as compared to the group with mild MetS (31.6% vs. 49.2%), but the difference was not significant ($p > 0.05$).

Patients with severe MetS had significantly higher values of BMI, body surface area, and waist circumference compared to patients with mild MetS (Table I).

Biological evaluation

There was a weak negative correlation between HDL-cholesterol and patients' BMI ($r = -0.205$, $p = 0.05$), but not between the former and waist circumference ($r = -0.191$, $p = 0.09$). The levels of biological parameters were not influenced by the patients' age or gender.

HDL-cholesterol was significantly lower, whereas triglycerides were significantly higher in patients with severe MetS (Table II). The other biological parameters, which are not components of MetS, did not differ between mild and severe MetS ($p > 0.05$).

Regarding the inflammatory biomarkers, only PTX-3 had significantly higher values in patients with severe MetS (Table II). The level of PTX-3 was not influenced by the patients' age or gender ($p > 0.05$).

Regarding the association of the inflammatory biomarkers with anthropometric and biological parameters, the only positive correlation was that of OPG levels with patients' BMI ($r = 0.264$, $p = 0.018$). PTX-3 and TNF-α were not correlated with BMI. None of the inflammatory parameters were correlated with waist circumference or with other biological parameters ($p > 0.05$).

Table I. Demographic and clinical data

Characteristics	No. of MetS components	Median values	*p*
Age (years)	3	50.18 (43.53–58.72)	0.089
	>3	57.31 (45.84–65.20)	
Gender (M/F) (%)	3	47.4/52.6	1
	>3	50.8/49.2	
Body surface area (m^2)	3	1.55 (1.42–1.69)	**0.002**
	>3	1.75 (1.62–1.90)	
Body mass index (BMI; kg/m^2)	3	28.90 (27.39–32.36)	**<0.001**
	>3	34.52 (31.01–37.28)	
Waist circumference (cm)	3	101 (98–110)	**0.001**
	>3	112 (102–124.5)	
Systolic blood pressure (mmHg)	3	160 (140–180)	0.7
	>3	160 (150–171)	
Diastolic blood pressure (mmHg)	3	90 (90–110)	0.7
	>3	95 (90–100)	

Data are expressed as median; 25–75th percentile. Bold values represent statistical significant ($p < 0.05$). BMI: body mass index; F: female; M: male; MetS: metabolic syndrome

The plasmatic values of TNF-α had a moderate positive correlation with PTX-3 ($r = 0.395$, $p < 0.001$) and OPG ($r = 0.221$, $p = 0.049$). The plasmatic levels of PTX-3, OPG, TNF-α, and hs-CRP ($p > 0.05$) were not correlated.

Cardiovascular evaluation
6MWT was negatively correlated with BMI ($r = -0.457$, $p < 0.001$) and waist circumference ($r = -0.397$, $p < 0.001$). Regarding the inflammatory biomarkers, only PTX-3 was negatively correlated with 6MWT ($r = -0.255$, $p = 0.02$).

The measured distance in 6MWT was significantly lower in patients with severe MetS as compared to the mild MetS group ($p = 0.005$). Thus, the severe MetS group had 48 patients (78.7%) with the 6-min walk test distance (6MWTD) below 610, whereas the mild MetS group had only 8 patients (42.8%; $p = 0.004$). The distance of 610 m was positively correlated with a higher number of MetS components ($p = 0.004$).

CCA-IMT was positively correlated with the patients' BMI ($r = 0.302$, $p = 0.006$). Moreover, both CCA-IMT and PWV were positively correlated with waist circumference ($r = 0.374$, $p = 0.001$ and $r = 0.253$, $p = 0.024$, respectively).

In addition, CCA-IMT was increased in patients with severe MetS (Table III). Forty-three patients (70.5%) with severe MetS presented a CCA-IMT above 0.8 mm as compared to seven patients (36.8%) with mild MetS ($p = 0.014$).

None of the investigated inflammatory biomarkers were correlated with CCA-IMT or PWV ($p > 0.05$).

Table II. Laboratory values

Characteristics	No. of MetS components	Median values	p
Fasting plasma glucose (mg/dl)	3	99 (88–131)	0.09
	>3	118 (104–134)	
Triglyceridemia (mg/dl)	3	178 (137–217)	**0.05**
	>3	199 (159.5–270)	
HDL-cholesterol (mg/dl)	3	42 (38–48)	**<0.001**
	>3	36 (33–39)	
HS-C reactive protein (ng/ml)	3	0.92 (0.71–1.41)	0.195
	>3	0.85 (0.595–1.11)	
Total cholesterol (mg/dl)	3	201 (175–235)	0.95
	>3	210 (173.5–234.5)	
LDL-cholesterol (mg/dl)	3	129.2 (100.6–155.4)	0.892
	>3	126 (88.4–149.8)	
Creatinine (mg/dl)	3	0.79 (0.68–0.91)	0.87
	>3	0.86 (0.75–0.995)	
PTX-3 (ng/dl)	3	0.36 (0.36–10.76)	**0.030**
	>3	10.04 (0.36–82.29)	
OPG (pg/dl)	3	306.66 (244.84–504.49)	0.15
	>3	430.30 (283.48–572.49)	
TNF-α (pg/dl)	3	557.75 (3.90–3,188.37)	0.53
	>3	1186.81 (59.40–3,359.94)	

Data are expressed as median; 25–75th percentile. Bold values represent statistical significant ($p < 0.05$). HDL-cholesterol: high-density lipoprotein cholesterol; hs-CRP: high-sensitivity C-reactive protein; LDL-cholesterol: low-density lipoprotein cholesterol; MetS: metabolic syndrome; PTX-3: pentraxin-3; OPG: osteoprotegerin; TNF-α: tumor necrosis factor-alpha.

ROC curve analysis for assessment of sensibility and specificity of the studied biomarkers in MetS severity assessment

The calculated PTX-3 cut-off value (10.7 ng/dl) differentiated between mild and severe MetS [AUC = 0.656; sensitivity (Se) = 47.1% (95% CI = 36.1%–62.3%); specificity (Sp) = 78.9% (95% CI = 54.4%–93.9%)]. Regarding OPG and TNF-α, receiver operating characteristic (ROC) analysis did not reach statistical significance.

In addition, the ROC curve for 6MWT and CCA-IMT were analyzed. Accordingly, the 6MWTD had a calculated cut-off value of 610 m, which made a significant difference between mild and severe MetS [AUC 0.712; Se = 78.69% (95% CI = 66.3%–88.1%); Sp = 57.9% (95% CI = 33.5%–79.7%)]. CCA-IMT had an AUC of 0.675 for a cut off

Table III. Cardiovascular parameters

Characteristics	No. of MetS components	Median values	p
6MWDT (m)	3	670 (700–560)	**0.005**
	>3	560 (450–600)	
Carotid stiffness index β	3	12.88 (−14.81–16.28)	0.982
	>3	12.62 (−11.09–14.93)	
Pulse wave velocity (m/s)	3	10.72 (6.02–12.22)	0.415
	>3	10.84 (9.45–12.224)	
CCA-IMT (mm)	3	0.8 (0.7–0.9)	**0.017**
	>3	0.9 (0.8–0.995)	

Data are expressed as median; 25–75th percentile. Bold values represent statistical significant ($p < 0.05$). 6MWTD: 6-min walk test distance; CCA-IMT: common carotid artery – intima media thickness; MetS: metabolic syndrome.

value of 0.8 mm, with a sensitivity of 70.5% (95% CI = 57.4%–81.5%) and a specificity of 63.16% (95% CI = 38.4%–83.7%).

Multivariate analysis of factors associated with MetS severity
To find out which parameter was independently associated with the severity of MetS, several predictive models using multivariate logistic regression were constructed. The most stable included the following variables: 6MWT, PTX-3, and CCA-IMT (Table IV). Based on previous reported results (28), the PTX-3 values were adjusted according to the patients' age. Only 6MWTD <610 m and CCA-IMT >0.8 mm were independently linked to severe MetS, in both analyses with or without adjustment of PTX-3 values according to the patients' age.

PTX-3 was negatively correlated with the 6MWT ($r = −0.255$; $p = 0.02$), which can explain why it was not independently associated with severe MetS. The 6MWT had a much larger probability to be linked to severe MetS (OR = 4.2 vs. 2.8).

Table IV. Multivariate analysis for the severity of MetS

Variables	Unadjusted for age		Adjusted for age	
	p	OR [95% CI]	p	OR [95% CI]
6MWTD > 610 m	0.016	4.246 [1.305–13.816]	0.024	4.668 [1.228–17.740]
PTX-3 > 10.7 ng/dl	0.121	2.837 [0.760–10.588]	0.115	2.990 [0.766–11.674]
CCA-IMT > 0.8 mm	0.020	4.027 [1.244–13.031]	0.020	4.209 [1.253–14.140]

6MWTD: 6-min walk test distance; CCA-IMT: common carotid artery – intima media thickness; MetS: metabolic syndrome; PTX-3: pentraxin-3; CI: confidence interval; OR: odds ratio

Discussion

This study describes the plasmatic profile of PTX-3, OPG, and TNF-α in patients with MetS, to establish their potential value for MetS risk assessment. Among the three biomarkers, PTX-3 had the highest correlation with the severity of MetS. It was found that PTX-3 plasmatic level was increased in patients with MetS, and a value higher than 10.7 ng/dl has a moderate sensitivity in the prediction of severe forms of the disease. In addition to this inflammatory biomarker, two other tests, 6MWT and CCA-IMT, were independently associated with severe MetS.

Inflammation in the vasculature is an important pathogenic link between cardiovascular diseases and MetS (26). Patients with MetS are more susceptible to develop diabetes mellitus, some cancers, and cardiovascular diseases (13) with an increased risk of morbidity and mortality. Since this syndrome consists of several cardiovascular risk factors, their combination could have a synergistic and multiplicative action, greatly amplifying the effects of each individual factor. It is often not possible to establish a cause–effect relationship between some risk factors and MetS and, sequentially, the cardiovascular risk. A better stratification of MetS' severity may allow us to understand which patients have a greater risk for cardiovascular events, leading to early introduction of therapeutic measures, whether pharmacological or not.

In this study, we included patients with only MetS, without clinical manifestation of atherosclerosis. Many studies have shown that there is a correlation between MetS and inflammatory mediators, including IL-6, TNF-α, PTX-3, and hs-CRP (10, 13, 21, 23, 29), but there are few data regarding their usage as biomarkers in the assessment of MetS' severity.

In this study, PTX-3 was correlated with MetS severity and its cut-off value of 10.7 ng/dl differentiated between mild and severe MetS. The same findings were reported by Karakas et al., who noticed that patients with severe MetS (five components) had higher values of PTX-3 compared to patients with mild or moderate MetS (three or four components) (9). Regarding hs-CRP, unlike this study, Karakas et al. reported that patients with severe MetS had higher hs-CRP as compared with mild MetS patients (9). We did not observe a different hs-CRP value in patients with severe as compared to mild MetS, or any correlation between the investigated inflammatory markers and hs-CRP. This result is similar to that reported by Miyazaki et al. (15) who, however, included patients with MetS and previous acute myocardial infarction.

The role of PTX-3 in atherosclerosis prompted us to evaluate whether a correlation exists between plasma PTX-3 and cardiometabolic risk factors in the syndrome. There was no correlation between PTX-3 and a specific component of MetS or other biological parameters. The results from the literature are controversial. Tabak et al. (24) found that PTX-3 is positively correlated with hs-CRP and LDL-cholesterol in patients with MetS. Yamasaki et al. (28) and Miyazaki et al. (15) showed that PTX-3 was inversely correlated with triglyceride levels and BMI in healthy subjects without MetS or associated cardiovascular diseases, and in patients with previous acute MI, respectively. Kardas et al. (10) and Zanetti et al. (29) showed that PTX-3 levels were positively correlated with triglycerides and negatively correlated with HDL-C levels in obese children and adolescents with MetS and cardiovascular diseases. A possible explanation of these controversial results consists in different inclusion criteria and different studied groups. It is possible that the relationships between PTX-3, atherosclerosis, and lipids are complex and are differently regulated under healthy and pathological conditions.

PTX-3 dynamics changes over time in association with the presence of several cardiovascular risk factors or the presence of MetS components. This is based on the observation that PTX-3 is positively associated with other inflammatory markers, but not with the metabolic profile. Both OPG and PTX-3 positively correlated with TNF-α. This was an expected result, knowing that PTX-3 secretion is stimulated by TNF-α, whereas OPG belongs to the TNF-α superfamily (4, 19). Therefore, PTX-3 could become a marker to identify subclinical atherosclerosis, but further studies are needed to establish what its exact role is in the inflammatory process associated with cardiovascular disease.

Endothelial dysfunction plays an important role in the development of atherosclerosis, leading to changes in the vessel intima and an increase in arterial stiffness. CCA-IMT is known to be a parameter that identifies subclinical atherosclerosis. It has been reported that CCA-IMT is a predictor of CV events, independently of blood pressure, lipid profile, and glucose levels in patients with MetS (8, 29). In addition, it has been proven that CCA-IMT is associated with the progression of MetS over time (29). In this study, CCA-IMT was positively correlated with anthropometric parameters, but not with PTX-3 or OPG. For CCA-IMT, a cut-off value of 0.8 mm differentiated between the mild and moderate forms of MetS. These observations were different from the results reported in Zanetti et al.'s study (29). They described a positive association between CCA-IMT and PTX-3 plasmatic levels, but after adjustment for HDL-cholesterol, this association did not persist (29). The results from this study were similar to those of Baragetti et al. (2). They reported that PTX-3 was no longer correlated with CCA-IMT after adjustment for age, sex, hypertension, diabetes, lipid profiles, cardiovascular events, and medical therapy (2). In this study, PTX-3 was not correlated with CCA-IMT in either uni- or multivariate analysis, before or after adjustment for age. These findings suggest that in addition to PTX-3 other factors play an important role in promoting carotid artery media thickening in MetS, and the inflammatory status is not the only mechanism that leads to endothelial dysfunction and atherosclerosis progression.

6MWTD is a rapid and inexpensive method to assess functional exercise capacity in patients with cardiovascular diseases or MetS (5). In the present study, 6MWT was inversely correlated with BMI and waist circumference, reflecting a low physical activity in patients with obesity or overweight. The measured distance was significantly lower in patients with severe MetS. The analysis showed that a distance of 610 m may differentiate between the mild and severe forms of MetS. PTX-3 negatively correlated with 6MWT in univariate analysis, but after multivariate analysis only six MWT and CCA-IMT were independently linked to severe MetS. Rubinsztajn et al. (20) reported no changes of 6MWT in COPD patients with or without MetS, but the other inflammatory markers like IL-6 and CRP were higher in patients with MetS, suggesting that respiratory illness rather than subclinical inflammation may be responsible for reduced physical activity. In another study performed in patients with cardiac surgeries, PTX-3 as inflammatory marker showed a close association with 6MWT distance, similarly to our data (6).

The strength of this study is that we studied several biomarkers involved in MetS and we evaluated the relationship between each of them and anthropomorphic and biochemical variables. However, this study has some limitations. A relatively small number of patients were included in the study, which might diminish the strength of the presented data. In addition, patients' long-term follow-up would have provided more information regarding the progression of carotid plaques and investigated biomarkers. It might be interesting to evaluate the biomarkers over time to assess the disease progression.

Conclusions

PTX-3 was correlated with the severity of MetS, with other inflammatory parameters and cardiovascular tests. CCA-IMT and 6MWTD are useful in differentiating between mild and severe MetS. PTX-3 could become a useful biomarker in the evaluation of subclinical atherosclerosis in patients with cardiometabolic risk factors and MetS, but further studies are needed to confirm its exact role in the inflammatory process associated with MetS.

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Conflict of interest

The authors declare no conflict of interest.

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