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Pentraxin 3: A Marker for the Presence and Severity of Coronary Artery Disease

Pentraxin 3: Koroner Arter Hastalığı Varlığının ve Şiddetinin Belirteci

ABSTRACT

Objective: Atherosclerosis, a major contributor to coronary artery disease (CAD), is characterized by chronic arterial inflammation. Pentraxin 3 (PTX-3), a biomarker of inflammation, serves as an indicator of both atherosclerosis and the progression of CAD. The aim of this study was to investigate the association between PTX-3 levels and the presence and severity of CAD, as determined by coronary computed tomography angiography (CCTA).

Method: In this study, 94 participants (54 with CAD and 40 controls) underwent CCTA and coronary artery calcium scoring (CACS) using computed tomography. PTX-3 levels were measured using the enzyme-linked immunosorbent assay (ELISA) method. CAD patients were categorized based on CCTA findings and further subdivided into three groups according to their CACS: Group I (CACS < 100), Group II (CACS 100–299), and Group III (CACS ≥ 300).

Results: Serum PTX-3 levels were significantly higher in the CAD group. A PTX3 cut-off value of 5.80 ng/mL predicted CAD with 68% sensitivity and 66% specificity. A strong positive correlation was observed between CACS and PTX-3 levels (r = 0.521, P < 0.001). In high-risk patients with a CACS ≥ 300, PTX-3 levels were significantly higher than those in low- and intermediate-risk groups a CACS < 300. However, no significant difference in PTX-3 levels was observed between the normal coronary group and the low- and intermediate-risk groups. Furthermore, no correlation was found between the degree of coronary artery stenosis and PTX-3 levels.

Conclusion: Pentraxin 3 might serve as a valuable biomarker for the diagnosis and severity of CAD.

Keywords: Agatston score, atherosclerosis, coronary artery calcification, coronary artery disease, coronary computed tomography angiography, Pentraxin 3

ÖZET

Amaç: Kronik arteriyel inflamasyon ile karakterize ateroskleroz koroner arter hastalığının (KAH) en önemli sebebidir. İnflamasyonun bir biyobelirteci olan Pentraksin 3 (PTX-3), hem aterosklerozun varlığı hem de KAH'ı şiddetinin bir göstergesi olarak kullanılmaktadır. Çalışmamızın amacı, PTX-3 düzeyleri ile koroner bilgisayarlı tomografik anjiyografi (KBTA) ile belirlenen KAH varlığı ve şiddeti arasındaki ilişkiyi araştırmaktır.

Yöntem: Çalışmada 94 katılımcıya (54 KAH ve 40 kontrol) bilgisayarlı tomografi kullanılarak KBTA ve koroner arter kalsiyum skorlaması (KAKS) yapılmış ve serum PTX-3 düzeyleri ELISA yöntemiyle ölçülmüştür. KAH hastaları KAKS'larına göre üç gruba ayrılmıştır: Grup I (<100), Grup II (100–299) ve Grup III (≥300). KAH hastaları KAKS'larına göre üçe ayrılmışıtır: Grup I (KAKS<100), Grup II (KAKS 100–299) ve Grup III (KAKS≥300).

Bulgular: Serum PTX-3 düzeyleri KAH grubunda anlamlı olarak daha yüksekti. PTX-3 cut-off değeri 5.80 ng/mL, KAH'ı %68 duyarlılık ve %66 özgüllük ile öngördürdü.

KAKS ve PTX-3 seviyeleri arasında güçlü bir pozitif korelasyon saptandı (r = 0.521, P < 0.001). PTX-3 seviyeleri; KAKS≥300 olan yüksek riskli hastalarda KAKS<300 olan düşük ve orta riskli gruplara göre anlamlı derecede yüksekti. Normal koroner grubu ile düşük ve orta riskli KAH grupları arasında PTX-3 düzeylerinde anlamlı bir fark gözlenmedi ve koroner arter stenoz derecesi ile PTX-3 düzeyleri arasında bir korelasyon bulunmadı.

Sonuç: PTX-3, KAH tanısı ve şiddeti için değerli bir biyobelirteç olarak kullanılabilir.

Anahtar Kelimeler: Agatston Skoru, ateroskleroz, koroner arter kalsifikasyonu, koroner arter hastalığı, koroner bilgisayarlı tomografik anjiyografi, Pentraxin 3

ORIGINAL ARTICLE
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Cardiovascular disease (CVD) remains a significant contributor to mortality in both Türkiye and Europe as a whole. The elevated occurrence of circulatory system disorders places a considerable strain on healthcare systems and government budgets. A 2017 report from the European Union (EU) indicated that circulatory system diseases were responsible for 1.71 million fatalities, representing approximately 36.7% of all recorded deaths. Similarly, in Türkiye, these diseases accounted for approximately 36.5% of total deaths.[1] The majority of these deaths are attributable to coronary artery disease (CAD) and stroke. Despite significant progress in therapy and prevention over the past three decades, CAD remains the leading cause of death in Europe.[2] The current global prevalence rate of coronary artery disease is 1,655 per 100,000, with this figure projected to rise to 1,845 per 100,000 by 2030.[3] Approximately 50% of deaths associated with CVD occur without any prior indications or diagnoses of cardiac conditions. This underscores the critical need to assess risk in asymptomatic individuals, which is essential for preventing such fatalities.[4]

Despite invasive coronary angiography (ICA) remaining the gold standard for diagnosing and treating CAD, non-invasive imaging is becoming an increasingly crucial aspect of the diagnostic process. In particular, coronary computed tomography angiography (CCTA) is poised to become a pivotal tool in the near future for the exclusion of CAD, with current guidelines placing it at the forefront of the assessment of stable coronary syndromes.[5] In addition to diagnosing CAD, CCTA applications may also determine the composition of atherosclerotic plaques in identified lesions. This enables the assessment of plaque vulnerability to acute coronary syndrome (ACS) and the prevention of future ischemic events through the optimization of medical treatment or the performance of coronary interventions.[6] The significance of biomarkers in diagnosing CAD is particularly important for its early detection, whether used alone or as part of imaging modalities. In recent times, a considerable number of biomarkers linked to the risk of CAD have been identified and investigated. These include various inflammation markers such as C-reactive protein (CRP), pentraxin, select interleukins, tumor necrosis factor alpha (TNF-α), adipokines, lipid-associated parameters, and hematological cell-derived indices.[7-11]

Pentraxin 3 (PTX-3) is part of the pentraxin superfamily, which includes C-reactive protein and serum amyloid P. Unlike CRP, which is synthesized by the liver, PTX-3 is produced in response to inflammatory stimuli across several cell types and organs, particularly within the arterial wall.[12] Research has demonstrated that PTX-3 serves as a more specific factor in plaque formation and inflammatory responses in coronary arteries. It has been shown that PTX-3 is created at the site of inflammation and is present in atherosclerotic lesions.[13] PTX-3 levels likely reflect a localized inflammatory response to arterial wall damage rather than a systemic response. Consequently, PTX-3 could serve as a more accurate indicator for identifying inflammation localized within the arterial wall.[14] Previous studies have utilized ICA to investigate the correlation between PTX-3, CAD, and atherosclerosis. However, the results of these studies have been inconclusive regarding the prediction and severity of CAD. The objective of this research was to examine serum PTX-3 levels in patients with varying degrees of atherosclerotic burden, as identified by CCTA, which is a more sensitive indicator of atherosclerosis.[15-18]

ABBREVIATIONS

ACS	Acute coronary syndrome
CACS	Coronary artery calcium scoring
CAD	Coronary artery disease
CCTA	Coronary computed tomography angiography
CRP	C-reactive protein
CVD	Cardiovascular disease
ELISA	Enzyme-linked immunosorbent assay
EU	European Union
ICA	Invasive coronary angiography
PTX-3	Pentraxin 3
TNF-α	Tumor necrosis factor alpha

Materials and Methods

This observational pilot study cross-sectionally evaluated 94 consecutive participants who presented with chest pain and underwent CCTA between June and September. Exclusion criteria included atrial fibrillation, age below 35 years, prior use of statins or anti-inflammatory drugs, chronic renal disease, chronic liver disease, autoimmune or acute infectious diseases, and established CAD or peripheral artery disease. Participants with a positive exercise electrocardiogram (ECG) or myocardial perfusion single-photon emission computed tomography (SPECT) indicating CAD were referred for direct ICA in accordance with clinical guidelines. To refine the definition of the normal coronary artery group, we aimed to exclude participants with microvascular disease from the normal group identified by CCTA.

Following the provision of informed consent, a range of clinical and laboratory data were collected, including demographic and medical variables such as sex, age, smoking history, body mass index (BMI), blood pressure, lipid profiles, and family history of CAD. Blood samples were obtained from the antecubital vein after an overnight fast of at least eight hours. Serum lipid levels and other biochemical markers were analyzed using a biochemical analyzer. Serum PTX-3 levels were measured using enzyme-linked immunosorbent assay (ELISA) kits (Invitrogen Human PTX-3 ELISA) according to the manufacturer's instructions. All samples were stored at -80 °C until analysis.

CCTA was performed on all participants using a 128-slice single-source scanner (Somatom Go Top; Siemens Healthcare, Forchheim, Germany). The Agatston score was used to assess the extent of coronary artery calcification, evaluated on the same computed tomography (CT) scanner.

Ethics approval was obtained from the İzmir Bakırçay University Non-Interventional Clinical Research Ethics Committee (Approval Number: 1155, Research Number: 1135, Date: 24.08.2023).

This study was conducted in accordance with the Declaration of Helsinki. No artificial intelligence (AI)-assisted technologies, including large language models (LLMs), chatbots, or image generators, were used in the production of this study.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD) and analyzed using the independent samples t-test. Categorical variables were described as frequencies (n) and percentages (%) and analyzed using the chi-squared test or

Table 1. Differences Between Coronary Artery Disease Group and Normal Coronary Group

	Coronary Artery Disease (n = 54)	Control (n = 40)	P
Female (%)	35.18%	37.5%	0.532
Age (years)	59.08 ± 9.78	60.23 ± 9.92	0.835
BMI (kg/m²)	27.65 ± 3.88	26.98 ± 4.08	0.584
Glucose (mg/dL)	105.83 ± 34.76	98.85 ± 54.74	0.489
Cholesterol (mg/dL)	215.45 ± 50.99	222.45 ± 37.89	0.324
LDL (mg/dL)	139.07 ± 41.78	149.27 ± 39.96	0.401
HDL (mg/dL)	52.76 ± 09.51	55.01 ± 13.90	0.701
Non-HDL (mg/dL)	172.52 ± 53.76	175.65 ± 52.73	0.821
Triglycerides (mg/dL)	190.39 ± 109.76	167.19 ± 98.78	0.087
Creatinine (mg/dL)	0.82 ± 0.12	0.77 ± 0.11	0.071
Smoking (%)	37.00%	35.00%	0.401
Diabetes mellitus (%)	24.07%	20.00%	0.361
Systolic BP (mmHg)	135.65 ± 12.55	132.45 ± 11.76	0.643
Diastolic BP (mmHg)	77.76 ± 10.55	76.98 ± 9.08	0.701
PTX-3	6.72 ± 2.02	5.75 ± 1.11	0.035

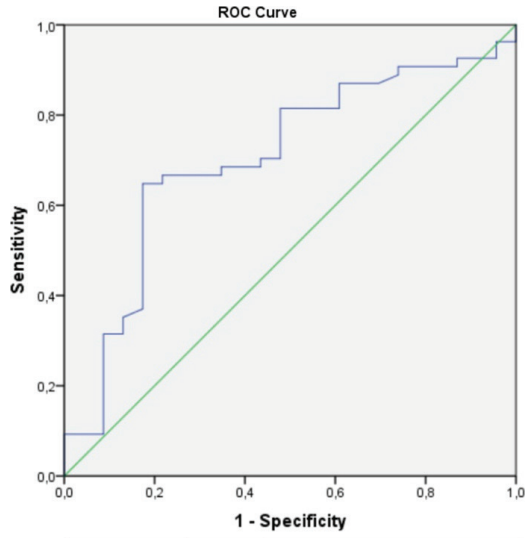
BMI, Body Mass Index; BP, Blood Pressure; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; PTX-3, Pentraxin 3.

Fisher's exact test, as appropriate. Pearson's correlation analysis was used to evaluate associations between PTX-3 levels and other continuous variables. Receiver operating characteristic (ROC) curves were constructed to assess the diagnostic efficacy of PTX-3 in identifying CAD. All statistical analyses were performed using SPSS software, version 29.0 (SPSS Inc., Chicago, IL, USA). A two-tailed p-value of less than 0.05 was considered statistically significant.

Results

The results indicated no statistically significant differences in age, sex, body mass index, or smoking status between the CAD and control groups. Additionally, the two groups exhibited similar lipid profiles, blood pressure levels, as well as comparable blood glucose and creatinine levels. However, a significant difference was observed in serum PTX-3 levels, which were markedly elevated in the CAD group compared to the normal coronary group (Table 1). The ROC analysis (Figure 1) demonstrated that a PTX-3 cut-off value of 5.80 ng/mL predicted CAD with a sensitivity of 68% and a specificity of 66%.

A statistically significant positive correlation was found between coronary artery calcium score (CACS) and serum PTX-3 levels ($r = 0.521$, $P < 0.001$) in the patient population. Patients classified as high-risk, characterized by a substantial atherosclerotic plaque load (Group III), indicated by a CACS (Agatston score) greater than 300, exhibited significantly elevated blood PTX-3 levels compared to those in the low- and intermediate-risk categories (Group I and Group II). No statistically significant differences in serum PTX-3 levels were detected between Group I (Agatston score < 100) and Group II (Agatston score 100–299), which represent low and moderate cardiac risk and plaque load, respectively. Furthermore,



AUC	P	Lower - Upper (95% Confidence Interval)
0.672	0.038	0.469 – 0.72

Figure 1. Receiver operating characteristic (ROC) curve analysis showing the cut-off value of pentraxin-3 for predicting coronary artery disease.

both Group I and Group II showed no significant differences when compared to the normal coronary artery group (Table 2). The data suggest a possible association between elevated serum PTX-3 levels and an increased risk of CAD and atherosclerotic plaque accumulation, as evidenced by the CACS.

However, the current investigation found no statistically significant association between the extent of intraluminal coronary artery stenosis identified by CCTA and serum PTX-3 levels.

Discussion

This study aimed to explore the potential relationship between PTX-3 levels and the presence and severity of CAD in patients with stable CAD. Our findings showed that serum PTX-3 concentrations were elevated in the CAD population compared to the control group without atherosclerotic lesions in the coronary arteries. These findings align with those reported by other researchers.[15-17,19] In previous studies, the diagnosis and severity of CAD were determined using ICA. In these studies, CAD was defined as intraluminal stenosis exceeding 50% in the coronary arteries. Disease severity was analyzed using tools such as the Gensini score, SYNTAX score (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery), or by examining the relationship between the number of vessels with stenosis greater than 50% and serum PTX-3 levels.[15-17,20] However, patients with less than 50% stenosis identified via ICA or those lacking significant intraluminal narrowing due to eccentric plaques—often classified as the "normal coronary artery group" in previous studies—may not accurately represent a truly normal population. The inclusion of patients with CAD in the control groups of these studies complicates the interpretation of their findings. Moreover, assessing CAD severity solely through ICA is limited, as this method does not account for eccentric plaques that may not result in significant intraluminal obstruction.[21,22] Our study examined the relationship between PTX-3 and CAD using

Table 2. Pentraxin 3 Levels in the Normal Coronary Artery Group and Coronary Artery Disease Groups Classified by Agatston Score, with Statistical Analysis of Differences Between the Normal Coronary Artery Group (Group 0) and CAD Groups (Groups I, II, III)

	Group 0 (n = 40) Normal PTX: 5.75 ± 1.11		
Group I (n = 19) Agatston < 100 PTX: 6.11 ± 1.05	P = 0.066	**Group I** (n = 19) Agatston < 100 PTX: 6.11 ± 1.05	
Group II (n = 17) 100 ≤ Agatston < 300 PTX: 6.27 ± 1.11	P = 0.061	P = 0.995	**Group II** (n = 17) 100 ≤ Agatston < 300 PTX: 6.27 ± 1.11
Group III (n = 18) Agatston ≥ 300 PTX: 8.51 ± 3.12	P < 0.001	P < 0.001	P = 0.017

PTX, Serum Pentraxin 3 Levels.

CCTA, which offers greater accuracy than ICA in identifying the CAD group and the true normal coronary artery group. This approach represents an important contribution to the medical literature.[21]

PTX-3 belongs to the pentraxin superfamily, which also includes CRP. Unlike CRP, PTX-3 is proposed to have an atheroprotective role[13,23] and demonstrates evidence of local action. PTX-3 inhibits the activity of fibroblast growth factor 2 (FGF2), reduces the migration of vascular smooth muscle cells (SMCs), and limits angiogenesis. In coronary plaques, PTX-3 accumulates in and around intraplaque hemorrhages, notably co-localizing with M2 macrophages, which play a critical role in tissue repair. PTX-3 may also provide protection against thrombosis following plaque rupture.[13,24]

Rolph et al.[13] were the first to identify PTX-3 in atherosclerotic lesions through immunohistochemistry, establishing PTX-3 as a specific marker for atherosclerotic plaques. Histological analyses of coronary plaques corroborate these findings, indicating higher PTX-3 levels in advanced compared to early atherosclerotic lesions and in unstable versus stable coronary plaques.[13,25] Elevated PTX-3 levels in unstable, vulnerable plaques may explain the independent association between high circulating PTX-3 levels and an increased risk of all-cause mortality, cardiac death, and adverse cardiac events, including cardiac death and rehospitalization for ACS or worsening heart failure in patients with CAD.[13,25,26]

PTX-3 secretion appears to be a targeted response to vascular injury, with its levels potentially correlating more significantly with advanced stages of atherosclerosis.[27] Studies evaluating serum PTX-3 levels and CAD severity using metrics such as the SYNTAX score,[16] Gensini score,[15] and the number of coronary arteries with > 50% stenosis,[17,18,20,28] based on ICA, have demonstrated a statistically significant relationship between elevated PTX-3 levels and more advanced stages of atherosclerosis and CAD severity.

The current research demonstrated a statistically significant association between serum PTX-3 levels and the presence of CAD as assessed by CCTA. This finding aligns with and supports the results of prior studies utilizing ICA. Additionally, a positive correlation was observed between serum PTX-3 levels and the CACS, a reliable measure of atherosclerotic burden in CAD. This finding is particularly significant in light of prior studies utilizing ICA, where PTX-3 serum levels were associated with the SYNTAX and Gensini scoring systems, as well as the count of vessels exhibiting stenosis greater than 50%.[15-18,28]

The detection of CAD using CCTA is considerably more sensitive than detection using ICA. CCTA can identify eccentric and small plaques that do not cause intraluminal narrowing and, therefore, may go undetected by ICA. Furthermore, ICA studies often classify coronary groups with less than 50% luminal stenosis as normal, even though these arteries may still be affected by CAD. This discrepancy arises from differing methodologies used in studies investigating the correlation between serum markers and CAD compared to those examining the extent and severity of CAD using CCTA and ICA.[7,8,21,22]

CACS reflect the overall burden of coronary atherosclerosis. While there has been ongoing debate about whether CACS indicates plaque stability or instability, the current consensus suggests that elevated CACS levels are more indicative of patient vulnerability rather than plaque vulnerability. CACS has demonstrated superior predictive capability for cardiovascular events compared to the Framingham risk score, with rapid progression of coronary calcium associated with poorer prognoses.[29] Sangiorgi et al.[30] found in their research that coronary calcium measurement is an effective technique for evaluating the presence of atherosclerotic plaque in specific arterial regions. Moreover, the quantity of calcium correlates with the overall extent of atherosclerotic plaque burden. However, their study revealed a lack of a strong predictive correlation between luminal narrowing and mural calcification, which they attributed to the phenomenon of remodeling. Findings from the Denmark Heart Registry using CCTA indicate that the principal factor influencing cardiovascular events and mortality risk is the total plaque burden, as assessed by the CACS, rather than the degree of stenosis alone. Consequently, patients with similar levels of CACS exhibit comparable risks for cardiovascular events, regardless of the presence of nonobstructive or obstructive CAD.[31] According to the results of our study, PTX-3 levels were significantly higher in patients with more advanced stages of atherosclerosis, particularly in those with a CACS ≥ 300. In light of the findings from the Denmark Registry, PTX-3 may be useful for identifying high-risk patients with advanced CAD. However, it appears to have limited utility in detecting patients with low CACS or non-calcified "vulnerable patients" with atherosclerotic plaques. A recent study, with findings similar to ours, used ICA

for CAD diagnosis and found that PTX-3 concentrations were significantly elevated in the CAD group compared to the control group. No association was detected between PTX-3 levels and angiographically significant atherosclerotic lesions in the coronary arteries, consistent with our findings.[17]

PTX-3 is produced at sites of inflammation and is present in atherosclerotic lesions. Consequently, PTX-3 levels reflect a localized inflammatory response to arterial wall damage rather than a systemic reaction. Therefore, PTX-3 blood levels are expected to increase in proportion to the atherosclerotic burden in coronary arteries.[13,14] This may explain why, in our study, PTX-3 levels showed a statistical association with CACS, a reliable indicator of atherosclerotic burden, but no such statistical association was observed with the degree of intraluminal coronary artery stenosis. Additionally, participants with a positive exercise ECG or myocardial perfusion SPECT predictive of CAD were directly referred for ICA in accordance with clinical recommendations and subsequently excluded from our cohort. This exclusion of participants with severe coronary artery stenoses likely reduced the incidence of severe coronary artery stenoses in the remaining CAD group, potentially attenuating the statistical association between PTX-3 levels and severe coronary artery stenosis.

The CAD cohort in our study was categorized into three groups based on their CACS (CACS, Agatston score), which assesses atherosclerotic burden, CAD prevalence, and associated risk, as outlined in the literature.[32] Serum PTX-3 levels were significantly elevated in the high-risk group with extensive and severe atherosclerosis (Agatston score ≥ 300) compared to the low- and moderate-risk groups. Our study found no statistical difference in PTX-3 levels between the low-risk, low-severity CAD group (Agatston score 0-99) and the moderate-severity, moderate-risk CAD group (Agatston score 100-299). Additionally, serum PTX-3 levels did not differ between these two groups and the normal coronary artery group.

This may explain the consistency observed between prior research employing ICA to examine the relationship between blood PTX-3 levels and the presence and severity of CAD, and the results of our investigation utilizing CCTA. Elevated serum PTX-3 levels are generally associated with advanced stages of atherosclerosis, as demonstrated in our CAD Group III and the CAD groups in ICA studies. In ICA investigations, cohorts with coronary artery stenosis below 50%, often functioning as control groups, may exhibit characteristics similar to those of patients with low to intermediate CAD risk in our analysis, classified as Groups I and II.

Limitations

This study has some limitations. It was conducted at a single center and included a relatively small cohort of patients. Additionally, there was no prospective monitoring of cardiovascular events and their relationship with serum PTX-3 levels. Participants with a positive exercise ECG or myocardial perfusion SPECT indicating CAD were referred for ICA and excluded from our cohort. This exclusion likely reduced the incidence of severe coronary artery stenoses in the remaining CAD group, potentially weakening the statistical association between PTX-3 levels and severe stenosis. Nonetheless, this study serves as a preliminary investigation that lays the groundwork for more extensive future research.

Conclusion

Serum PTX-3 levels were significantly elevated in individuals with CAD identified by CCTA compared to those without CAD. A PTX-3 threshold of 5.80 ng/mL predicted CAD with a sensitivity of 68% and a specificity of 66%. PTX-3 levels showed a positive correlation with the CACS and were significantly elevated in the high-risk and severe CAD group (CACS ≥ 300) compared to low- and moderate-risk CAD patients based on CACS. These findings suggest that PTX-3 might serve as a valuable biomarker for the diagnosis and assessment of CAD severity.

Ethics Committee Approval: Ethics committee approval was obtained from the İzmir Bakırçay University Non-Interventional Clinical Research Ethics Committee (Approval Number: 1155, Research Number: 1135, Date: 24.08.2023).

Informed Consent: Written informed consent was obtained from the participants.

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References

1. Timmis A, Vardas P, Townsend N, et al; Atlas Writing Group, European Society of Cardiology. European Society of Cardiology: Cardiovascular disease statistics 2021. *Eur Heart J*. 2022;43(8):716-799. Erratum in: *Eur Heart J*. 2022;43(8):799. [CrossRef]
2. Hartley A, Marshall DC, Salciccioli JD, Sikkel MB, Maruthappu M, Shalhoub J. Trends in mortality from ischemic heart disease and cerebrovascular disease in Europe: 1980 to 2009. *Circulation*. 2016;133(20):1916-1926. [CrossRef]
3. Khoja A, Andraweera PH, Lassi ZS, et al. Risk factors for early-onset versus late-onset coronary heart disease (CHD): Systematic review and meta-analysis. *Heart Lung Circ*. 2023;32(11):1277-1311. [CrossRef]
4. Obisesan OH, Osei AD, Uddin SMI, Dzaye O, Blaha MJ. An update on coronary artery calcium interpretation at chest and cardiac CT. *Radiol Cardiothorac Imaging*. 2021;3(1):e200484. [CrossRef]
5. Baeßler B, Götz M, Antoniades C, Heidenreich JF, Leiner T, Beer M. Artificial intelligence in coronary computed tomography angiography: Demands and solutions from a clinical perspective. *Front Cardiovasc Med*. 2023;10:1120361. [CrossRef]
6. Dimitriadis K, Pyrpyris N, Theofilis P, et al. Computed tomography angiography identified high-risk coronary plaques: From diagnosis to prognosis and future management. *Diagnostics*. 2024;14(15):1671. [CrossRef]
7. Okan T, Topaloglu C. Association of ratios of monocyte/high-density lipoprotein cholesterol and neutrophil/high-density lipoprotein cholesterol with atherosclerotic plaque type on coronary computed tomography. *Cardiovasc J Afr*. 2024;34:1-6.

8. Okan T, Doruk M, Ozturk A, Topaloglu C, Dogdus M, Yilmaz MB. Evaluation of plasma atherogenic index, triglyceride-glucose index and other lipid ratios as predictive biomarkers of coronary artery disease in different age groups. *Diagnostics (Basel)*. 2024;14(14):1495. [CrossRef]
9. Attiq A, Afzal S, Ahmad W, Kandeel M. Hegemony of inflammation in atherosclerosis and coronary artery disease. *Eur J Pharmacol*. 2024;966:176338. [CrossRef]
10. Guo T, Huang L, Liu C, et al. The clinical value of inflammatory biomarkers in coronary artery disease: PTX3 as a new inflammatory marker. *Exp Gerontol*. 2017;97:64-67. [CrossRef]
11. Zhu Y, Xian X, Wang Z, et al. Research progress on the relationship between atherosclerosis and inflammation. *Biomolecules*. 2018;8(3):80. [CrossRef]
12. Fornai F, Carrizzo A, Forte M, et al. The inflammatory protein pentraxin 3 in cardiovascular disease. *Immun Ageing*. 2016;13(1):25. [CrossRef]
13. Otani T, Moriguchi-Goto S, Nishihira K, et al. Intralesional pentraxin 3 increases with atherosclerotic disease progression, but may protect from thrombosis: Friend or foe? *Thromb Res*. 2024;234:134-141. [CrossRef]
14. Norata GD, Garlanda C, Catapano AL. The long pentraxin PTX3: A modulator of the immunoinflammatory response in atherosclerosis and cardiovascular diseases. *Trends Cardiovasc Med*. 2010;20(2):35-40. [CrossRef]
15. Liu H, Guan S, Fang W, Yuan F, Zhang M, Qu X. Associations between pentraxin 3 and severity of coronary artery disease. *BMJ Open*. 2015;5(4):e007123. [CrossRef]
16. Yahia M, Elmasry OS, Ra'ouf MA. The relationship between serum pentraxin-3 levels and severity of coronary heart disease. *World J Cardiovasc Dis*. 2018;8:370-380. [CrossRef]
17. Knapp M, Gil-Mika M, Sawicki R, et al. Pentraxin 3 as a marker of development and severity of stable coronary artery disease. *Adv Med Sci*. 2024;69(2):391-397. [CrossRef]
18. Premnath SM, Nanda SK, Ray L, Arokiaraj MC, Ravichandran K. Association of serum pentraxin 3 and high-sensitivity c-reactive protein with severity of coronary stenosis. *Int J App Basic Med Res*. 2022;12:249-253. [CrossRef]
19. Hermus L, Schuitemaker JH, Tio RA, et al. Novel serum biomarkers in carotid artery stenosis: Useful to identify the vulnerable plaque? *Clin Biochem*. 2011;44(16):1292-1298. [CrossRef]
20. Vuković-Dejanović V, Bogavac-Stanojević N, Spasić S, et al. Association of serum pentraxin-3 and high-sensitivity c-reactive protein with the extent of coronary stenosis in patients undergoing coronary angiography. *J Med Biochem*. 2015;34(4):440-449. [CrossRef]
21. Rampidis G, Rafailidis V, Kouskouras K, et al. Relationship between coronary arterial geometry and the presence and extend of atherosclerotic plaque burden: A review discussing methodology and findings in the era of cardiac computed tomography angiography. *Diagnostics (Basel)*. 2022;12(9):2178. [CrossRef]
22. Nakazato R, Shalev A, Doh JH, et al. Aggregate plaque volume by coronary computed tomography angiography is superior and incremental to luminal narrowing for diagnosis of ischemic lesions of intermediate stenosis severity. *J Am Coll Cardiol*. 2013;62(5):460-467. [CrossRef]
23. Ristagno G, Fumagalli F, Bottazzi B, et al. Pentraxin 3 in cardiovascular disease. *Front Immunol*. 2019;10:823. [CrossRef]
24. Sica A, Mantovani A. Macrophage plasticity and polarization: In vivo veritas. *J Clin Invest*. 2012;122(3):787-795. [CrossRef]
25. Rolph MS, Zimmer S, Bottazzi B, Garlanda C, Mantovani A, Hansson GK. Production of the long pentraxin PTX3 in advanced atherosclerotic plaques. *Arterioscler Thromb Vasc Biol*. 2002;22(5):e10-e14. [CrossRef]
26. Chu Y, Teng J, Feng P, Liu H, Wang F, Li X. Pentraxin-3 in coronary artery disease: A meta-analysis. *Cytokine*. 2019;119:197-201. [CrossRef]
27. Jenny NS, Blumenthal RS, Kronmal RA, Rotter JI, Siscovick DS, Psaty BM. Associations of pentraxin 3 with cardiovascular disease: The multi-ethnic study of atherosclerosis. *J Thromb Haemost*. 2014;12(6):999-1005. [CrossRef]
28. Nerkiz P, Doganer YC, Aydogan U, et al. Serum pentraxin-3 level in patients who underwent coronary angiography and relationship with coronary atherosclerosis. *Med Princ Pract*. 2015;24(4):369-375. [CrossRef]
29. Alexopoulos N, Raggi P. Calcification in atherosclerosis. *Nat Rev Cardiol*. 2009;6(11):681-688. [CrossRef]
30. Sangiorgi G, Rumberger JA, Severson A, et al. Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden in humans: A histologic study of 723 coronary artery segments using nondecalcifying methodology. *J Am Coll Cardiol*. 1998;31(1):126-133. [CrossRef]
31. Mortensen MB, Dzaye O, Steffensen FH, et al. Impact of plaque burden versus stenosis on ischemic events in patients with coronary atherosclerosis. *J Am Coll Cardiol*. 2020;76(24):2803-2813. [CrossRef]
32. Grundy SM, Stone NJ. Coronary artery calcium: Where do we stand after over 3 decades? *Am J Med*. 2021;134(9):1091-1095. [CrossRef]