Turk Kardiyol Dern Ars 2021;49(2):120-126 doi: 10.5543/tkda.2021.99537

ORIGINAL ARTICLE

Human neutrophil peptides 1-3 level in patients with acute myocardial infarction and its relation with coronary artery disease severity

Akut miyokart enfarktüsü hastalarında serum insan nötrofil peptid 1-3 ve koroner arter hastalığı ciddiyeti ile ilişkisi

Fahrettin Katkat, M.D.[1], Sinan Varol, M.D.[1], Nilgün Işıksaçan, M.D.[3], Fatma Nihan Turhan Çağlar, M.D.[2], Fatih Akın, M.D.[4], Dilay Karabulut, M.D.[2], Ertuğrul Okuyan, M.D.[1]

[1]Department of Cardiology, Bağcılar Training and Research Hospital, İstanbul, Turkey
[2]Department of Cardiology, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey
[3]Department of Biochemistry, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey
[4]Department of Cardiology, Muğla Sıtkı Koçman University School of Medicine, Muğla, Turkey

ABSTRACT

Objective: Inflammation plays a crucial role in the pathogenesis and clinical outcome of atherosclerosis. Among the various inflammatory factors, antimicrobial peptides, such as alpha-defensins, seem to contribute to the development and progression of atherosclerosis. The aim of this study was to evaluate the plasma levels of human neutrophil peptide-1, -2, and -3 (HNP1–3) in patients with acute myocardial infarction (AMI) and to assess its relationship with the severity of coronary artery disease.

Methods: Plasma HNP1–3 levels in patients with AMI and controls with angiographically normal coronary arteries were measured by solid-phase enzyme-linked immunosorbent assay. In the patient group, coronary artery disease severity was assessed using the SYNergy between percutaneous intervention with TAXus and cardiac surgery score (SS).

Results: HNP1–3 levels were significantly higher in the group with AMI than in the controls (6.5±5.8 ng/mL vs. 2.8±2.5 ng/mL, p<0.001). The receiver operator characteristic (ROC) analysis yielded a cut-off value of 3.13 ng/mL for differentiating patients with AMI from the controls (area under the curve: 0.739, 95% confidence interval: 0.629–0.831, p<0.001). HNP1–3 levels in the high SS tertile (≥33) were slightly but statistically nonsignificantly higher than that in the low (≤22) and intermediate SS tertiles (high SS: 7.0±6.1 ng/mL, intermediate SS: 5.9±6.2 ng/mL, low SS: 5.3±3.8 ng/mL; p=0.639).

Conclusion: Patients with AMI had higher plasma HNP1–3 levels than the controls, but this did not show a significant correlation with angiographic disease severity. The nonsignificant trend toward higher SS in patients with higher HNP1–3 levels warrants future studies on larger populations.

ÖZET

Amaç: Ateroskleroz patogenezi ve klinik sonuçlarında inflamasyon kritik rol oynamaktadır. Çeşitli inflamasyon faktörleri arasında alfa-defensinler gibi antimikrobiyal peptitler, ateroskleroz gelişimi ve ilerlemesine katkıda bulunabilir. Bu çalışmanın amacı akut miyokart enfarktüsü (AMI) olan hastalarda insan nötrofil peptid 1-2 ve 3 (HNP1-3) plazma seviyelerini ve koroner arter hastalığı yaygınlığı ile ilişkisini araştırmaktır.

Yöntemler: AMI olan hastalar ile normal koroner arterler saptanan kontrol grubu hastalarının plazma HNP1-3 seviyeleri, "solid-phase enzyme-linked immunosorbent assay" ile ölçüldü. Çalışma grubunda koroner arter hastalığı yaygınlığı "SYNergy between percutaneous intervention with TAXus and cardiac surgery score (SNYTAX Score: SS)" ile değerlendirildi.

Bulgular: Serum HNP1-3 seviyesi AMI hastalarında kontrol grubuna göre anlamlı derecede yüksekti (6.5±5.8 ng/mL'e karşı 2.8±2.5 ng/mL p<0.001). ROC analizinde AMI hastalarını kontrol grubundan ayırmada kestirim değeri 3.13 ng/mL olarak bulundu (Eğri altında kalan alan: 0.739, 95% güven aralığı: 0.629–0.831, p<0.001). HNP1-3 seviyesi yüksek SS tertil grubunda, düşük ve orta tertil grubuna gore hafifçe fakat istatistiksel anlamlı olmayan şekilde yüksekti. (Yüksek SS: 7±6.1 ng/mL vs orta SS: 5.9±6.2 vs düşük SS: 5.3±3.8 ng/mL, p=0.639).

Sonuç: Akut miyokart enfarktüsü olan hastalar, kontrol grubuna gore daha yüksek HNP1-3 seviyesine sahipti; fakat bu anjiyografik hastalığın yaygınlığı ile anlamlı korelasyon göstermemekteydi. Yüksek HNP1-3 seviyesi olan hastaların SYNTAX skorunda anlamlı olmayan artış eğilimini değerlendirmek için daha geniş popülasyonlarda yapılacak çalışmalara ihtiyaç vardır.

Received: August 27, 2019 *Accepted:* September 8, 2020
Correspondence: Fahrettin Katkat, M.D. Department of Cardiology, Bağcılar Training and Research Hospital, 34100, İstanbul, Turkey
Tel: +90 532 711 01 47 e-mail: fahrettin_katkat@hotmail.com

Atherosclerotic cardiovascular disease is the leading cause of mortality worldwide.[1] It is now widely accepted that inflammation plays a key role in all stages of atherosclerosis, from subclinical onset to clinically evident acute myocardial infarction (MI) (AMI).[2] Some of the well-defined atherosclerotic inflammatory markers are acute-phase reactants such as C-reactive protein (CRP); cytokines such as interleukin (IL)-1, IL-6, and IL-8; tumor necrosis factor alpha; cellular adhesion molecules; and matrix metalloproteinases.[3]

Antimicrobial proteins and peptides, also known as host defense peptides, are essential proteins for innate immunity.[4] They act against microbial invasion, including invasion by gram-negative and gram-positive bacteria, viruses, fungi, and even cancerous cells; hence, they also contribute to adaptive immune modulation. Human host defense peptides are detected in various sites of the body, including in saliva, tears, neutrophils, bone marrow, skin, intestines, and genitourinary tract. Recently, their immunomodulating functions and proinflammatory and anti-inflammatory effects in chronic inflammatory diseases, such as arthritis, asthma, colitis, and cancer, have attracted substantial attention, and studies have focused on their role in inflammatory diseases and potential therapeutic applications.[5]

Defensins, also termed human neutrophil peptides (HNPs)-1, -2, and -3, are the first defined antimicrobial peptides in humans.[4] They are highly expressed in neutrophils, and nearly 5% of total polymorphonuclear (PMN) leukocyte protein consists of HNPs.[6, 7] PMN activation causes the release of HNP1–3 from azurophilic granules.[6] Recently, HNP1–3 have been associated with atherosclerosis.[5] HNP1–3 inhibit both low-density lipoprotein (LDL) degradation and tissue-type plasminogen activator-related fibrinolysis. High levels of HNP1–3 are detected in the atherosclerotic coronary and carotid arteries.[6-8] Nassar et al.[9] demonstrated a correlation between HNP1–3 measured in skin biopsies and angiographic coronary artery disease (CAD) severity in patients with stable CAD.

Studies on the role of HNP1–3 in acute coronary syndromes and its association with disease severity are rather limited. Coronary artery complexity is associated with major adverse clinical events after AMI.[10] The SYNergy between percutaneous intervention with TAXus and cardiac surgery (SYNTAX) score (SS) is one of the most accepted and studied CAD severity scoring systems.[11] It was developed as a universal angiographic scoring system for quantifying epicardial coronary artery lesions according to the number, location, and complexity of the lesions. SS is a good predictor of adverse cardiovascular events, including cardiac death and MI, and its prognostic role in patients with AMI has been widely evaluated.[12, 13]

Abbreviations:

AMI	*Acute myocardial infarction*
CAD	*Coronary artery disease*
CAG	*Coronary angiogram*
CRP	*C-reactive protein*
HNP	*Human neutrophil peptide*
IL	*Interleukin*
LDL	*Low-density lipoprotein*
MI	*Myocardial infarction*
PMN	*Polymorphonuclear*
ROC	*Receiver operator characteristic*
STEMI	*ST-segment elevation myocardial infarction*
SS	*The SYNergy between percutaneous intervention with TAXus and cardiac surgery score*
SYNTAX	*The SYNergy between percutaneous intervention with TAXus and cardiac surgery*
WBC	*White blood cell*

The aim of this study was to evaluate HNP1–3 plasma levels in patients with acute ST-segment elevation MI (STEMI) and to assess its association with coronary complexity using SS.

METHODS

Study population

From July 30, 2018 to October 30, 2018, 40 consecutive patients admitted to Bağcılar Training and Research Hospital (İstanbul, Turkey) with a diagnosis of STEMI and 40 control patients were included in the study. The patients with STEMI had typical sustained symptoms lasting at least 30 minutes but less than 12 hours with ≥0.1 mV new ST-segment elevation in ≥2 contiguous leads or suspected new-onset bundle branch block on an electrocardiogram. Coronary angiogram (CAG) of these patients showed severe stenosis or total occlusion of the culprit lesion (thrombolysis in MI flow grade 0 or 1). Patients with Type II, IV, and IV AMI were excluded from the study.

The control group consisted of patients with typical chest pain who had a positive noninvasive ischemic stress test but angiographically normal coronary arteries. The decision to perform CAG on these patients was made by their primary physician who was blinded to the study.

Patients with known CAD, estimated glomerular filtration rate <60 mL/min, clinically significant valvular disease, uncontrolled hypertension, heart failure, serious hepatic failure, acute/chronic infection, fever, immune disease, rheumatic disease, cancer, and osteoporosis and who were aged >75 years were excluded.

Definitions

Hypertension was defined as being under antihypertensive treatment or having systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg. Chronic renal failure was defined as having a plasma creatinine level >1.5 mg/dL. Diabetes was defined as having a history of known diabetes, taking antidiabetic medications, or having fasting plasma glucose levels >126 mg/dL. Hyperlipidemia was defined as using an antihyperlipidemic medication in the last 6 months or having plasma total cholesterol levels ≥200 mg/dL and LDL levels ≥130 mg/dL.

All patients provided written informed consent. The study was approved by Clinical Research Ethics Committee of Bağcılar Training and Research Hospital on 01/08/2018 as a (2018.08.1.01.076) protocol number. The study protocol complied with the Declaration of Helsinki.

Laboratory measurements

Venous blood samples were collected from all patients to measure HNP1–3, hemogram, and conventional biochemical parameters. Blood samples were collected from the patients with STEMI within the first 2 hours of admission, and samples from the controls were obtained just after inclusion in the study and before angiography.

HNP1–3 analysis

Venous blood samples were collected in ethylenediamine tetraacetic acid tubes to measure HNP1–3. The tubes were centrifuged at 25°C at 3,500 rpm for 10 minutes to separate the serum and were stored at –70°C in polypropylene tubes until the analysis. Hemolyzed and lipemic samples were excluded. HNP1–3 were measured using a ready-to-use solid-phase enzyme-linked immunosorbent assay on the basis of the sandwich principle with an HK317 kit (Hycult Biotech, Uden, Netherlands). The assay was performed according to the manufacturer's instructions, and absorbance was measured at 450 nm using a microplate reader.

Coronary angiography

CAG was performed using the femoral approach. The cineangiography system was an Axiom Artis (Siemens Healthineers, Erlangen, Germany). All angiograms were recorded to compact discs in Digital Imaging and Communication in Medicine format and subsequently evaluated off line and visually by 2 interventional cardiologists blinded to the study.

Coronary artery disease severity

CAD was determined using the SS. Significant vessel disease was defined as the presence of ≥50% luminal-diameter stenosis in at least 1 major coronary artery. Each coronary lesion with a diameter stenosis ≥50% in vessels ≥1.5 mm was required to be scored. The SS was calculated using the SS calculator (www.syntaxscore.com), and tertiles were determined (low: ≤22, intermediate: 23–32, and high: ≥33) as previously described in the SYNTAX trial.[14]

Statistical analysis

Statistical analysis was performed using MedCalc Statistical Software, version 12.7.7 (MedCalc Software bvba; Ostend, Belgium; http://www.medcalc.org; 2013). Data are reported as the mean and standard deviation for continuous variables. Abnormally distributed variables were determined using the 1-sample Kolmogorov–Smirnov test. The differences among normally distributed variables were determined using Student's *t*-test, and the differences between abnormally distributed variables were defined using Mann–Whitney U test. Categorical data were compared with chi-square test. The 3 SS groups were compared using the Kruskal–Wallis test. The correlation of parametric variables was tested using the Pearson test, and nonparametric variables were tested using the Spearman test. Receiver operator characteristic (ROC) curve analysis was performed to determine the HNP1–3 cut-off level that would differentiate patients with STEMI from the controls. A 2-sided p value <0.05 was considered significant.

RESULTS

Table 1 shows the demographic characteristics of the patients with STEMI (n=40; 14 men [35%]; aged 58.5±11 years) and the controls (n=40; 21 men [52.5%]; aged 57±12 years). The 2 groups had a similar frequency of diabetes, hyperlipidemia, hyperten-

sion, smoking, and family history of CAD. Table 1 also shows the laboratory findings. The patient group had significantly higher white blood cell (WBC) levels than the control group (13.6±4.4 vs. 6.1±2.6, p<0.001). The CRP levels were not different between the groups.

Table 1. Demographic features and laboratory findings of the patient and control group

	Patient group	Control group	*p*
Sex, male, n (%)	14 (35.0)	21 (52.5)	0.176
Age, years	58.5±11	57±12	0.825
Diabetes, n (%)	14 (35.0)	16 (40.0)	0.818
HT, n (%)	16 (40.0)	22 (55.0)	0.263
Smoking, n (%)	22 (55.0)	22 (55.0)	1.00
HL, n (%)	20 (50.0)	19 (47.5)	1.00
Family history of CAD, n (%)	18 (45.0)	23 (57.5)	0.371
Creatinine (mg/dL)	0.83+0.3	0.86+0.3	0.787
WBC, (10e3/uL)	13.6+4.4	6.1+2.6	<0.001
CRP (mg/dL), median (IQR)	0.7 (0.1-17)	0.7 (0.1-10)	0.567
HNP1-3 (ng/mL), median (IQR)	3.7 (0.9-24.1)	2.2 (0.2-14.4)	<0.001

Values are presented as n (%), median (interquartile range), or mean±standard deviation.
CAD: coronary artery disease; CRP: C-reactive protein; HL: hyperlipidemia; HNP1-3: human neutrophil peptides-1, -2, and -3; HT: hypertension; HNP1-3: Human neutrophil peptide 1-3; IQR: interquartile range; WBC: white blood cell.

The patient group had significantly higher HNP1–3 levels than the controls (6.5±5.8 ng/mL vs. 2.8±2.5 ng/mL, p<0.001). Fig. 1A shows the differences between the patients with STEMI and the controls. The ROC curve analysis showed that the HNP1–3 cut-off level was 3.13 ng/mL (95% confidence interval: 0.629–0.831) for differentiating patients with STEMI from the controls with 70% sensitivity and 75% specificity (Fig. 1B). Furthermore, HNP1–3 levels exhibited a moderate correlation with WBC (r=0.323, p=0.003), whereas they were not correlated with age, blood glucose, lipids, and CRP (Fig. 2).

The patient group was divided into 3 groups according to the SS. There were 23 patients (28.8%) in the lower SS tertile, 12 patients (15%) in the intermediate SS tertile, and 5 patients (6.3%) in the high SS tertile. Despite a tendency toward higher levels with more complex CAD anatomy, there was no statistically significant difference in HNP1–3 levels among the 3 SS groups (Table 2).

DISCUSSION

Our findings show that patients with STEMI have elevated plasma levels of HNP1–3; yet, the association of HNP1–3 levels with CAD complexity is relatively modest.

Plasma HNP1–3 in AMI has been previously evaluated in only one study. Zhao et al.[15] compared

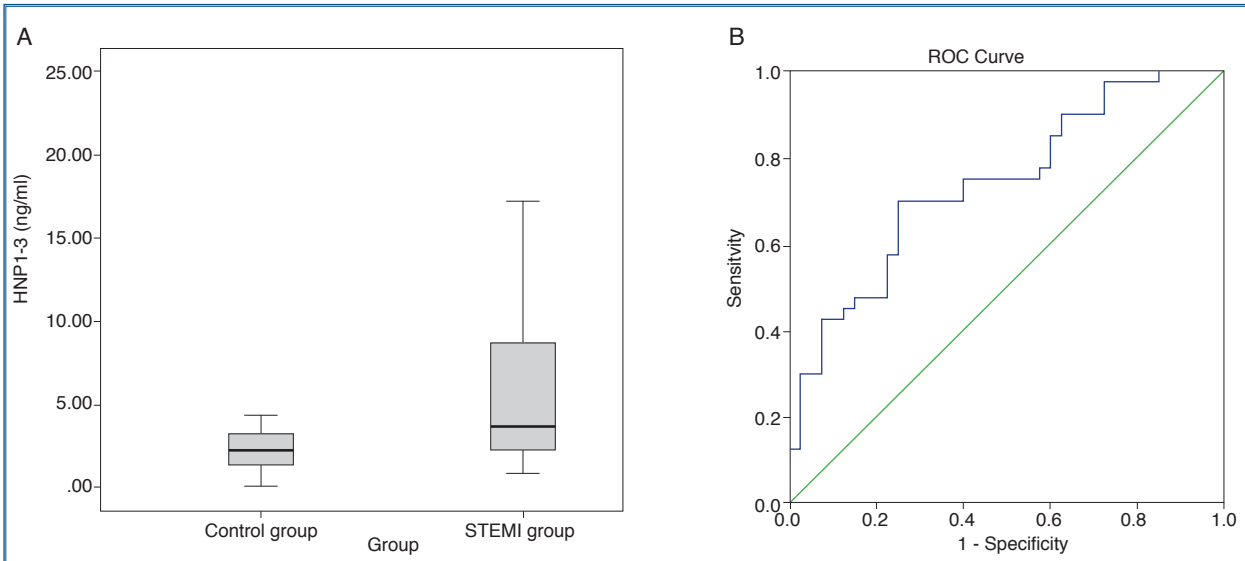
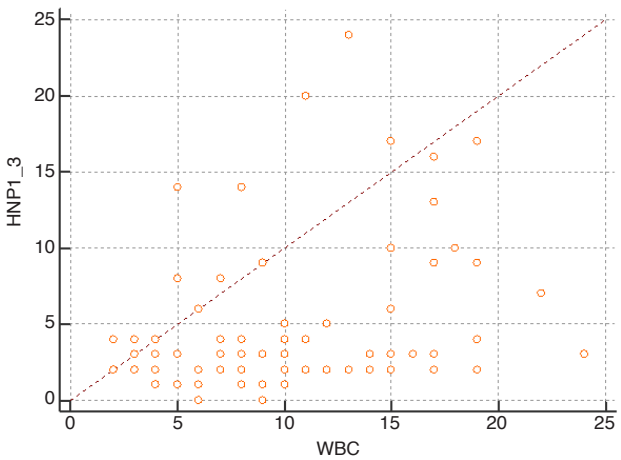


Figure 1. (A) HNP 1-3 in patients with STEMI and in controls. **(B)** The ROC analysis of HNP 1-3 for differentiating STEMI. HNP1-3: human neutrophil peptides-1, -2, and -3; ROC: receiver operating characteristic; STEMI: ST-segment elevation myocardial infarction.

Table 2. Laboratory findings in SYNTAX score tertiles

	Low SS tertile	Intermediate SS tertile	High SS tertile	*p*
HNP, (ng/mL), median (IQR)	6.4 (1.4-10.5)	3.4 (1.5-20.1)	4.1 (0.9-24.1)	0.639
WBC, (10e3/uL)	13.7+4.2	13.4+4.1	13.6+6.4	0.197
CRP, (mg/dL), median (IQR)	0.6 (0.1-17)	0.6 (0.1-4.8)	4.2 (0.2-10.9)	0.982

Values are presented as median (IQR) or mean±standard deviation.
CRP: C-reactive protein; HNP: human neutrophil peptide; IQR: interquartile range; SYNTAX: SYNergy between percutaneous intervention with TAXus and cardiac surgery; WBC: white blood cell.



		Age	Age	Glucose	LDL-C	WBC	CRP
HNP1-3	r	-.073	-.059	.025	.323	.187	
	p	0.5	0.61	0.83	0.003	0.1	

Figure 2. Correlation analyses of HNP 1-3 with age, blood glucose, LDL-C, WBC, and CRP. CRP: C-reactive protein; HNP1-3: human neutrophil peptides-1, -2, and -3; LDL-C: low-density lipoprotein cholesterol; WBC: white blood cell.

HNP1–3 levels among patients with acute STEMI, patients with stable CAD, and controls and showed that patients with STEMI had the highest HNP1–3 levels, followed by the patients with CAD and the controls. In that study, HNP1–3 levels remained elevated in the first 5 days after the onset of STEMI. The authors suggested that HNP1–3 may play a key role in the progression of CAD and the development of acute coronary events.[15] Our study confirms their findings on the increased HNP1–3 levels in patients with STEMI. However, the association between HNP1–3 levels and the severity of CAD could not be confirmed.

Ungan et al.[16] studied the association between HNP1–3 and the extent of CAD in patients with stable angina pectoris. They measured the extent of CAD using the Gensini score and showed higher HNP1–3 levels in patients with higher Gensini scores. To our knowledge, our study is the first to evaluate HNP1–3 levels according to SS in patients with AMI. The different findings between our study and that of Ungan et al.[16] may be explained by the differences in the patient characteristics (acute vs. chronic CAD), the number of included patients (40 vs. 107), and the differences between the 2 scoring systems.

Many previous studies have evaluated the association between SS and inflammatory biomarkers (WBC and neutrophil-to-lymphocyte ratio) in both patients with stable and those with acute CAD.[16-20] Similar to those studies, we observed higher WBC levels in the group with AMI than in the controls but could not confirm an association with disease severity. CRP, a downstream marker of inflammation, correlates with the extent of cardiac injury in the acute phase of MI.[21,22] In this study, despite the group with AMI having a higher mean CRP level than the controls, the difference was not statistically significant.

Inflammation plays a key role in the development and progression of atherosclerosis.[2,3,23] Biomarkers such as CRP, PMNs, and ILs have been widely investigated in this context and have shown promising results as diagnostic and prognostic biomarkers. HNPs are released from PMNs during acute and chronic inflammatory situations.[23–26] Owing to their relation to chronic

inflammatory conditions, recent studies have focused on the roles HNPs in atherosclerosis.[6, 23] HNPs form complexes with LDL and alter LDL metabolism.[23–26] Recent studies have indicated that HNPs have a 2-sided effect on atherosclerosis by both accelerating LDL clearance from plasma and stimulating LDL deposition and retention in the vasculature, resulting in the development of atherosclerosis even in individuals with normal plasma cholesterol levels.[27] The stimulation of human coronary artery endothelial cells with HNPs results in monocyte adhesion and transmigration, accelerated foam cell formation, and activation of thrombosis.[28] The intimal and medial smooth muscle cells of atherosclerotic arteries demonstrate increased HNP levels.[7] They act as a link between inflammation and thrombosis, creating larger and neutrophil-rich clots with increased fiber density and decreasing fibrinolysis and response to anticoagulants.[29]

Limitations

This study has several limitations. It is a single-center study with a relatively small number of patients. HNP1–3 levels were measured only once; therefore, biological intraindividual variation over time remains to be investigated. The exact interval between pain onset and blood collection was not evaluated; yet, the total ischemic time may have affected the HNP results. Previous drug usage, such as statins, which are known to affect inflammation, was also not evaluated. We only calculated the WBC count; however, the absolute neutrophil count would be more valuable because HNPs are released from PMNs. The control group consisted of patients with typical chest pain who had a positive noninvasive ischemic stress test but angiographically normal coronary arteries. Some of these patients may have endothelial dysfunction. Moreover, in this group, we could not exclude patients with endothelial dysfunction and microvascular angina.

Conclusion

Plasma HNP1–3 levels are increased in patients with STEMI compared to those in controls, but they do not show a significant correlation with angiographic disease severity. The nonsignificant trend toward higher SS in patients with higher HNP1–3 levels warrants future studies on larger populations.

Ethics Committee Approval: Ethics committee approval for this study was received from the Ethics Committee of Bağcılar Training and Research Hospital (Approval Date: August 1, 2018; Approval Number: 2018.08.1.01.076).

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept - F.K., E.O., S.V.; Design - F.K., E.O., S.V., F.N.T.Ç., E.O., N.I., D.K.; Supervision - E.O., F.K.; Data - F.K., S.V.; Analysis - F.K., S.V., F.A., D.K., F.N.T.Ç., N.I.; Literature search - F.K., S.V., N.I., F.N.T.Ç., F.A., D.K., E.O.; Writing - F.K., S.V., N.I., F.N.T.Ç., F.A., D.K., E.O.; Critical revision - F.K., E.O., S.V., F.A.

Funding: No funding was received for this research.

Conflict-of-interest: None.

REFERENCES

1. Pepió Vilaubí JM, Orozco-Beltrán D, Gonçalves AQ, Rodriguez Cumplido D, Aguilar Martin C, Lopez-Pineda A, et al. Adherence to European Clinical Practice Guidelines for Secondary Prevention of Cardiovascular Disease: a cohort study. Int J Environ Res Public Health 2018;15:1233. [Crossref]
2. Chen H, Yin K. J. AIBP, inflammation, and atherosclerosis. J Lipid Res 2018;59:1081-3. [Crossref]
3. Yu E, Hsu HY, Huang CY, Hwang LC. Inflammatory biomarkers and risk of atherosclerotic cardiovascular disease. Open Med (Wars) 2018;13:208-13. [Crossref]
4. Guangshun W. Human antimicrobial peptides and proteins. Pharmaceuticals (Basel) 2014;7:545-94. [Crossref]
5. Mookherjee N, Anderson MA, Haagsman HP, Davidson DJ. Antimicrobial host defence peptides: functions and clinical potential. Nat Rev Drug Discov 2020;19:311-32. [Crossref]
6. Abu-Fanne R, Maraga E, Abd-Elrahman I, Hankin A, Blum G, Abdeen S, et al. α-defensins induce a post-translational modification of low density lipoprotein (LDL) that promotes atherosclerosis at normal levels of plasma cholesterol. J Biol Chem 2016;291:2777-86. [Crossref]
7. Quinn K, Henriques M, Parker T, Slutsky AS, Zhang H. Human neutrophil peptides: a novel potential mediator of inflammatory cardiovascular diseases. Am J Physiol Heart Circ Physiol 2008;295:H1817-24. [Crossref]
8. Higazi AA, Lavi E, Bdeir K, Ulrich AM, Jamieson DG, Rader DJ, et al. Defensin stimulates the binding of lipoprotein (a) to human vascular endothelial and smooth muscle cells. Blood 1997;89:4290-8. [Crossref]
9. Nassar H, Lavi E, Akkawi S, Bdeir K, Heyman SN, Raghunath PN, et al. α-Defensin: link between inflammation and atherosclerosis. Atherosclerosis 2007;194:452-7. [Crossref]
10. Askin L, Tasolar MH, Turkmen S, Kaya H. Comparison of the predictive roles of risk scores of in-hospital major adverse cardiovascular events in patients with non-ST-Elevation myocardial infarction undergoing percutaneous coronary intervention. Med Princ Pract 2018;27:459-65. [Crossref]

11. Bundhun PK, Yanamala CM, Huang F. Percutaneous coronary intervention, coronary artery bypass surgery and the SYNTAX score: a systematic review and meta-analysis. Sci Rep 2017;7:43801. [Crossref]
12. Suh YJ, Han K, Chang S, Kim JY, Im DJ, Hong YJ, et al. SYNTAX score based on coronary computed tomography angiography may have a prognostic value in patients with complex coronary artery disease: an observational study from a retrospective cohort. Medicine (Baltimore) 2017;96:e7999. [Crossref]
13. Bryniarski KL, Tokarek T, Bryk T, Rutka J, Gawlik I, Żabówka A, et al. Com, intima-media thickness and ankle-brachial index are correlated with the extent of coronary artery disease measured by the SYNTAX score. Postepy Kardiol Interwencyjnej 2018;14:52-8. [Crossref]
14. Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 2009;360:961-72. [Crossref]
15. Zhao H, Yan H, Yamashita S, Li W, Liu C, Chen Y, et al. Acute ST-segment elevation myocardial infarction is associated with decreased human antimicrobial peptide LL-37 and increased human neutrophil peptide-1 to 3 in plasma. J Atheroscler Thromb 2012;19:357-68. [Crossref]
16. Ungan 1, Caglar FNT, Biyik İ, Ciftci S, Sahin A, Akturk IF. The correlation between plasma human neutrophil peptide 1-3 levels and severity of coronary artery disease. Arch Med Sci Atheroscler Dis 2016;1:133-38.
17. Sari I, Sunbul M, Mammadov C, Durmus E, Bozbay M, Kivrak T, et al. Relation of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio with coronary artery disease severity in patients undergoing coronary angiography. Kardiol Pol 2015;73:1310-6. [Crossref]
18. Kurtul S, Sarli B, Baktir AO, Demirbas M, Saglam H, Doğan Y, et al. Neutrophil to lymphocyte ratio predicts SYNTAX score in patients with non-ST segment elevation myocardial infarction. Int Heart J 2015;56:18-21. [Crossref]
19. Ates AH, Canpolat U, Yorgun H, Kaya EB, Sunman H, Demiri E, et al. Total white blood cell count is associated with the presence, severity and extent of coronary atherosclerosis detected by dualsource multislice computed tomographic coronary angiography. Cardiol J 2011;18:371-7.
20. Kostis JB, Turkevich D, Sharp J. Association between leukocyte count and the presence and extent of coronary atherosclerosis as determined by coronary arteriography. Am J Cardiol 1984;53:997-9. [Crossref]
21. Orn S, Manhenke C, Ueland T, Damås JK, Mollnes TE, Edvardsen T, et al. C-reactive protein, infarct size, microvascular obstruction, and left-ventricular remodelling following acute myocardial infarction. Eur Heart J 2009;30:1180-6. [Crossref]
22. Reindl M, Reinstadler SJ, Feistritzer HJ, Klug G, Tiller C, Mair J, et al. Relation of inflammatory markers with myocardial and microvascular injury in patients with reperfused ST-elevation myocardial infarction. Eur Heart J Acute Cardiovasc Care 2017;6:640-9. [Crossref]
23. Van Leeuwen M, Gijbels MJ, Duijvestijn A, Smook M, van de Gaar MJ, Heeringa P, et al. Accumulation of myeloperoxidase-positive neutrophils in atherosclerotic lesions in LDLR mice. Arterioscler Thromb Vasc Biol 2008;28:84-9. [Crossref]
24. Lopez-Bermejo A, Chico-Julia B, Castro A, Recasens M, Esteve E, Biarnes J, et al. Alpha defensins 1, 2, and 3. Potential roles in dyslipidemia and vascular dysfunction in humans. Arterioscler Thromb Vasc Biol 2007;27:1166-71. [Crossref]
25. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. JAMA 1998;279:1477-82. [Crossref]
26. Bdeir K, Cane W, Canziani G, Chaiken I, Weisel J, Koschinsky ML, et al. Defensin promotes the binding of lipoprotein(a) to vascular matrix. Blood 1999;94:2007-19.
27. Higazi M, Abdeen S, Abu-Fanne R, Heyman SN, Masarwy A, Bdeir K, et al. Opposing effects of HNP1 (α-defensin-1) on plasma cholesterol and atherogenesis. PLoS One 2020;15:e0231582. [Crossref]
28. Quinn KL, Henriques M, Tabuchi A, Han B, Yang H, Cheng WE, et al. Neutrophil peptides mediate endothelial-monocyte interaction, foam cell formation, and platelet activation. Arterioscler Thromb Vasc Biol 2011;31:2070-9. [Crossref]
29. Abu-Fanne R, Stepanova V, Litvinov RI, Abdeen S, Bdeir K, Higazi M, et al. Neutrophil α-defensins promote thrombosis in vivo by altering fibrin formation, structure, and stability. Blood 2019;133:481-93. [Crossref]

Keywords: Myocardial infarction; human neutrophil peptide 1, -2, -3; atherosclerosis

Anahtar Kelimeler: Miyokart enfarktüsü; human neutrophil peptide-1, -2 ve 3; ateroskleroz