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Original Investigation / Özgün Araştırma

Relation of interleukin-6 level with coronary artery disease severity in patients undergoing coronary angiography

Koroner anjiyografi yapılan hastalarda interlökin-6 düzeyi ile koroner arter hastalığının ciddiyeti arasındaki ilişki

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ABSTRACT

Objective: Atherosclerosis plays an important role in the pathogenesis of coronary artery disease (CAD). There is a closer relationship between atherosclerosis and inflammatory cytokines. Commonly used scoring systems for risk stratification in clinical practice are GENSINI and SYNergy between PCI with TAXUS and Cardiac Surgery (SYNTAX) scores for determining disease severity and method of revascularization. The aim of this study was to investigate the relationship between interleukin (IL)-6 levels and both GENSINI and SYNTAX scores in patients with CAD.

Methods: In total, 118 patients who underwent coronary angiography were enrolled in the study. GENSINI and SYNTAX were calculated for determining disease severity. IL-6 level was measured using immunometric assay method.

Results: There were no significant differences between the groups with respect to mean age, blood pressure, heart rate, and use of alcohol. Gender and smoking status were significantly different between the groups. GENSINI and SYNTAX scores of patients were significantly higher in the CAD group than in the controls. IL-6 level was significantly higher in the CAD group than in the controls. In the correlation analysis, IL-6 level significantly correlated with GENSINI and SYNTAX scores and was an independent predictor of abnormal coronary angiography. Optimal cut-off level of IL-6 was 7.81 pg/mL to assess the ability of IL-6 to differentiate the presence of CAD (area under curve, 0.78; sensitivity, 78.3%; and specificity, 70.7%).

Conclusion: Patients with CAD have higher IL-6 levels compared with the controls. IL-6 level correlated with both GENSINI and SYNTAX scores. Moreover, IL-6 was an independent predictor of abnormal coronary angiography. An IL-6 value of ≥7.81 pg/mL predicted the presence of CAD with a sensitivity of 78.3% and a specificity of 70.7%.

Keywords: Coronary artery disease, Inflammation, IL-6, GENSINI score, SYNTAX score

ÖZ

Amaç: Ateroskleroz koroner arter hastalığının patogenezinde çok önemli rol oynamaktadır. Ateroskleroz ile enflamatuvar sitokinler arasında çok sıkı bir ilişki bulunmaktadır. GENSINI ve SYNTAX skorlaması koroner arter hastalığının şiddetinin ve uygulanacak olan revaskülarizyon yönteminin belirlenmesinde kullanılan skorlama yöntemleridir. Bu çalışmanın amacı koroner arter hastalarında interlökin-6 düzeyi ile GENSINI ve SYNTAX skorları arasındaki ilişkiyi ortaya çıkarmaktır.

Yöntemler: Koroner anjiyografi yapılan 118 hasta çalışmaya dahil edilmiştir. Hastalığın şiddeti GENSINI ve SYNTAX skorları hesaplanarak yapılmıştır. IL-6 düzeyleri kemilüminesan yöntem kullanılarak ölçülmüştür.

Bulgular: Gruplar arasında ortalama yaş, kan basıncı, nabız ve alkol kullanımı açısından bir farklılık yoktu. Cinsiyet ve sigara kullanımı açısından gruplar arasında anlamlı bir fark vardı. Koroner arter hastalarının GENSINI ve SYNTAX skorları kontrol grubundan anlamlı derecede yüksekti. Korelasyon analizlerinde IL-6 düzeyi ile GENSINI ve SYNTAX skorları arasında pozitif yönlü bir korelasyon olduğu ve IL-6'nın anormal koroner anjiyografinin bağımsız bir belirleyicisi olduğu ortaya çıkmıştır. Koroner arter hastalığını tespit edebilmek için IL-6'nın optimal cut-off değeri 7,81 pg/mL olarak tespit edildi (Area under curve=0,78, sensitivity=%78,3, specificity=%70,7).

Sonuç: Koroner arter hastaları kontrol grubuyla karşılaştırıldığında daha yüksek IL-6 düzeylerine sahiptir. IL-6 düzeyi ile GENSINI ve SYNTAX skorları arasında pozitif yönlü bir korelasyon vardır. IL-6 anormal koroner anjiyografinin bağımsız bir belirleyicisidir. 7,81 pg/mL üzerindeki IL-6 değerleri koroner arter hastalığını tespit etmede %78,3 sensitiviteye ve %70,7 spesifisiteye sahiptir.

Anahtar kelimeler: Koroner arter hastalığı, enflamasyon, IL-6, GENSINI skoru, SYNTAX skoru

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INTRODUCTION

Coronary artery disease (CAD) is the most common heart disease in the world. Hypertension, obesity, smoking, diabetes, sedentary life style, hyperlipidemia, and a family history of CAD are some of the main risk factors for CAD. Although many precautions have been taken to prevent CAD, such as dietary and lifestyle modifications, optimization of blood lipid levels, and regulation of blood glucose levels, it is a very important public health problem and the most common cause of death in the world (1).

Atherosclerosis plays an important role in the pathogenesis of CAD. Inflammatory cytokines lead to endothelial cell activation and contribute to inflammatory responses in patients with CAD. Therefore, atherosclerosis is a kind of chronic immune/inflammatory disease of the vessels. Many researchers have investigated the effect of inflammation on CAD. These studies showed that inflammation plays a key role in the initiation and propagation of CAD (2, 3). There are many inflammatory markers related to CAD, including C-reactive protein (CRP), homocysteine, matrix metalloproteinases, interleukin (IL)-6, IL-8, and IL-27. IL-6 is the sign of synthesis of acute phase proteins. IL-6 levels increase with tissue injury, infections, ischemic diseases, neoplasms, and trauma (4). Recently, the clinical trials related to CAD showed that IL-6 may be an indicator of increased risk for CAD (5). In addition to these improvements, the major concern of cardiologist is the risk stratification of patients with CAD to determine prognosis, mortality, severity of disease, and appropriate revascularization methodologies. Two commonly used scoring systems for risk stratification in clinical practice are GENSINI and SYNergy between PCI with TAXUS and Cardiac Surgery (SYNTAX) scores for determining disease severity and methods of revascularization. Even though these scoring systems have many advantages, they need invasive coronary interventions for determining risk scores. The aim of this study was to investigate the relationship between IL-6 levels and both GENSINI and SYNTAX scores in patients with CAD.

METHODS

Study Population

In total, 150 patients with suspicion of CAD who underwent coronary angiographic examination were evaluated for this study. Exclusion criteria of the study were acute and chronic infection, history of connective tissue disease, cardiomyopathy, myocarditis, previously documented CAD, congenital heart disease, pre-excitation syndromes, and impaired renal function (defined as a plasma creatinine value higher than 106.08 μmol/L or 1.2 mg/dL). After the exclusion criteria were applied, 118 patients were enrolled in the study. Demographic information, smoking and alcohol use, and blood pressures were recorded. All patients were informed about the study and written informed consent was obtained from patient who participated in this study. The local ethics committee of Marmara University approved the study.

Biochemical Assessment

Blood specimens were collected from the patients (n=118) into serum separator tubes (SST) with no additives and K_2-ethylenediaminetetraacetic acid (EDTA)-containing tubes (Becton Dickinson, NJ, USA) in a fasting state before coronary angiography. The samples in SST were allowed to clot for 20 min and centrifuged at 1300×g for 10 minutes. Serum samples were aliquoted and stored at −80°C under proper conditions until analysis of IL-6. We measured serum glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), sodium (Na^+), potassium (K^+), creatinine, total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL), and high-density lipoprotein cholesterol (HDL) using standard kits (COBAS, Integra, Roche Diagnostic Systems, Basel, Switzerland). Complete blood counts of all patients were analyzed on an LH 780 auto-analyzer (Beckman Coulter Inc., FL, USA). IL-6 was measured with a solid-phase, enzyme-labeled, chemiluminescent sequential immunometric assay (IMMULITE 2000, Siemens Health Care, UK). Within-run precision values were 4.5%-3.3% and between-run precision values were 5.3%-7.2% for 89-112 pg/mL IL-6, according to the manufacturer's claim.

Coronary Angiographic Evaluation

Coronary angiography examination was performed on all patients by the femoral approach, and high-quality cine-angiograms were used for analysis. Diameter stenosis ≥50% was accepted as significant using quantitative angiography. Fifty-eight patients had at least one significant lesion. Patients who have at least one significant lesion was accepted as patients with CAD. Sixty patients without a significant lesion were accepted as the control group. SYNTAX score was calculated by two experienced invasive cardiologist as suggested before (6) using an online calculator (http://www.SYNTAXscore.com). If any controversy was found, judgment was made by consensus. GENSINI score for determining severity of CAD (7) was calculated according to stenosis as follows: 1 point for 25% stenosis, 2 points for 26%-50% stenosis, 4 points for 51%-75% stenosis, 8 points for 76%-90% stenosis, 16 points for 91%-99% stenosis, and 32 points for totally occluded arteries. The score was then multiplied by a factor that represents the importance of the lesion in the coronary arterial tree.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) 16.0 statistical package for Windows (SPSS Inc.; versiyon 16.0, Chicago, IL, USA). Continuous data were expressed as mean±standard deviation, whereas categorical data were presented as percentage. The Chi-square test was used for comparison of categorical variables, whereas the student t-test and the Mann-Whitney U test were used to compare parametric and nonparametric continuous variables, respectively. For correlation analysis, Pearson test was used. Receiver operating characteristic (ROC) analysis was used to assess the ability of IL-6 to differentiate the presence of CAD. Intra- and interobserver variability was calculated as the absolute difference between two measurements. A value of $p<0.05$ was considered statistically significant.

RESULTS

According to coronary angiographic examination, 58 patients (female/male, 18/40; mean age, 58.2±11.3 years) had significant CAD, whereas 60 patients (female/male, 36/24; mean age, 57.3±11.8 years) had no CAD (p=0.487 for age). There were no significant differences between the groups with respect to the mean ages, systolic blood pressure, diastolic blood pressure,

Table 1. Baseline characteristics and clinical data of the study population

	Patient group (n=58)	Control group (n=60)	p
Age (years)	58.2±11.3	57.3±11.8	0.487
Female gender (n)	18	36	**0.002**
Systolic blood pressure (mmHg)	136.6±20.7	140.7±19.5	0.194
Diastolic blood pressure (mmHg)	76.9±12.0	78.8±10.8	0.191
Heart rate (beat/minute)	75.7±13.1	75.4±10.1	0.518
Smoking (n)	33	17	**0.002**
Alcohol use (n)	6	7	0.819
SYNTAX score	10.7±7.3	0.1±0.2	**<0.001**
GENSINI score	47.1±30.5	2.2±3.3	**<0.001**

Data are expressed as mean ± SD or as number and percentages. Bold values indicate p<0.05.

Table 2. Comparison of laboratory findings of patient and control groups

	Patient group (n=58)	Control group (n=60)	p
Interleukin-6 levels (pg/mL)	21.0±22.6	6.6±7.8	**<0.001**
White blood cell counts	8.0±2.2	7.7±2.5	0.229
Hemoglobin (gr)	13.3±1.8	13.2±1.6	0.494
Fasting glucose (mg/dL)	128.1±55.6	121.4±47.1	0.539
Creatinine (mg/dL)	0.92±0.18	0.87±0.20	0.164
Total cholesterol (mg/dL)	205.7±50.8	219.3±57.6	0.168
Triglycerides (mg/dL)	165.1±69.6	188.8±81.6	0.120
Low density lipoprotein (mg/dL)	126.4±38.7	124.0±42.8	0.948
High density lipoprotein (mg/dL)	41.5±8.5	46.2±13.6	0.071
AST (U/L)	30.2±18.0	24.2±12.1	0.111
ALT (U/L)	26.3±14.1	23.4±13.1	0.160
Na (mmol/L)	138.9±5.3	140.3±3.0	0.127
K (mmol/L)	4.3±0.5	4.5±0.4	0.082

Data are expressed as mean±SD. Bold values indicate p<0.05.
AST: aspartate amino transferase; ALT: alanine amino transferase; Na: sodium; K: potassium

heart rates, and alcohol use. Gender and smoking status were significantly different between the two groups (p=0.002 and p=0.002, respectively). Sociodemographic and clinical data of the two groups are displayed in Table 1. GENSINI and SYNTAX scores of patients were significantly higher in the CAD group than in the control group, as expected (p<0.001, respectively). The mean values of GENSINI and SYNTAX scores were 2.2±3.3 and 0.1±0.2 for the control group and 47.1±30.5 and 10.7±7.3 for the CAD group, respectively.

Table 3. Correlation of IL-6 and WBC with severity of coronary artery disease

	Syntax score		Gensini score	
	r	p	r	p
IL-6	**0.484**	**<0.001**	**0.529**	**<0.001**
WBC	**0.167**	**0.070**	**0.104**	**0.263**

IL: interleukin; WBC: white blood cell count. Bold values indicate p<0.05

Table 4. Logistic regression analysis to determine the independent predictors of abnormal coronary angiography

	Odds Ratio (OR)	95% Confidence Interval for OR	p
Age	1.026	0.987-1.067	0.194
Gender	2.439	0.917-6.488	0.074
Interleukin-6	1.113	1.048-1.182	**0.001**
Smoking	0.417	0.156-1.113	0.081

Bold values indicate p<0.05.

Laboratory findings of the two groups are shown in Table 2. The IL-6 level was significantly higher in the CAD group compared to the control group. There was no difference in other laboratory findings. In the correlation analysis, we found that the IL-6 level significantly correlated with the GENSINI and SYNTAX scores (r=0.529, p<0.001 and r=0.484, p<0.001, respectively) in the CAD group (Table 3). The multiple logistic regression analysis showed that the IL-6 level was an independent predictor of abnormal coronary angiography [odds ratio (95% CI), 1.113 (1.048–1.182); p=0.001] (Table 4). The ROC curve analysis showed that the optimal cutoff level of IL-6 was 7.81 pg/mL to assess the ability of IL-6 to predict the presence of CAD (area under curve, 0.78; sensitivity, 78.3%; and specificity, 70.7%) (Figure 1).

DISCUSSION

In this study, we investigated the relationship between IL-6, both GENSINI and SYNTAX scores, and their association with CAD. Our results demonstrated that IL-6 levels correlated with GENSINI and SYNTAX scores in patients with CAD. Moreover, the IL-6 level was an independent predictor of abnormal coronary angiography. An IL-6 value of 7.81 pg/mL or higher predicted the presence of CAD with a sensitivity of 78.3% and a specificity of 70.7%.

It is obvious that inflammation plays a crucial role in atherosclerosis and cardiovascular disease (8). There are many inflammatory markers, such as tumor necrosis factor (TNF) alpha, IL-1, CRP, and IL-6, whose relations to the inflammatory process in CAD were shown in previous studies (9). Tanindi et al. (10) reported that IL-6 was associated with more extensive and severe CAD. They determined the sensitivity and specificity value of IL-6 for

determining CAD as 46% and 86%, respectively. In our study, the optimal cutoff value of IL-6 was 7.81 pg/mL and sensitivity and specificity were 78.3% and 70.7%, respectively.

Some studies were conducted to investigate the role of IL-6 for predicting the mortality in patients with cardiovascular diseases. In a prospective study, the relationship between IL-6 and the mortality of hospitalized patients with CAD was also examined. They reported that IL-6 was positively associated with an increased risk of all-cause and cardiovascular mortality (11). Contrary to that study, Tuomisto et al. (12) reported that CRP and TNF-α, but not IL-6, were significant independent predictors of total mortality among men. Volpato et al. reported that high IL-6 levels strongly affected the risk of mortality associated with the presence of CAD (13). In a recent study, it was found that IL-6 levels were correlated with the severity of CAD. In that study, the severity of CAD was evaluated by the GENSINI score (14). In addition to these reports, there are some studies about the therapeutic use of IL-6 inhibition. An IL-6 receptor blocking agent (tocilizumab) has been used for the treatment of rheumatoid arthritis (RA), and its use in preventing CAD is controversial. Provan et al. reported that tocilizumab treatment decreases the arterial stiffness measurements that are determined by pulse wave velocity, which is a marker of cardiovascular disease risk in patients with RA (15). It is reported that tocilizumab has antiarrhythmic potential and decreases the corrected QT interval; it may also be used to treat pericarditis associated with RA by controlling systemic inflammation (16, 17).

It is a big challenge for invasive cardiologists or cardiovascular surgeons to decide the most beneficial revascularization method. The SYNTAX score is used as a guidance system by the cardiologists. We suggested that a marker of inflammation, such as IL-6, plays a role in risk stratification, disease severity, and determining the method of revascularization. Although there are studies in the literature that investigate the relationship between IL-6 and the severity of CAD, our study is unique in its design because it combines SYNTAX and GENSINI scores in one study. In the studies by Cotsman et al. (5) and Rajpal et al. (14), plasma IL-6 levels showed positive correlation with GENSINI and SYNTAX scores, respectively. Jernbeg et al. (18) showed that the combination of N-terminal pro-brain natriuretic peptide and IL-6 is a useful tool in the identification of patients with a definite survival benefit from an early invasive strategy. Consistent with these studies, there was a positive correlation between IL-6 levels and not only GENSINI but also SYNTAX scores in our study.

Study Limitations

There are several limitations of our study. First, this was a cross-sectional study and the patients were not followed up. Therefore, we could not show the association of inflammatory markers with adverse cardiac events, and we are not able to evaluate the prognostic value of IL-6 in patients with CAD. Second, we did not investigate other inflammatory markers, such as high sensitive CRP, IL-1-beta, TNF-alpha, homocysteine, and matrix metalloproteinase. Therefore, it is not possible to compare the results with these markers. Third, we did not evaluate other cardiovascular risk factors, such as sedentary life style, body mass index, and waist circumference. Finally, we did not evaluate the medication history of the participants. These factors may also affect the inflammatory status of the patients. Future prospective and large population studies should be performed to elucidate the effectiveness of IL-6 to predict the presence, severity, and extent of CAD.

CONCLUSION

We demonstrated that patients with CAD have higher IL-6 levels compared with those in the control group. The IL-6 level positively correlated with both GENSINI and SYNTAX scores. Moreover, the IL-6 level was an independent predictor of abnormal coronary angiography. An IL-6 value of 7.81 pg/mL or higher predicted the presence of CAD with a sensitivity of 78.3% and a specificity of 70.7%.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Marmara University.

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REFERENCES

1. Hansson GK, Robertson AK, Söderberg-Nauclér C. Inflammation and atherosclerosis. Annu Rev Pathol 2006; 1: 297-329. [CrossRef]
2. Yan ZQ, Hansson GK. Innate immunity, macrophage activation and atherosclerosis. Immune Rev 2007; 219: 187-203. [CrossRef]
3. Saadeddin SM, Habbab MA, Ferns GA. Markers of inflammation and coronary artery disease. Med Sci Monit 2002; 8: 5-12.
4. Papanicolaou DA, Wilder RL, Manolagas SC, Chrousos GP. The pathophysiologic roles of interleukin-6 in human disease. Ann Intern Med 1998; 128: 127-37. [CrossRef]

5. Gotsman I, Stabholz A, Planer D, Pugatsch T, Lapidus L, Novikov Y, et al. serum cytokine tumor necrosis factor-alpha and ınterleukin-6 associated with the severity of coronary artery disease: ındicators of an active ınflammatory burden? Isr Med Assoc J 2008; 10: 494-8.
6. SYNTAX Working Group. SYNTAX score calculator. (accessed January 15): Avaible from: http://www.SYNTAXscore.com.
7. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol 1983; 51: 606. [CrossRef]
8. Libby P, Ridker PM, Hansson GK; Leducq Transatlantic Network on Atherothrombosis. Inflammation in atherosclerosis: from pathophysiology to practice. J Am Coll Cardiol 2009; 54: 2129-38. [CrossRef]
9. Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, et al; Intermountain Heart Collaborative Study Group. Which white blood cell subtypes predict increased cardiovascular risk? J Am Coll Cardiol 2005; 45: 1638-43. [CrossRef]
10. Tanindi A, Sahinarslan A, Elbeg S, Cemri M. Relationship Between MMP-1, MMP-9, TIMP-1, IL-6 and Risk Factors, Clinical Presentation, Extent and Severity of Atherosclerotic Coronary Artery Disease. Open Cardiovasc Med J 2011; 5: 110-6. [CrossRef]
11. Su D, Li Z, Li X, Chen Y, Zhang Y, Ding D, et al. Association between serum interleukin-6 concentration and mortality in patients with coronary artery disease. Mediators Inflamm 2013; 2013: 726178. [CrossRef]
12. Tuomisto K, Jousilahti P, Sundvall J, Pajunen P, Salomaa V. C-reactive protein, interleukin-6 and tumor necrosis factor alpha as predictors of incident coronary and cardiovascular events and total mortality A population-based, prospective study. Thromb Haemost 2006; 95: 511-8. [CrossRef]
13. Volpato S, Guralnik JM, Ferrucci L, Balfour J, Chaves P, Fried LP, et al. Cardiovascular disease, interleukin-6, and risk of mortality in older women: the women's health and aging study. Circulation 2001; 103: 947-53. [CrossRef]
14. Rajpal S, Rana MA, Peter E, Shah S, Pardue S, Gebregziabher H, et al. Relationship of syntax score with markers of vascular inflammation. J Am Coll Cardiol 2014; 63: A2066. [CrossRef]
15. Provan SA, Berg IJ, Hammer HB, Mathiessen A, Kvien TK, Semb AG. The impact of newer biological disease modifying anti-rheumatic drugs on cardiovascular risk factors: a 12-month longitudinal study in rheumatoid arthritis patients treated with rituximab, abatacept and tociliziumab. PLoS One 2015; 26: e0130709. [CrossRef]
16. Lazzerini PE, Acampa M, Capecchi PL, Fineschi I, Selvi E, Moscadelli V, et al. Antiarrhythmic potential of anticytokine therapy in rheumatoid arthritis: tocilizumab reduces corrected QT interval by controlling systemic inflammation. Arthritis Care Res (Hoboken) 2015; 67: 332-9. [CrossRef]
17. Yoshida S, Takeuchi T, Sawaki H, Imai T, Makino S, Hanafusa T. Successful treatment with tocilizumab of pericarditis associated with rheumatoid arthritis. Mod Rheumatol 2014; 24: 677-80. [CrossRef]
18. Jernberg T, Lindahl B, Siegbahn A, Andren B, Frostfeldt G, Lagerqvist B, et al. N-terminal pro-brain natriuretic peptide in relation to inflammation, myocardial necrosis, and the effect of an invasive strategy in unstable coronary artery disease. J Am Coll Cardiol 2003; 42: 1909-16. [CrossRef]

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