

The utility of mean platelet volume as a predictor of postoperative atrial fibrillation following coronary artery bypass grafting

Koroner arter baypas greftleme sonrası postoperatif atriyal fibrilasyonun bir prediktörü olarak ortalama trombosit hacminin kullanımı

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Abstract

Aim: Atrial fibrillation is the most common arrhythmia following coronary artery bypass grafting (CABG). The predictors of postoperative atrial fibrillation (POAF) following CABG are controversial. The aim of this study was to evaluate the predictivity of mean platelet volume (MPV) in the development of atrial fibrillation following CABG and other risk factors affecting POAF.

Methods: A total of 227 patients who underwent on-pump CABG in the cardiovascular surgery department of our hospital between May 2016 and January 2019 were included in this retrospective cohort study. Patients were divided into two groups as those who underwent POAF and those who did not (non-POAF group). Patients' demographic data such as age, gender, height, weight and BMI, biochemical parameters, comorbidities, smoking status, ejection fraction, the number of bypassed vessels, the use of intra-aortic balloon pump and inotropic agents, total drainage, neurological and other complications, operation time, duration of admission in intensive care unit and in the ward, and mortality status were recorded and comparatively analyzed.

Results: No statistically significant differences were found between the groups in terms of gender, body mass index, the incidences of diabetes mellitus, hypertension, chronic obstructive pulmonary disease, pulmonary arterial hypertension, renal failure, smoking status, the number of bypassed vessels, the use of intra-aortic balloon pump, inotropic agents, and biochemical parameters ($P < 0.05$ for all) except red cell distribution width (RDW), urea and mean platelet volume (MPV). MPV, RDW and urea values were significantly higher in the POAF group ($P = 0.004$, $P = 0.018$ and $P = 0.006$, respectively). Multivariate regression analysis revealed that age, MPV and the amount of total drainage were independent risk factors for developing POAF (OR=1.080, OR=1.371, OR=1.001; $P = 0.001$, $P < 0.001$, $P = 0.024$, respectively).

Conclusion: MPV can be used as a predictor for the development of POAF following on-pump CABG. MPV is a quite simple parameter, which can be readily obtained in routine complete blood count. However, our results should be supported by further prospective, multicenter and large-scale studies.

Keywords: Postoperative atrial fibrillation, Mean platelet volume, Coronary artery bypass grafting, Biochemical parameters

Öz

Amaç: Atriyal fibrilasyon koroner arter baypas greftleme (KABG) sonrası en sık görülen aritmidir. CABG'yi takiben postoperatif atriyal fibrilasyonun (POAF) belirleyicileri tartışmalıdır. Bu çalışmanın amacı, CABG'yi takiben POAF gelişimi ve POAF'ı etkileyen diğer risk faktörleri için ortalama trombosit hacminin (MPV) kullanımını değerlendirmektir.

Yöntemler: Bu retrospektif kohort çalışmamıza Mayıs 2016-Ocak 2019 tarihleri arasında hastanemizin kardiyovasküler kliniğinde pompalı CABG uygulanan toplam 227 hasta dahil edildi. Hastalar, POAF ve POAF olmayan gruplar olarak iki gruba ayrıldı. Hastaların yaş, cinsiyet, boy, kilo ve BMI gibi demografik verileri, biyokimyasal parametreler, komorbiditeler, sigara içme durumu, ejeksiyon fraksiyonu, baypas edilen damar sayısı, aort içi balon pompası (IABP) ve inotropik ajanlar, toplam drenaj, nörolojik ve diğer komplikasyonlar, operasyon süresi, yoğun bakım ünitesinde ve koğuştta yatış süresi ve mortalite durumu kaydedildi ve karşılaştırmalı olarak analiz edildi.

Bulgular: Gruplar arasında cinsiyet, vücut kitle indeksi, diabetes mellitus insidansı, hipertansiyon, kronik obstrüktif akciğer hastalığı, pulmoner arteriyel hipertansiyon, böbrek yetmezliği, sigara içme durumu, baypas edilen damar sayısı, IABP, inotropik ajanlar ve biyokimyasal parametreler (kırmızı hücre dağılım genişliği (RDW), üre ve MPV hariç anlamlı bir fark bulunmadı. MPV, RDW ve üre değerleri POAF grubunda POAF olmayanlara göre istatistiksel olarak anlamlı derecede yüksekti (sırasıyla $P = 0.004$, $P = 0.018$ ve $P = 0.006$). Çok değişkenli regresyon analizinde, yaş ve toplam drenaj miktarı POAF gelişiminin bağımsız risk faktörleri olarak bulundu (sırasıyla OR=1,080, OR=1,371, OR=1,001; $P = 0.001$, $P < 0.001$, $P = 0.024$).

Sonuç: MPV, pompalı CABG'yi takiben POAF gelişimi için bir belirteç olarak kullanılabilir. MPV, rutin tam kan sayımında kolayca elde edilebilen oldukça basit bir parametredir. Ancak, sonuçlarımız prospektif, çok merkezli ve büyük ölçekli çalışmalarda desteklenmelidir.

Anahtar kelimeler: Postoperatif atriyal fibrilasyon, Ortalama trombosit hacmi, Koroner arter baypas greftleme, Biyokimyasal parametreler

Introduction

Postoperative atrial fibrillation (POAF) is the most common arrhythmia following coronary artery bypass grafting (CABG). The incidence of POAF has been reported between 10% and 40% after CABG operation [1,2]. Although it is usually self-limiting, POAF is an important predictor of morbidity and mortality and increased healthcare costs. POAF is accompanied by cerebrovascular accidents, increased cardiac insufficiency and decreased left ventricular hemodynamic performance [3,4]. The risk of POAF following cardiac surgery is also influenced by several pre-existing cardiac and pulmonary disorders in addition to epidemiological and intraoperative factors. There are studies in the literature investigating the reasons underlying POAF [5]. The most commonly reported risk factor for POAF is age [6]. The other reported risk factors include male gender, low ejection fraction, chronic obstructive pulmonary disease, chronic renal dysfunction and preoperative withdrawal of beta-blockers [7,8]. However, there is no an exact consensus on the risk factors affecting the development of POAF.

Platelets are associated with thrombosis and inflammation, both of which play crucial roles in the pathogenesis of AF [9]. Large platelets increase thrombotic potency. The mean platelet volume (MPV), which corresponds to the average platelet size in the blood, is a readily measurable marker for reflecting platelet activation. MPV increases with the production of platelets. An elevated MPV level shows a higher tendency of coagulation in the blood, which increases the risk of thrombosis, stroke and cardiovascular disease [10]. MPV is a focus of interest as an independent cardiovascular risk factor. Recently, the mean platelet volume, a parameter that is routinely detected in complete blood count and is usually not paid attention to by clinicians, has been examined as a new expression of markers in several diseases including atherosclerosis, cerebral infarction and active inflammatory disorders [11,12]. Easy availability of MPV measurement without any additional cost encourages its wider use in clinical practice. MPV values have been found higher in persons with increased cardiovascular risk [13]. However, the number of studies investigating the relationship between MPV and the development of postoperative AF is limited [2,14]. Therefore, the objective of this study was to retrospectively evaluate the practicability of MPV level for the development of POAF following CABG and the other risk factors affecting POAF.

Materials and methods

Patient population & study design

A total of 227 patients who underwent coronary artery bypass grafting operation in the cardiovascular clinic of our hospital between May 2016 and January 2019 were included in this study. Preoperative standard 12-lead electrocardiography was routinely obtained in all patients and those with sinus rhythms were enrolled in the study. Patients were divided into two groups as those who developed postoperative AF and those who did not (POAF group and non-POAF group). Patients' demographic data such as age and gender, height, weight and BMI values, biochemical parameters, comorbidities, smoking status, ejection fraction, the number of bypassed vessels, the

usage of an intra-aortic balloon pump (IABP), administered inotropic agents, total drainage, neurological and other complications, operation time, and duration of admission in intensive care unit (ICU) and in the ward, and mortality status were recorded and retrospectively analyzed. Patients with significant valvular heart disease, pulmonary or neurological disease, acute coronary syndrome, congestive heart failure, atrial flutter, peripheral vascular disease, those with infections, malignancy, overt hypothyroidism or hyperthyroidism, chronic renal or hepatic disease and overt/active hematological disorders, and patients taking anti-arrhythmic drugs previously and those with current use of oral contraceptives were excluded from the study.

Evaluations

Standard on-pump CABG operation requiring cardiopulmonary bypass was performed in all included patients by the same surgeon. Following anesthesia induction, the patient was given supine position. The operations were performed through median sternotomy, with aortic cannulation at mild hypothermia using a single right atrial cannula, membrane oxygenator, a single cross clamp, and a roller pump with initially antegrade and then retrograde blood cardioplegia via the coronary sinus.

The patients were continuously monitored with a five-lead telemetry during admission in the ICU. Following discharge from the ICU, the patients were followed-up with 12-lead electrocardiography (ECG) every day. New-onset POAF was defined as AF occurring during hospitalization following CABG as specified by the Society of Thoracic Surgeons. Accordingly, atrial fibrillation (AF) lasting at least 10 minutes on the telemetry and requiring medical treatment following surgery in a patient without preoperative AF was defined as POAF.

Complete blood count was performed in patients undergoing CABG by obtaining blood samples following a 12-hour fasting period. Pre- and postoperative hemoglobin (Hb), hematocrit (Hct), white blood cell (WBC), red cell distribution width (RDW), MPV, neutrophil (Neut), platelet count (PLT), C-reactive protein (CRP), urea, creatinine, aspartate transaminase (AST), alanine transaminase (ALT) and troponin levels were measured. In addition, systolic and diastolic blood pressure were measured preoperatively and at the 1st, 2nd, 4th, 8th, 16th and 24th postoperative hours. The parameters obtained were compared between the patients with and without POAF. MPV values were measured from blood samples collected in 2 mL tubes containing tripotassium ethylenediaminetetraacetic acid using an automatic blood counter (Beckman Coulter LH 750, Fullerton, CA, USA).

Ethical statement

The study protocol was approved by the ethics committee of Pamukkale University Medical Faculty. All patients were informed about the study objectives in detail and gave verbal and written consent. The study was conducted in accordance with the principles of Declaration of Helsinki.

Statistical analysis

Data obtained in the study were statistically analyzed with SPSS 20.0 for Windows (SPSS, IBM Inc., Chicago, IL, USA) package software. Normality of the data was analyzed with the Kolmogorov-Smirnov test. The continuous variables were expressed as mean (SD), and the categorical variables, as

frequency and percentage. Since the data were normally distributed, continuous variables were compared between the two groups with Mann-Whitney U test. Categorical variables were compared with the Chi-square or Fisher Exact tests. The data were subjected to univariate regression analysis in order to determine the risk factors affecting POAF. The significant data in the univariate analysis were then subjected to multivariate analysis in order to detect the independent risk factors for POAF development. *P*-value <0.05 was considered statistically significant.

Results

Among 227 patents included in the study, 23.3% (n=53) were females and 76.7% (n=174) were males. Forty-four (19.4%) patients developed AF following CABG. No statistically significant difference was observed between the patients with and without POAF in terms of gender (*P*=0.928). The mean age in POAF and non-POAF patients, and overall were 69.89 (7.44) years, 62.79 (10.21) years and 64.17 (10.12) years, respectively. The mean age of the POAF group was statistically significantly higher compared to the non-POAF group (*P*<0.001). The mean body mass index (BMI) was 27.95 (4.45) kg/m² in POAF patients, and 28.49 (5.25) kg/m² in patients without POAF. No statistically significant difference was found between the POAF and non-POAF patients in terms of BMI (*P*=0.768). Comorbidities and smoking statuses of the patients are presented in Table 1.

There were no statistically significant differences between the patients with and without POAF in terms of diabetes mellitus, hypertension, COPD, pulmonary arterial hypertension (PAH), and renal failure incidences or smoking status (for all *P*>0.05).

The mean left atrial diameters of those in the POAF and non-POAF groups were similar, with 4.21±1.05 cm and 4.02±0.74 cm, respectively (*P*=0.442). One vessel was bypassed in 2 (4.5%) patients, 2 vessels in 7 (15.9%) patients, 3 vessels in 15 (34.1%) patients, 4 vessels in 12 (27.3%) patients, 5 vessels in 5 (11.4%) patients, 6 vessels in 2 (4.5%) patients and 7 vessels in 1 (2.3%) patient in the POAF group, and in the non-POAF group, 1 vessel was bypassed in 10 (5.5%) patients, 2 vessels in 19 (10.4%) patients, 3 vessels in 58 (31.7%) patients, 4 vessels in 58 (31.7%) patients, 5 vessels in 28 (15.3%) patients, and 6 vessels in 10 (5.5%) patients. No statistically significant was observed between the patients with and without POAF in terms of the number of vessels bypassed (*P*=0.436). Intra-aortic balloon pump (IABP) was used in 7 (15.9%) patients with POAF and 7 (39%) patients without POAF. The rate of patients with IABP was statistically significantly higher in the POAF group (*P*=0.008). Inotropic agents were used in 15 (34.9%) and 41 (22.9%) patients with and without POAF, respectively. There was no statistically significant difference between the two groups in terms of the use of inotropic agents (*P*>0.05). The mean ejection fraction (EF) was 49.27 (8.52) in patients with POAF, and 51.7 (9.38) in those without. EF value was significantly lower in POAF group (*P*=0.042). The total amount of drainage was 75.49 (648.4) mL and 585.4 (402.06) mL in POAF and non-POAF groups, respectively, which was significantly higher in

patients with POAF (*P*=0.011). Biochemical outcomes of the patients are presented in Table 2.

Table 1: Clinical characteristics and comorbidities of patients with and without POAF

		AF		Non-AF		<i>P</i> -value
		n	%	n	%	
Gender	Female	11	25.0	42	23.0	0.928
	Male	33	75.0	141	77.0	
DM	Yes	19	45.2	70	40.0	0.656
	No	23	54.8	105	60.0	
HT	Yes	24	57.1	88	50.3	0.531
	No	18	42.9	87	49.7	
COPD	Yes	0	0.0	12	6.6	0.13
	No	44	100.0	169	93.4	
PAH	Yes	7	15.9	17	9.3	0.313
	No	37	84.1	166	90.7	
RF	Yes	2	4.5	15	8.2	0.537
	No	42	95.5	168	91.8	
Smoking	Yes	18	43.9	85	48.3	0.739
	No	23	56.1	91	51.7	

DM: diabetes mellitus; HT: hypertension, COPD: chronic obstructive pulmonary disease, PAH: pulmonary arterial hypertension, RF: renal failure

Table 2: Biochemical parameters of patients with and without POAF

	AF		Non-AF		<i>P</i> -value
	Mean	SD	Mean	SD	
Hb	13.11	1.54	13.36	1.96	0.411
Hct	40.23	4.86	40.63	5.72	0.715
WBC	8.68	2.68	8.32	2.61	0.284
RDW	16.52	1.25	16.32	2.65	0.018
MPV	9.82	2.92	8.37	1.52	0.004
NEUT	6.3	2.86	6.22	3.05	0.501
PLT	235.16	63.85	228.6	65.88	0.349
CRP	18.57	33.11	15.06	25.52	0.731
Urea	46.05	14.32	42.34	22.87	0.006
Creatinine	1	0.25	1	0.6	0.101
AST	28.7	26.94	42.77	54.97	0.159
ALT	22.02	24.44	25.41	20.87	0.096

Hb: hemoglobin, Hct: hematocrit, WBC: white blood cells, RDW: red cell distribution width, MPV: mean platelet volume, NEUT: neutrophils, PLT: platelets, CRP: C-reactive protein, AST: aspartate aminotransferase, ALT: alanine aminotransferase

Hemoglobin, hematocrit, WBC, neutrophil and platelet count, CRP, creatinine, AST, and ALT values were similar between the two groups (*P*>0.05 for all). However, the mean MPV value was significantly higher in the POAF group (*P*=0.004), along with RDW (*P*=0.018) and urea (*P*=0.006) values.

The mean operational time was 241.43 (43.42) minutes in the patients with POAF and 246.5 (42.56) minutes in patients without, which were similar (*P*=0.409). There were no statistically significant differences between the groups in terms of cross clamp duration, and the durations of admission to the ICU and wards (*P*=0.345 and *P*=0.633, respectively) The most common postoperative complications were low cardiac output syndrome, myocardial infarction, pneumonia, mediastinitis, wound site infections and bleeding. No statistically significant differences were found between the two groups in terms of postoperative complications (*P*=0.624 for all). Two (4.5%) and 3 (1.6%) patients died in the POAF and non-POAF groups, respectively (*P*=0.249).

Age, IABP, EF, RDW, MPV, urea and total drainage variables, all of which were significant in the univariate regression analysis, were included in the multivariate regression analysis. MPV, age and total drainage were the independent risk factors associated with POAF (OR=1.080, OR=1.371, OR=1.001; *P*=0.001, *P*<0.001, *P*=0.024, respectively) (Table 3).

Table 3: Independent risk factors associated with POAF

	OR	95% CI		<i>P</i> -value
		Lower	Upper	
Age	1.080	1.031	1.131	0.001
MPV	1.371	1.151	1.634	<0.001
Total drainage	1.001	1.000	1.003	0.024

OR: Odds ratio

Discussion

In this retrospective cohort study, we investigated whether there was a correlation between the mean platelet volume (MPV) and the development of postoperative atrial fibrillation. Our results indicate that MPV was significantly higher in the patients who developed POAF compared to those who did not.

AF is one of the most common complications following CABG. There are numerous studies in the literature reporting risk factors such as age, ejection fraction (EF) and left atrial diameter for the development of POAF [2]. In our study, while the mean left atrial diameter was similar between the groups, the mean age was significantly higher, and EF was significantly lower in patients who developed POAF. In the multivariate analysis we performed to determine the independent risk factors associated with POAF, age was statistically significant. In the present study, the mean age of the patients was 64.17 years. Similarly, in a study by Aberer et al. [15] examining the effect of MPV on acute ischemic stroke, the mean age of the patients was 62.64 years.

The number of studies investigating the relationship between biomedical parameters and the development of POAF are limited [3,14,16]. After understanding the predictive and prognostic value of MPV for many medical conditions, the number of studies on this issue has increased [14-21]. The predictive effect of MPV was examined in many diseases, including cardiovascular disorders. However, there is no consensus in the literature about the correlation between MPV and cardiovascular diseases. For example, some studies found an association between a high MPV level and the risk of stroke [22-24], while others could not [15]. MPV levels were high in patients with arrhythmogenic right ventricular cardiomyopathy or dysplasia (ARVC/D) [17]. In another study by Degerli et al. [18], MPV was a reliable indicator of acute mesenteric ischemia. In a study conducted by Chung et al. [24], MPV was higher in patients with congestive heart failure compared to the control group. Gawlita et al. [20] reported high MPV levels in persons with coronary artery disease. On the other hand, it was reported that MPV levels may be associated with postoperative adverse events [25]. In a study by Icli et al. [26], MPV was significantly higher in patients with mitral valve prolapsus.

MPV is considered to reflect the reactivity or activation of platelets as a simple marker [27,28]. Platelet size has been shown as predictive and prognostic biomarkers of cardiovascular events [29,30]. Larger platelets are metabolically more reactive than smaller ones. Reactive platelets contain a greater amount of prothrombotic materials and are associated with a greater aggregability in response to adenosine diphosphate (ADP), increased thromboxane A2 and B2 and glycoprotein IIb-IIIa receptor expression and decreased in-vitro aggregation with prostacyclin [31].

MPV was investigated by many studies as a cardiovascular risk factor. However, the number of studies investigating the association between MPV and atrial fibrillation are limited [2,32]. The results of this study indicate that MPV was statistically significantly higher in the group with postoperative AF compared to the group without. In addition, multivariate analyses revealed that MPV was an independent risk

factor for developing POAF. In this regard, our study is one of the limited studies on this issue in the literature.

Limitations

The main limitation of our study was its single-centered, retrospective design. The number of our patients was higher compared to similar studies. The number of parameters studied among the patients with and without postoperative atrial fibrillation constitutes the strong aspect of this study.

Conclusion

The results of our study indicate that MPV can be used as a predictor for the development of POAF after on-pump CABG. MPV is a quite simple parameter, which can be readily obtained in routine complete blood count. We think that this parameter can be a reliable marker of atrial fibrillation, which is one of the common arrhythmias encountered following coronary artery bypass grafting. However, our results should be supported by prospective and multicenter studies.

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