PERINATAL JOURNAL

Original Article

Perinatal Journal 2026; 34(1):1199-1210

https://doi.org/10.57239/prn.26.034100120

Correlation between plasma Pentraxin-3 (ptx3) levels and Carotid Intima-Media Thickness (CIMT) in patients at intermediate to high cardiovascular risk

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Abstract

Globally, mortality is still largely driven by atherosclerotic cardiovascular disease, making early identification of silent or asymptomatic atherosclerosis particularly important in individuals with intermediate to high cardiovascular risk. Inflammation throughout the body contributes significantly to the development of atherosclerosis, and pentraxin three has been proposed as a biomarker that may reflect disease progression, although its clinical relevance still requires further confirmation. Carotid intima media thickness is widely recognized as a noninvasive method to evaluate the severity and advancement of atherosclerotic changes. The study employed an observational cross-sectional design to examine the correlation between plasma pentraxin-3 levels and carotid intima-media thickness in patients with intermediate to high cardiovascular risk as determined by a general risk assessment model. Participants underwent carotid ultrasound examination and blood sampling for pentraxin three analysis, and the data were evaluated using correlation analysis. The findings showed no meaningful association between plasma pentraxin three concentration and carotid intima media thickness in this patient group, whereas carotid intima media thickness demonstrated a clear positive relationship with increasing age and overall cardiovascular risk. In conclusion, plasma pentraxin three levels do not appear to be significantly related to carotid intima media thickness in individuals with intermediate to high risk of cardiovascular disease.

Keywords: Atherosclerosis, Pentraxin-3 (PTX3), Carotid Intima-Media thickness, Framingham general CVD risk score 2008

Introduction

The global public health system continues to face major challenges due to cardiovascular disease, affecting populations in both high income and low income regions. According to global health reports, it is responsible for a substantial proportion of overall mortality, with the majority of related deaths occurring in developing countries, and the burden is expected to rise further in the future.

Most cardiovascular diseases are rooted in atherosclerosis, a multifaceted condition whose progression is influenced by both genetic predisposition and environmental exposures mediated by established risk factors, including abnormal lipid profiles, elevated blood pressure, impaired glucose metabolism, and excess body weight. As atherosclerosis advances, it can disrupt normal blood flow and lead to ischemic manifestations, while instability or rupture of atherosclerotic plaques may trigger sudden and severe cardiovascular events.

Atherosclerosis does not inevitably lead to clinical cardiovascular events in every affected individual, yet a higher extent of subclinical disease is associated with an increased likelihood of future events. Commonly used risk stratification models incorporate factors such as advancing age, biological sex, and elevated blood pressure. Professional guidelines from major cardiovascular organizations advocate for comprehensive risk evaluation in individuals without symptoms based on these traditional factors. Nevertheless, validation studies have demonstrated that such scoring systems offer only moderate accuracy in predicting outcomes. As a result, there is a growing need for supplementary diagnostic methods or biological markers that can better identify hidden or asymptomatic atherosclerosis, particularly in individuals classified as having intermediate cardiovascular risk.

Measurement of carotid intima media thickness using carotid ultrasonography provides a noninvasive means of identifying early atherosclerotic alterations before symptoms develop. Intima media thickness of the common carotid artery is commonly recognized as a reliable surrogate indicator of subclinical atherosclerosis, reflecting early arterial wall

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remodeling.

Evidence from multiple studies indicates a close association between carotid atherosclerosis and coronary artery disease as well as cerebrovascular disease. However, this examination requires specialized equipment, specific techniques, and trained, experienced operators to obtain accurate results. Therefore, there is a need for readily available and easily measurable risk biomarkers that can provide additional value in cardiovascular risk stratification.

Accumulating data suggest that systemic inflammation is a key contributor to the pathogenesis and progression of atherosclerosis. Inflammatory biomarkers such as C-reactive protein, interleukin-6, tumor necrosis factor-α, and pentraxin-3 have been linked to atherosclerotic processes and poor cardiovascular outcomes. Although pentraxin-3 belongs to the same protein family as C-reactive protein, it is considered more specific to vascular inflammation, as it is produced locally by atherogenesis-related cells rather than primarily by the liver. This biomarker has been identified within atherosclerotic plaques, with higher concentrations observed in more advanced lesions compared with early fatty changes, suggesting its association with disease progression. Consequently, pentraxin three may offer more precise information about atherosclerotic activity than general inflammatory markers. Previous population based studies have also demonstrated relationships between pentraxin three levels, traditional cardiovascular risk factors, subclinical vascular disease, and cardiovascular mortality.

Given the existing evidence, the current study sought to assess the link between plasma pentraxin-3 levels and carotid intima–media thickness as a marker of atherosclerosis severity in subjects with intermediate to high cardiovascular risk based on a widely utilized risk assessment model.

Methods

1.Study design: An observational analytic study with a cross-sectional design was conducted.

2. Study population

The participants in this study were individuals classified as having intermediate to high cardiovascular risk according to the Framingham Risk Score 2008. All subjects were recruited from patients visiting the outpatient cardiology clinic at Dr. Soetomo General Hospital in Surabaya over the study period spanning June to August 2016.

3. Study sample

The study sample comprised patients identified as having intermediate to high cardiovascular risk based on the Framingham General Cardiovascular Disease Risk Score 2008 who visited the outpatient cardiology clinic at Dr. Soetomo General Hospital in Surabaya during June to August 2016. Individuals were included only if they fulfilled the predetermined inclusion and exclusion criteria and voluntarily agreed to participate by providing informed consent.

4. Sampling technique

This study applied a consecutive sampling approach, whereby all patients who satisfied the eligibility criteria were enrolled in sequence as they presented to the clinic, and recruitment continued until the predetermined sample size was reached.

5. Sample size estimation

The minimum required sample size for this study was calculated using the following sample size estimation formula:

$$n = \left[\frac{Z_\alpha + Z_\beta}{0.5.\ln\left(\frac{1+r}{1-r}\right)}\right]^2 + 3$$

Where the following parameters were defined:

n = the required sample size
Zα = 1.96 (type I error set at 5%)
Zβ = 0.842 (statistical power of 80%)

r = the expected correlation coefficient between PTX3 and CIMT, estimated at 0.5

Based on this calculation, the minimum sample size required for this study was 30 subjects.

Study variables

The independent variable in this study was plasma pentraxin-3 (PTX3) level, while the dependent variable was CIMT.

Study instruments

The 2008 Framingham General Cardiovascular Disease Risk Score was applied to determine cardiovascular risk, incorporating demographic, lipid, blood pressure, and clinical variables, including age, sex, cholesterol levels, smoking status, blood pressure treatment, and diabetes mellitus. Individuals categorized as having intermediate risk, defined by a score between ten and nineteen percent, as well as those classified as high risk with a score of twenty percent or higher, were eligible for inclusion in the study.

Study procedures

A comprehensive clinical evaluation was performed on individuals visiting the cardiology, diabetes, geriatric, and employee clinics at Dr. Soetomo General Hospital, Surabaya, including medical history assessment, physical examination, twelve-lead electrocardiography, routine laboratory investigations, and cardiovascular risk estimation using the Framingham Risk Score.

Patients who fulfilled the predefined inclusion and exclusion criteria were subsequently invited to take part in the study, and participation was granted only after written informed consent had been obtained from the patient or an authorized family member.

Venous blood was drawn from each participant to determine plasma pentraxin three concentrations and was subsequently delivered to a certified clinical laboratory for processing. The samples were treated with appropriate anticoagulants and centrifuged under controlled temperature conditions shortly after collection to separate plasma components. To reduce the influence of platelets, an additional high speed centrifugation step was carried out.

Plasma specimens were either analyzed immediately or divided into aliquots and preserved at low temperature until laboratory assessment. Measurement of pentraxin three levels was performed using an enzyme linked immunosorbent assay and read with a microplate reader supported by dedicated analysis software.

Evaluation of carotid intima media thickness was conducted with the participant lying in a supine position and the head rotated away from the side being examined. Image acquisition and interpretation were carried out in accordance with recommendations from a professional echocardiography society. Measurements were obtained from the far wall of both common carotid arteries at a standardized location beyond the carotid bulb, using multiple imaging planes and an automated edge detection system to ensure accuracy and reproducibility.

Data processing and statistical analysis

After collection, all data were systematically coded, entered into the database, checked for accuracy, and edited prior to statistical evaluation. The assessed variables comprised plasma pentraxin-3 levels, carotid intima–media thickness, and the Framingham General Cardiovascular Disease Risk Score 2008. Continuous data were expressed as mean and standard deviation or as median and range according to their distribution, while categorical data, including sex and baseline characteristics, were reported as frequencies and percentages. All descriptive findings were presented in tables.

Further inferential analysis was performed to evaluate the relationship between plasma pentraxin-3 concentrations and carotid intima media thickness. Depending on data distribution, Pearson correlation was applied to normally distributed data, whereas Spearman rank correlation was used for non-normally distributed variables. A two-tailed significance level of 0.05 with 80% statistical power was adopted, and all inferential findings were summarized in tables.

The strength of the correlation was expressed by the correlation coefficient (r) and interpreted as follows:

0.00–0.30: weak correlation
0.31–0.50: moderate correlation
0.51–1.00: strong correlation

All statistical analyses were performed using SPSS

software, version 23.0.

Results and Discussion

A cross-sectional study with a correlational approach was conducted among outpatients with intermediate to high cardiovascular risk, as determined by the Framingham General Cardiovascular Disease Risk Score 2008, who visited the cardiology outpatient clinic at Dr. Soetomo General Hospital in Surabaya from June to August 2016. Consecutive sampling was applied, and participants were enrolled based on established inclusion and exclusion criteria. Comprehensive clinical assessments, including laboratory investigations, plasma pentraxin-3 measurement, and carotid intima media thickness evaluation, were performed in all eligible individuals. Ultimately, thirty-eight subjects were analyzed statistically.

Baseline characteristics of study subjects

Baseline profiles of the thirty-eight study participants comprised demographic information (age and sex), cardiovascular risk scores, and categorization by cardiovascular risk level. Major cardiovascular risk factors, including diabetes mellitus, hypertension, smoking, and dyslipidemia, as well as physical examination findings such as systolic and diastolic blood pressure, were recorded. Laboratory findings, plasma pentraxin-3 concentrations, and carotid intima–media thickness measurements were also obtained and are presented in Table one.

Shapiro–Wilk testing revealed non-normal distributions for pentraxin-3 concentrations, carotid intima–media thickness, and cardiovascular disease risk scores. Therefore, categorical data were summarized using frequencies and percentages, and numerical data were reported as medians accompanied by minimum and maximum values.

Among the participants included in the analysis, the distribution between men and women was equal. Ages ranged from early middle adulthood to late elderly, with the central tendency indicating that most subjects were in their early sixties. On physical examination, median systolic and diastolic blood pressure values were consistent with elevated blood pressure levels. Participants were classified as having excess body weight based on body mass index criteria, with the median body mass index falling within the overweight range.

With regard to cardiovascular risk factors, lipid abnormalities were the most frequently observed condition, followed by elevated blood pressure and diabetes mellitus. Cigarette smoking was relatively uncommon among the study population. Risk stratification using the Framingham General Cardiovascular Disease Risk Score placed the majority of subjects in the intermediate risk category, while a smaller proportion, with the overall median risk score reflecting moderate cardiovascular risk. The central values for plasma pentraxin three concentration and carotid intima media thickness indicated measurable inflammatory activity and subclinical atherosclerotic changes within the study group.

Table 1. Characteristics of basic data of research subjects (n=38)

Variable	n (%) or Median (Min-Max)
Gender	
Male	
Women	19 (50,0%)
FRS	19 (50,0%)
Medium	
Height	
Hypertension	25 (65,8%)
Ya	
No	13 (34,2%)
Diabetes	
Ya	
No	22 (57,9%)

Dyslipidemia	16 (42,1%)
Ya	
No	
Smoking	15 (39,5%)
Ya	
No	23 (60,5%)
Age (years)	
Body Mass Index (kg/m2)	24 (63,2%)
Systolic blood pressure (mmHg)	14 (36,8%)
Diastolic blood pressure (mmHg)	
SK (mg/dL)	3 (7,9%)
GDP (mg/dL)	35 (92,1%)
GD2JPP (mg/dL)	62 (40 - 78)
Total Cholesterol (mg/dL)	25,6 (19,9 – 43,1)
LDL-Cholesterol (mg/dL)	140 (120 – 180)
HDL-Cholesterol (mg/dL)	90 (70 – 100)
CVD Risk (%)	0,99 (0,49 – 1,45)
PTX3 (ng/mL)	105 (75 – 269)
CIMT (mm)	145,5 (98 – 474)
	202 (151 – 285)
	130 (81 – 242)
	46 (33 – 75)
	15,9 (10,0 – 30,0)
	0,13 (0,08 – 3,87)
	0,97 (0,69 – 1,917)

ivariate analysis of plasma PTX3 levels on the characteristics of study subjects

The correlation of PTX3 levels to the variables is shown in Table two. The correlation test is carried out with Spearman's rho test, where there is a correlation.

Table 2. Bivariate analysis of plasma PTX3 levels on study subject characteristics (n = 38)

Variabel	p*	r
Age (years)	p = 0,577	r = 0,093
Body Mass Index (BMI) (kg/m2)	p = 0,949	r = -0,011
CVD Risk (%)	p = 0,705	r = 0,063
Serum Creatinine (mg/dL)	p = 0,988	r = -0,002
Fasting Blood Sugar (mg/dL)	p = 0,212	r = -0,207
Blood Sugar 2JPP (mg/dL)	p = 0,820	r = -0,038
Systolic Blood Pressure (mmHg)	p = 0,787	r = -0,045
Diastolic Blood Pressure (mmHg)	p = 0,559	r = -0,098
Total Cholesterol (mg/dL)	p = 0,587	r = 0,091
HDL cholesterol (mg/dL)	p = 0,022	r = -0,371
LDL cholesterol (mg/dL)	p = 0,944	r = -0,012

* Analyzed using the Spearman's rho correlation test (two-tailed significance; α = 0.05).

Correlation testing revealed that plasma pentraxin three concentrations were not significantly associated with age, body mass index, overall cardiovascular risk score, serum creatinine levels, fasting and postprandial blood glucose.

Table 3 Differences in plasma PTX3 levels to the characteristics of the study subjects (n = 38)

Variabel	p*
Gender	0,672
Hypertension	0,375
Diabetes	0,881
Dyslipidemia	0,232
Smoking	0,311
Statin Consumption	0,146

In addition, comparisons of pentraxin three levels of major cardiovascular risk factors, namely diabetes mellitus, hypertension, dyslipidemia, and smoking, as well as according to statin use, are summarized in Table three.

As shown in Table three, plasma pentraxin three concentrations did not differ significantly between men and women. Likewise, no meaningful differences were identified when comparing pentraxin three levels in subjects with or without diabetes mellitus, hypertension, dyslipidemia, or a history of smoking. In addition, pentraxin three concentrations were comparable between participants who were receiving statin therapy and those who were not, with all comparisons yielding p values above the threshold for statistical significance.

Bivariate analysis of CIMT according to study subject characteristics

The correlations between CIMT and the study variables are presented in Table 4. Correlation analyses were performed using Spearman's rho.

Table 3 Bivariate analysis of CIMT correlation to study subject characteristics (n = 38)

Variabel	p*	r
Age (years)	p = 0,003*	r = 0,471
Body Mass Index (kg/m2)	p = 0,933	r = -0,014
Cardiovascular risk (%)	p = 0,001*	r = 0,505
Serum Creatinine (mg/dL)	p = 0,510	r = 0,110
Fasting Blood Sugar (mg/dL)	p = 0,911	r = -0,019
Blood Sugar 2JPP (mg/dL)	p = 0,383	r = -0,145
TDS (mmHg)	p = 0,866	r = 0,028
TDD (mmHg)	p = 0,364	r = -0,151
Total cholesterol (mg/dL)	p = 0,756	r = -0,052
HDL cholesterol (mg/dL)	p = 0,885	r = 0,024
LDL cholesterol (mg/dL)	p = 0,864	r = 0,029

* Analyzed using the Spearman's rho correlation test (two-tailed significance; α = 0.05)

As presented in Table four, carotid intima media thickness demonstrated a statistically significant association with age, with the correlation coefficient

indicating a moderate positive relationship. A similar pattern was observed for overall cardiovascular disease risk, which also showed a significant and moderately positive correlation.

According to the results summarized in Table five, carotid intima media thickness did not differ significantly between male and female participants. Likewise, comparisons based on the presence or absence of diabetes mellitus, hypertension, dyslipidemia, and smoking history revealed no statistically meaningful differences in carotid intima media thickness.

Table 4. CIMT differences in research subject characteristics (n = 38)

Variabel	p
Gender	0,204
Hypertension	0,723
Diabetes	0,754
Dyslipidemia	0,146
Smoking	0,191
Statin Consumption	1,000

*Analyzed using the Mann–Whitney U test (two-tailed significance; α = 0.05)

No significant variation in carotid intima media thickness was also observed between subjects who were receiving statin therapy and those who were not, with all p values exceeding the threshold for statistical significance.

Correlation analysis between plasma PTX3 Levels and CIMT in patients with intermediate to high cardiovascular risk

The associations between plasma pentraxin three concentrations and carotid intima media thickness are summarized in Tables six and seven. These relationships were evaluated using Spearman rank correlation analysis, and statistical significance was determined using a p value threshold of less than zero point zero five.

Table 5. Analysis of correlation of plasma PTX3 Levels with CIMT values in subjects with medium-high risk CVD (n = 38)

CVD Risk	p*	r
Medium – High Risk CVD	0,358	0,153

* Analyzed using the Spearman's rho correlation test (two-tailed significance; α = 0.05)

Table 6. Analysis of correlation of plasma PTX3 Levels with CIMT values in subjects with medium-high risk CVD (n = 38)

CVD Risk	p*	r
Medium Risk CVD (n= 25)	0,635	0,100
CVD High Risk (n = 13)	0,477	0,228

* Analyzed using the Spearman's rho correlation test (two-tailed significance; α = 0.05)

When the participants were further evaluated within each cardiovascular risk category, the results remained consistent, showing no meaningful relationship between pentraxin three concentration and carotid intima media thickness in either risk group.

Pentraxin three is an inflammatory mediator released by several cell types involved in vascular inflammation, including endothelial cells, macrophages, and neutrophils, following stimulation by proinflammatory cytokines that are abundant within atherosclerotic plaques.

Carotid intima media thickness measurement represents a sensitive and noninvasive approach for detecting and assessing the extent of atherosclerotic changes. Within this context, the present correlational study was conducted to explore the potential relationship between plasma pentraxin three levels with elevated cardiovascular risk as determined by a standardized risk assessment model.

Baseline characteristics of study subjects

Advancing age, biological sex, elevated blood pressure, tobacco use, lipid abnormalities, and diabetes mellitus are well established contributors to the constitute the fundamental determinants. These risk factors seldom exist independently and typically interact in a multifaceted and synergistic manner, thereby accelerating atherosclerotic progression. Within the study population, lipid disorders represented the most common modifiable risk factor, followed by hypertension, diabetes mellitus, and smoking, whereas age and sex constituted the principal nonmodifiable components of cardiovascular risk.

Findings from long term population research have shown that the likelihood of developing coronary heart disease rises markedly after midlife, with men facing a higher lifetime probability than women. Sudden cardiac death related to coronary disease is particularly frequent among middle aged men, highlighting the strong influence of age and sex on cardiovascular outcomes. In addition, elevated pulse pressure combined with increased systolic blood pressure has been shown to confer a level of cardiovascular risk comparable to a substantial rise in systolic pressure alone. This observation emphasizes the critical role of large artery stiffness as an important determinant of cardiovascular risk in older individuals.

Diabetes mellitus has consistently and independent contributor to cardiovascular disease, with evidence indicating a markedly higher risk among affected individuals, especially in women. Beyond metabolic disorders, cardiovascular disease is closely linked to lifestyle related factors, including cigarette smoking, unhealthy dietary patterns, and insufficient physical activity, all of which promote the development of dyslipidemia, diabetes mellitus, and hypertension.

Global health reports suggest that the majority of cardiovascular deaths could be avoided through the adoption of healthier lifestyles, underscoring the substantial preventive potential of behavioral modification.

Correlation between plasma PTX3 levels and study subject characteristics

Despite extensive investigation into the involvement of pentraxin three in vascular biology and cardiovascular disease, the direct causal link between circulating pentraxin three concentrations and cardiovascular outcomes has not yet been clearly established. Clinical studies have reported associations between pentraxin three levels and acute myocardial infarction, while experimental research using animal models has suggested that pentraxin three may play a protective role against atherosclerotic development.

The analysis demonstrated that plasma pentraxin-3 levels were not significantly related to various demographic and clinical parameters, including age, blood pressure measurements, body mass index, lipid profiles, renal function, and fasting and postprandial glucose levels. Furthermore, no significant differences in pentraxin-3 concentrations were found across groups defined by major cardiovascular risk factors or by sex.

Previous investigations Zanetti et al. (2009) have conflicting evidence regarding the association of pentraxin-3 with metabolic and cardiovascular risk factors. In contrast, Yamasaki et al. (2009) described positive associations between pentraxin three concentrations and triglyceride levels, along with inverse relationships with high density lipoprotein cholesterol. Other reports have shown negative correlations between pentraxin three levels and indicators of adiposity, including body mass index and triglycerides. Research examining pentraxin three expression within visceral adipose tissue has suggested links with multiple metabolic and inflammatory parameters, such as lipid profiles, inflammatory markers, and adipokines, while showing no clear association.

The association between pentraxin three and conventional cardiovascular risk factors has also been evaluated in population based studies, many of which have found no meaningful relationship between pentraxin three levels and conditions such as hypertension, diabetes mellitus, dyslipidemia, or smoking status. In contrast, investigations conducted in selected high risk groups have reported that pentraxin three levels may correlate with age, vascular stiffness, blood pressure indices, and markers of immune activation, while showing inverse relationships with certain lipid parameters. Notably, among healthy individuals (Baragetti et al., 2013).

Correlation between CIMT and study subject characteristics

As a systemic pathological condition, atherosclerosis involves multiple arterial territories. Elevated carotid intima media thickness has been linked to cardiovascular risk factors and to current and future cardiovascular events, indicating the global burden of atherosclerosis. Therefore, carotid intima media thickness is widely accepted as a surrogate measure of atherosclerotic disease.

Carotid intima media thickness in the present study was determined using the maximum value obtained from repeated measurements, referred to as the maximum-of-maximum method. While a uniform standard for carotid intima media thickness measurement has yet to be established, the assessment protocol adhered to guidelines from a recognized echocardiography society. Interpretation of these measurements should be adjusted for age, sex, and population characteristics.

A moderate positive association was observed between carotid intima media thickness and age, and between carotid intima–media thickness and global cardiovascular risk scores. This observation aligns with earlier evidence of age-related increases in carotid intima media thickness and with studies reporting greater thickness values among individuals at higher cardiovascular risk.

The analysis showed no significant associations between carotid intima media thickness and blood pressure, body mass index, lipid parameters, glucose measurements, or renal function. Additionally, carotid intima–media thickness did not vary significantly by sex, statin therapy, or major

cardiovascular risk factors such as diabetes mellitus, hypertension, smoking, and dyslipidemia.

Earlier studies, such as that reported by Koskinen et al. (2009), have shown variable results. Investigations in younger cohorts have linked intima–media thickness progression to obesity, dyslipidemia, and insulin resistance, while studies involving more diverse age groups have found carotid intima media thickness to be associated with several cardiovascular risk factors, including age, hypertension, dyslipidemia, and diabetes mellitus.

CIMT in patients with intermediate to high cardiovascular risk

The findings showed no significant relationship between plasma pentraxin-3 levels and atherosclerotic burden measured by carotid intima–media thickness among individuals with intermediate to high cardiovascular risk, including when the intermediate- and high-risk groups were analyzed independently.

In agreement with earlier reports, including the study by Knoflach et al. (2012), large cohort studies have shown no significant relationship between circulating pentraxin-3 concentrations and intima–media thickness of major arterial segments. While pentraxin-3 has been linked to the extent and severity of atherosclerotic disease, especially in patients with multivessel involvement, it does not seem to reflect arterial wall thickening as a marker of early atherosclerotic changes. Similar observations have been reported in population based studies demonstrating that pentraxin three levels do not predict intima media thickness progression and are not associated with the maximal rate of arterial wall thickening. Other research has likewise failed to demonstrate a meaningful relationship between pentraxin three concentrations and carotid intima media thickness, suggesting that pentraxin three may not adequately reflect early or subclinical atherosclerotic changes (Baragetti et al. , 2013).

Several clinical and experimental observations suggest that pentraxin three is closely linked to vascular alterations and immune regulation (Yano et al., 2010). Evidence from animal models indicates that this molecule may play a protective role against atherosclerosis by acting as a regulatory signal during both local and systemic inflammation, limiting excessive neutrophil accumulation and thereby dampening inflammatory reactions (Yilmaz et al., 2010). Further clinical findings reveal that plasma pentraxin three parallels the activity of indoleamine two three dioxygenase, an enzyme produced by antigen presenting cells that suppresses immunoinflammatory pathways, particularly those driven by T helper type one responses (Deban et al., 2010; Jylhävä et al., 2011).

Observational evidence indicates that higher circulating pentraxin three is accompanied by increased neutrophil abundance and enhanced activity of matrix metalloproteinase nine, suggesting engagement of the local innate immune system. Although this protein is stored within polymorphonuclear cell granules and released upon their activation, it also counterbalances inflammation by reducing leukocyte adhesion and migration through inhibition of P selectin–dependent mechanisms, thereby limiting excessive neutrophil infiltration and exerting protective effects against atherosclerosis. During early atherosclerotic changes, pentraxin three may mainly function as a regulatory molecule that restrains inflammation, whereas in more advanced lesions or clinically evident cardiovascular conditions it may become more closely linked to pro inflammatory pathways.

Overall, these results align with prior evidence indicating that the prognostic relevance of pentraxin three is confined to specific clinical scenarios such as symptomatic cardiovascular disease, heart failure, or acute coronary events, while it shows limited value in detecting early atherosclerosis or subtle vascular alterations. Consequently, plasma pentraxin three is unlikely to be a useful marker for screening healthy populations or individuals with subclinical atherosclerotic changes.

Study limitations

Several methodological limitations should be acknowledged. All biochemical analyses were performed in a single laboratory, and variability of pentraxin three within the same individual over time was not evaluated. Circulating pentraxin three demonstrated wide dispersion, with most participants presenting levels below the established

reference range, which required the application of extrapolated values for statistical assessment.

This predominance of low values may be explained by the inclusion of relatively healthy participants. Additional limitations concern the ultrasonographic, which was conducted by a single examiner without assessment of intra observer reliability. The study was also limited by its single center design and restricted population coverage, reducing the generalizability of the results. Moreover, background medical treatments such as lipid lowering, glucose lowering, and blood pressure lowering therapies were not standardized or restricted, potentially affecting vascular measurements.

Consequently, confirmation of these findings will require rigorously designed investigations involving larger and more diverse populations, multicenter collaboration, repeated assessment of biomarkers, and controlled therapeutic regimens to ensure greater robustness and validity of the conclusions.

Conclusion

The analysis revealed no significant relationship between plasma PTX3 concentrations and carotid intima–media thickness in patients at intermediate to high cardiovascular risk.

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