Plateletcrit and Platelet Distribution Width as Independent Predictors of Coronary Artery Ectasia

Hikmet Hamur[1], Kamuran Kalkan[2], Hakan Duman[3], Murtaza Emre Durakoğlugil[3], Zafer Küçüksu[4], Sinan İnci[5], Erkan Yıldırım[2]

[1] Erzincan University Faculty of Medicine, Department of Cardiology, Erzincan, Turkey
[2] Erzurum Regional Training and Research Hospital, Clinic of Cardiology, Erzurum, Turkey
[3] Recep Tayyip Erdoğan University Faculty of Medicine, Department of Cardiology, Rize, Turkey
[4] Mengücek Gazi Training and Research Hospital, Clinic of Cardiology, Erzincan, Turkey
[5] Aksaray State Hospital, Clinic of Cardiology, Aksaray, Turkey

ABSTRACT

Introduction: Coronary artery ectasia (CAE) is characterised by an abnormal dilatation of the coronary arteries. Platelet volume indices, including the mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT) and platelet count, are indicators of platelet activation. In this study, we investigated platelet volume indices in patients with CAE.

Patients and Methods: The study group included 51 patients (38 men; mean age: 52 ± 9.9 years) with isolated CAE and 50 individuals with normal coronary arteries (39 men; mean age: 54 ± 11.3 years). Admission platelet volume indices were measured as part of the automated complete blood count.

Results: Platelet count, MPV, PCT and PDW were higher in CAE than in the control group ($p< 0.05$). Multivariate analysis revealed PDW (odds ratio: 0.22, 95% confidence interval: 0.06-0.73, $p= 0.013$) and PCT (odds ratio: 3.41, 95% confidence interval: 1.66-6.98, $p\leq 0.001$) as independent predictors of CAE.

Conclusion: This study demonstrates that PCT and PDW are independent predictors of CAE.

Key Words: Coronary artery ectasia; coronary artery disease; mean platelet volume; platelet distribution width

Plateletkrit ve Trombosit Dağılım Genişliği Koroner Arter Ektazisinin Bağımsız Öngördürücüsüdür

ÖZET

Giriş: Koroner arter ektazisi (KAE), koroner arterlerin anormal genişlemesi ile karakterize edilir. Ortalama trombosit hacmi (OTH), trombosit dağılım genişliği (TDG), plateletkrit (PKT) dahil olmak üzere trombosit hacmi endeksleri ve trombosit sayısı trombosit aktivasyonunun göstergeleridir. Bu çalışmada KAE'li hastalarda trombosit hacmi endeksleri incelendi.

Hastalar ve Yöntem: Çalışmaya, izole KAE'si olan 51 (38 erkek; ortalama yaş: 52 + 9.9 yıl) hasta ve koroner arterleri normal olan 50 (39 erkek; ortalama yaş: 54 + 11.3 yıl) sağlıklı birey dahil edildi. Başvuruda trombosit hacmi endeksleri otomatik tam kan sayımı parçası olarak ölçüldü.

Bulgular: Trombosit sayımı, OTH, PKT ve TDG, KAE grubunda kontrol grubuna göre daha yüksekti ($p< 0.05$). Çok değişkenli lojistik regresyon analizinde, TDG (Odds oranı: 0.22, %95 güven aralığı: 0.06-0.73, $p= 0.013$) ve PKT'nin (Odds oranı: 3.41, %95 güven aralığı: 1.66-6.98, $p\leq 0.001$) KAE'nin bağımsız öngördürücüleri olduğu gösterildi.

Sonuç: Bu çalışma, PKT ve TDG'nin KAE'nin bağımsız belirleyicileri olduğunu göstermektedir.

Anahtar Kelimeler: Koroner arter ektazisi; koroner arter hastalığı; ortalama trombosit hacmi; trombosit dağılım genişliği

Correspondence

Hikmet Hamur

E-mail: hikmethamur@hotmail.com
Submitted: 06.02.2016
Accepted: 21.03.2016

INTRODUCTION

Coronary artery ectasia (CAE), a frequent angiographic finding, is defined as the dilation of the luminal arterial diameter 1.5 or more times greater than the diameter of the normal portion of the artery[1]. CAE may predispose patients to adverse coronary events, such as vasospasm, thrombosis, dissection and myocardial infarction; however, the underlying mechanism of the abnormal luminal dilatation is stil unclear[2-5].

Platelet volume indices, including the mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT) and platelet count, are indicators of platelet activity, and these are routinely reported in automated full blood counts[6,7]. Platelet volume, a marker of platelet activation, is measured with MPV[8]. PDW, which reflects the variation in the size of circulating platelets, is also an indicator of platelet activation[9]. PCT, the product of MPV and platelet count, projects the number of platelets in a unit blood volume and is a marker of total platelet mass[10]. PCT is related to coronary artery disease (CAD)[6]. MPV is a potentially useful marker of platelet function and cardiovascular diseases[11]. There exists a significant association between MPV and CAD[12,13]. Larger platelets, which are more haemostatically active, may play a specific role in the development of coronary artery ectasia[14].

To date, only MPV has been evaluated in patients with CAE; however, PDW and PCT, which reflect the total platelet mass, have been ignored. In this study, we evaluated platelet volume indices, including PDW and PCT, in patients with CAE.

PATIENTS and METHODS

Study Population

The study group included 51 patients (38 men; mean age: 52 ± 9.9 years) with isolated CAE who had ectatic coronaries without any stenotic lesion among those who had undergone coronary angiography due to the suspicion of CAD. The control group consisted of 50 consecutive participants (39 men; mean age: 54 ± 11.3 years) who had normal coronary angiograms during the study period. Patients with any of the following were excluded: acute coronary syndrome, previous coronary artery bypass grafting, history of antiplatelet or anticoagulant use or percutaneous coronary intervention, myocardial infarction, left ventricular systolic dysfunction, acute or chronic inflammatory disease, renal and hepatic deficiency, hypothyroidism, hyperthyroidism, thrombocytopaenia, haemolytic failure, autoimmune or neoplastic disease, recent major surgery or systemic failure, respiratory tract disease (chronic obstructive pulmonary disease, chronic bronchitis, pulmonary embolism), primary pulmonary hypertension, isolated right heart insufficiency, congenital heart disease or advanced stage valve disease as well as patients with baseline anaemia (haemoglobin < 13 g/dL for males, haemoglobin < 12 g/dL for females) and a history of blood transfusion in the last 3 months. The protocol was approved by the local ethics committee and complied with the Declaration of Helsinki.

Following an assessment of the detailed medical history and a complete physical examination, age, sex, family history of CAD, current smoking status, history of hypertension, dyslipidaemia, diabetes mellitus (DM) and body mass index [BMI; weight (kg)/height squared (m^2)] and glomerular filtration rate (GFR) were recorded for all patients. GFR was calculated from serum creatinine using the Cockcroft-Gault equation [(140 -age) × (weight in kg) × (0.85 if female)/(72 × creatinine)].

Laboratory Analysis

Blood samples were drawn from an antecubital vein before coronary angiography after a fasting period of 12 h. Blood glucose, creatine and lipid profiles were recorded. These parameters were analysed using an autoanalyser (AU 2700 plus analyzer, Beckman Coulter, Tokyo, Japan).

Haematological parameters, including white blood cell, haemoglobin, mean cell volume (MCV), mean cell haemoglobin (MCH), mean cell haemoglobin concentration (MCHC), red cell distribution width (RDW), platelet count, MPV, PCT and PDW were measured as part of the automated complete blood count (CBC) using a Coulter LH 780 Hematology Analyzer (Beckman Coulter Inc, Miami, FL, USA).

Clinical Definitions

Hypertension was defined as a systolic pressure of > 140 mmHg and/or a diastolic pressure of > 90 mmHg recorded at least twice or the use of antihypertensive medication. DM was defined as a fasting plasma glucose level of > 126 mg/dL, glucose levels of > 200 mg/dL at any measurement or active antidiabetic treatment. Hypercholesterolaemia was acknowledged as total cholesterol levels of > 200 mg/dL or a previous history of statin use. A positive family history of CAD was defined as documented evidence of premature CAD in a first-degree relative (men < 55 and women < 65 years of age).

Coronary Angiography

Coronary angiography was performed using the Judkins technique without nitroglycerin using 6-Fr right and left heart catheters. Angiograms were analysed by two interventional cardiologists who were blinded to the clinical status and laboratory measurements. After obtaining images by standard approaches, each angiogram was interpreted by two independent cardiologists. The diagnosis of CAE was acknowledged if dilation was present exceeding a 1.5-fold of the diameter of adjacent normal coronary segments[15]. When there was no identifiable adjacent normal segment, the mean diameter of the corresponding coronary segment in the control group served as the normal value. Significant coronary artery stenosis was defined as ≥ 50% stenosis of the major coronary arteries. The severity of ectasia was evaluated and categorised[16]. In decreasing order of severity, the diffuse ectasia of two or three vessels was classified as type I, diffuse disease in one vessel and localised disease in

another vessel as type II, diffuse ectasia of one vessel only as type III and localised or segmental ectasia as type IV.

Statistical Analysis

Continuous variables are expressed herein as the mean ± standard deviation and categorical variables are shown as percentages. The one sample Kolmogorov-Smirnov test was used to evaluate the distribution of continuous variables. Continuous variables between two groups were compared using the Student's t-test or Mann-Whitney U test, where applicable. Categorical variables were compared using the chi-square or Fisher's exact test. Multivariate logistic regression analyses were performed in order to determine the independent predictors of CAE. Receiver operating characteristics (ROC) curve analysis was performed using MedCalc statistic software (version 13.2.0, Mariakerke, Belgium) to predict cut-off values of PCT and PDW for CAE. Two-tailed p values of < 0.05 were considered significant. Data were analysed using SPSS version 17 (SPSS Inc., Chicago, IL, USA).

RESULTS

Baseline Characteristics

The baseline characteristics of the study groups are presented in Table 1. The basic clinical and demographic characteristics, including age and sex, were similar in both groups. BMI values and the presence of DM, hypertension, smoking, dyslipidaemiaand a family history of CAD were not significantly different between the groups (p> 0.05). In addition, the estimated GFR, lipid parameters and medications did not differ (p> 0.05).

Blood Count Parameters

White blood cell count, haemoglobin level, MCV, MCH and MCHC were not significantly different between the groups (p> 0.05). However, RDW, platelet count, MPV, PCT and PDW were significantly higher in the CAE than in the control group (p< 0.05).

Multivariate and ROC Analyses

Multiple logistic regression analysis identified PDW [odds ratio: 0.216, 95% confidence interval (CI): 0.064-0.727, p= 0.013] and PCT (odds ratio: 3.408, 95% CI: 1.660-6.997, p≤ 0.001) as independent predictors of CAE (Table 2).

The cut-off values of PCT and PDW for identifying CAE were 0.18 with a sensitivity of 82.4% and specificity of 76.0% [area under the curve (AUC), 0.823; 95% CI, 0.734-0.891; p< 0.001] and 13.1 with a sensitivity of 66.7% and specificity of 78.0% (AUC, 0.763; 95% CI, 0.668-0.842; p< 0.001), respectively, in ROC analyses (Figure 1).

DISCUSSION

The present study evaluated platelet volume indices, such as MPV, PDW and PCT values, in patients with CAE. To the best of our knowledge, this study is the first to show that PDW and PCT are independent predictors of CAE.

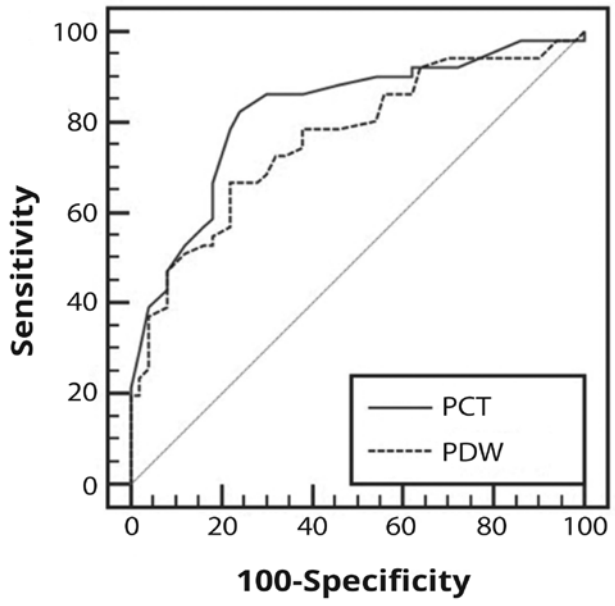

Figure 1. Receiver operating characteristic (ROC) curve of plateletcrit (PCT) and platelet distribution width (PDW) for predicting coronary artery ectasia (CAE).

The aetiology of CAE still remains unknown. Inflammatory diseases have been blamed in 20%-30% of cases and congenital CAE in approximately one-third of cases[17]. Infectious agents, toxicity and trauma may also have a place in the pathogenesis of CEA[18]. However, atherosclerosis seems to be the main aetiologic factor of CAE. Accordingly, histopathological changes within the arterial wall in CAE are similar to those of atherosclerosis, except there is a prominent loss of the musculoelastic arterial wall in CAE. Histologic examinations identified diffuse hyalinisation, lipid deposition, destruction of the intima and media and regional calcification in ectasia to be similar to atherosclerosis. Invasion of the arterial media results in the destruction of musculoelastic elements and thinning of the arterial wall. Interestingly, ectasia was not observed in lesions where the media was unaffected[19-21]. Therefore, the same basic pathophysiology may exist in coronary ectasia and stenosis. Ectasia of the coronary arteries may cause significant complications due to distal embolisation resulting from stasis in the dilated segments and impaired coronary flow[22].

Platelets play critical roles in inflammation, thrombosis and cardiovascular pathophysiology. Platelet activation is one of the crucial factors associated with CAD[23,24]. Inflammatory mediators, including interleukin (IL)-1, IL-3 and IL-6, promote megakaryocyte proliferation, which results in increased platelet count[25,26]. Therefore, higher platelet counts may indicate a proinflammatory state with thrombocyte activation and prothrombotic milieu[27]. Platelets with dense granules are bigger in size and metabolically more active[28,29]. Increased MPV is associated with acute coronary syndrome, carotid artery disease, sepsis, deep vein thrombosis, pulmonary embolism,

Table 1. Demographic, biochemical, haematological and angiographic characteristics of the study groups

	CAE group (n= 51)	Control group (n= 50)	p value
Age, years	52 (31-74)	54 (33-75)	0.094
Sex, male, n (%)	38 (74.5%)	39 (78.0%)	0.680
BMI, kg/m^2	24.5 (16.0-36.4)	24.0 (16.2-35.7)	0.252
Diabetes mellitus, n (%)	18 (35.3%)	14 (28.0%)	0.431
Hypertension, n (%)	19 (37.3%)	15 (30.0%)	0.440
Smoking, n (%)	16 (31.4%)	13 (26.0%)	0.551
Dyslipidaemia, n (%)	27 (52.9%)	23 (46.0%)	0.485
Family history of CAD, n (%)	9 (17.6%)	6 (12.0%)	0.425
White blood cell count, ×10^9/l	7.6 (4.9-9.8)	7.3 (4.6-9.9)	0.796
Haemoglobin, g/dL	14.0 (12.1-16.1)	14.2 (12.4-17.5)	0.648
MCV, fL	92 (77-103)	89 (76-105)	0.357
MCH, pg	32 (25-36)	31 (26-35)	0.837
MCHC, g/dL	33 (30-36)	33 (31-37)	0.814
Red cell distribution width (%)	15.0 (12.0-18.4)	14.3 (11.4-18.6)	0.044
Platelet count, ×10^9/l	246 (156-457)	203 (132-384)	0.010
Mean platelet volume, fL	9.2 (6.7-12.9)	8.3 (6.6-12.4)	0.043
PDW (%)	14.3 (9.1-17.1)	11.3 (9.4-16.4)	< 0.001
PCT (%)	0.25 (0.15-0.33)	0.12 (0.10-0.25)	< 0.001
GFR, mL/min/1.73 m^2	81 (72-105)	79 (72-103)	0.629
LDL cholesterol, mg/dL	135 (45-237)	132 (62.0-206)	0.967
HDL cholesterol, mg/dL	38 (22-64)	40 (23-65)	0.067
Triglyceride, mg/dL	151 (43-635)	134 (49-506)	0.315
Previous medications, %			
Aspirin, n (%)	14 (27.5%)	12 (24.0%)	0.692
Statin, n (%)	5 (9.8%)	5 (10.0%)	0.974
ACE inhibitors/ARB, n (%)	6 (11.8%)	7 (14.0%)	0.737
b-blocker, n (%)	5 (9.8%)	8 (16.0%)	0.353
CCB, n (%)	5 (9.8%)	4 (8.0%)	0.750
Ectasia group[a]			
I, n (%)	8 (15.7%)		
II, n (%)	11 (21.6%)		
III, n (%)	23 (45.0%)		
IV, n (%)	9 (17.7%)		

CAD: Coronary artery disease, BMI: Body mass index, MCV: Mean cell volume, MCH: Mean cell haemoglobin, MCHC: Mean cell haemoglobin concentration, PDW: Platelet distribution width, PCT: Plateletcrit, GFR: Glomerular filtration rate, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, ACE: Angiotensin converting enzyme, ARB: Angiotensin receptor blocker, CCB: calcium channel blocker.
[a] Corrected TIMI frame count.

coronary slow flow phenomenon and coronary collateral vessels[28-34]. Previous studies investigated MPV only in CAE; however, PDW and PCT, which project the total platelet mass, have not been evaluated. PCT indicates the number of circulating platelets in a unit volume of blood, analogous to the haematocrit for erythrocytes[10]. PDW is more specific than MPV for the identification of platelet activity and is a simple, practical and specific marker for enhanced coagulation[9].

Higher MPV values were demonstrated in patients with CAE and CAD than in subjects with normal coronary angiograms[14]. Elevated PCT values on admission are independently associated with long-term adverse outcomes in patients with STEMI who undergo primary angioplasty[35]. It was reported that increased RDW and PDW in slow coronary flow (SCF) patients may cause microvascular blood flow resistance due to impaired cell

Table 2. Multiple logistic regression analyses investigating the effect of variables on CAE

Variables	Multivariate OR (95% CI)	p value
RDW (%)	1.684 (0.736-3.853)	0.217
PLT count, x10^9/l	0.987 (0.960-1.015)	0.354
MPV, fL	0.861 (0.318-2.336)	0.769
PDW (%)	0.216 (0.064-0.727)	0.013
PCT (%)	3.408 (1.660-6.997)	0.001

CAE: Coronary artery ectasia, CI: Confidence interval, OR: Odds ratio, RDW: Red cell distribution width, PLT: Platelet, MPV: Mean platelet volume, PDW: Platelet distribution width, PCT: Plateletcrit.

deformability and that PCT provides reliable data regarding total platelet mass and may be a useful predictor of SCF[34]. Another study showed that PCT has an important predictive value for saphenous vein graft disease, with an implication for its possible use as a marker for antiplatelet therapy to prevent graft degeneration in patients undergoing bypass surgery[11]. Similarly, in the present study, platelet count, MPV, PCT and PDW were higher in the CAE group than in the control group, and PCT and PDW were independent predictors of CAE. In patients with CAE, PDW and PCT may be used as a marker for more aggressive antiplatelet treatment. Further large-scale and comprehensive studies are required to support these results.

Limitations of the Study

A limitation of this study is the small number of patients. Another limitation of this study is that no patient was assessed with intravascular ultrasonography. Therefore, the presence of minimal atherosclerotic plaques could not be definitively ruled out. This was not a prospective controlled study; thus, we cannot draw cause-and-effect relationships from our findings.

CONCLUSION

To the best of our knowledge, this study is the first to show the role of PCT and PDW in patients with CAE. This study demonstrated that PCT and PDW are independent predictors of CAE. Thus, PCT and PDW may provide an important, simple, effortless and cost-effective tool for predicting coronary artery ectasia.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Consept/Design: HH, KK,HD, EY
Analysis/Interpretation: MD, HH, SI
Data Acquisition: ZK, HH
Writing: HH
Final Approval: All of authors

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