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Original Article

Predictive value of platelet to lymphocyte ratio and mean platelet volume in atrial fibrillation after isolated coronary artery bypass graft operation

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Abstract

Aim: The relationship between inflammation and the development of atrial fibrillation and the relationship between platelet to lymphocyte ratio and mean platelet volume in relation to inflammation were investigated in patients with atrial fibrillation after isolated coronary artery bypass graft operation.

Material And Methods: Clinical and laboratory data of 132 patients, who did not have preoperative atrial fibrillation and underwent isolated coronary artery bypass graft operation using cardiopulmonary pump, were analyzed retrospectively. Patients were divided into two groups as patients with developed atrial fibrillation and those without atrial fibrillation. Concomitant diseases, preoperative drug use, echocardiographic and angiographic findings, preoperative, intraoperative and postoperative laboratory parameters were obtained from medical records and compared statistically.

Results: Of the 132 patients, 68 with atrial fibrillation (mean age: 68.3+/-10.7 years, 50 males and 18 females) and 64 patients without atrial fibrillation (mean age: 64.5+/-9.8 years, 55 males and 9 females) were identified, and difference in the mean age was statistically significant (p=0.016). Postoperative platelet to lymphocyte ratio and mean platelet volume values (280.3+/-112.3; 9.9+/-1.7) were also significantly higher in those with atrial fibrillation group than preoperative values (129.2+/-49.3; 9.6+/-1.6, p<0.0001, p<0.0009).

Conclusıon: According to our study higher values of postoperative platelet to lymphocyte ratio and mean platelet volume are correlated with development of atrial fibrillation after coronary artery bypass graft operation.

Keywords: Atrial fibrillation; coronary artery bypass graft operation; inflammation; mean platelet volume; platelet to lymphocyte ratio.

INTRODUCTION

Atrial fibrillation (AF) and/or flutter (AFL) are the most common complications of cardiac surgery. The rate of atrial fibrillation after coronary artery bypass grafting varies between 25-40%. Patients with postoperative atrial fibrillation have significantly higher prolonged hospital stay and the incidence of various complications such as cardiovascular events, renal failure, infections and cerebral infarctions(1).

Studies have shown that the development of atrial fibrillation is related to inflammation.Various inflammatory markers such as C reactive protein, tumor necrosis factor alpha, interleukin-2, interleukin-6 and interleukin-8 are associated with atrial fibrillation (2).

In recent years studies have shown that platelet/lymphocyte ratio (PLR) can be used as an inflammatory marker (3). Similarly, mean platelet volume (MPV) is a marker of platelet activation and function and has been shown to increase in response to inflammation and thrombosis (4).

In this study, the relationship between inflammation and the development of atrial fibrillation and the relationship between PLR and MPV in relation to inflammation were investigated in patients with atrial fibrillation after isolated coronary artery bypass graft operation (CABG).

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MATERIAL and METHODS

Study Population

This study is a single center and retrospectively designed and approved by the local ethics committee, consisting 132 randomised patients who underwent isolated coronary artery bypass graft operation between February 2012–December 2016. The exclusion criteria were; concomitant valvular surgery, the presence of a permanent pacemaker, preoperative atrial fibrillation, malignancy and infection, use of amiodaron and digitals, re-do surgery, LVEF<30%, emergent surgery and off-pump surgery.

Concomitant diseases, preoperative drug use, echocardiographic and angiographic findings, preoperative, intraoperative and postoperative parameters were obtained from medical records. Total white blood cells, neutrophils, lymphocytes and platelets were measured by using automated blood counter, Cell-Dyn 3700, Abbott, Germany, in fifteen minutes after handling of blood. Platelet to lymphocyte ratio was computed as the ratio of platelets (1000/uL) to lymphocytes (1000/Ul) obtained from the blood samples, preoperatively and postoperatively first three days.

Surgical Technique

All operations were performed by using cardiopulmonary bypass pump after median sternotomy.

Postoperative Atrial Fibrillation

Patients were followed up with 5-lead monitors and standard D-II leads in intensive care until hemodynamically stable. Patient received the service was followed up to 6-8 times for daily rhythm and blood pressure. When atrial fibrillation or other arrhythmias occurred in patients during this periods, arrhythmia was documented by drawing a 12-lead ECG. The day on which the atrial fibrillation started on the electrocardiograph was accepted as the day and the hour of onset of atrial fibrillation.

Statistical Analysis

Statistical analysis of the study was done using the SPSS 19.0 package program. Descriptive measure of all variables was calculated. Categorical variables were presented with frequency and percentage ratios and numerical variables with mean ± SD tables. The normality analysis of continuous numerical variables was performed by the Kolmogorov-Smirnov test. Nonparametric tests were used for group comparisons. The Mann-Whitney U test was used in the case of two independent groups, and the Wilcoxon Sign Sequence test was used to compare two dependent groups (repeated measures). Monte Carlo corrected chi-square analysis was used to determine the relationship between categorical variables. Results of comparison and correlation analysis are shown on the tables. Significant results were visualized using related graphics. At the end of the study, p <0.05 was considered statistically significant by taking the type-I error value as 5%.

RESULTS

Of the 132 patients, 68 with atrial fibrillation (mean age: 68.37+/-10.73, 50 males and 18 females) and 64 without atrial fibrillation (mean age: 64.58±9.83, 55 males and 9 females) were identified, and difference in the mean age was statistically significant (p=0.016). The other baseline characteristics like concomitant diseases and gender did not show a statistically significant difference between the groups (Table 1).

Risk factors for atrial fibrillation like age, HT, DM, COPD, Congestive Heart Failure and beta blocker use were evaluated and there was a statistically difference in age group (AF+ group 68.37+/-10.73, AF- group 64.58+/- 9.83, p=0.016), there were no statistically difference in other groups.

Similarly, there was no statistically significant difference in preoperative medications between the groups (Table 2).

There was no statistically significant difference in ejection fraction, cardiopulmonary bypass time, intensive care unit length of stay and length of postoperative hospital stay between the two groups (Table 3).

But there was statistically significant difference in the extubation times (Table 3) and mortality rates.

The mortality rate was 4.4% (n=3) in cases with atrial fibrillation and 1.5% (n=1) in cases without atrial fibrillation.

Table 1. Demographic and Comorbidity Characteristics of Patients

		AF + (n=68)	AF - (n=64)	
		Average±SS	p	
Age	year	68.37±10.73	64.58±9.83	0.016*
		N (%)	N (%)	
Gender	Male	50 (73.5)	55 (85.9)	0.077
	Female	18 (26.5)	9 (14.1)	
HT	+	49 (72.1)	43 (67.2)	0.544
	-	19 (27.9)	21 (32.8)	
DM	+	32 (47.1)	33 (51.6)	0.606
	-	36 (52.9)	31 (48.4)	
COPD	+	16 (23.5)	19 (29.7)	0.425
	-	52 (76.5)	45 (70.3)	
HL	+	21 (30.9)	24 (37.5)	0.423
	-	47 (69.1)	40 (62.5)	

AF: Atrial Fibrillation, COPD: Chronic Obstructive Pulmonary Disease, DM: Diabetes Mellitus, HL: Hyperlipidemia. HT: Hypertension

Table 2. Treatment Characteristics of Patients

Treatment		AF +	AF -	
		N (%)	N (%)	p
ACE Inhibitor	+	31 (45.6)	33 (51.6)	0.494
	-	37 (54.4)	31 (48.4)	
β-blocker	+	19 (27.9)	19 (29.7)	0.825
	-	49 (72.1)	45 (70.3)	
ARB	+	4 (5.9)	1 (1.6)	0.196
	-	64 (94.1)	63 (98.4)	
CaChannelblocker	+	13 (19.1)	12 (18.8)	0.957
	-	55 (80.9)	52 (81.2)	
Clopidogrel	+	9 (13.2)	5 (7.8)	0.314
	-	59 (86.8)	59 (92.2)	
Statin	+	20 (29.4)	21 (32.8)	0.673
	-	48 (70.6)	43 (67.2)	
Nitrate	+	7 (10.3)	4 (6.2)	0.403
	-	61 (89.7)	60 (93.8)	
ASA	+	24 (35.3)	19 (29.7)	0.494
	-	44 (64.7)	45 (70.3)	
Furosemide	+	2 (2.9)	0 (0)	0.168
	-	66 (97.1)	64 (100)	

AF: Atrial Fibrillation, ACE: Angiotensin Converting Enzyme, ARB: Angiotensin Receptor Blocker, ASA: Acetyl Salicylic Acid

Table 3. Clinical Characteristics of Patients According to Groups

AF state		AF +	AF -	
		Average ± SS		P
EF	%	49.19±8.68	50.84±8.03	0.247
Cross		50.71±13.33	51.98±12.65	0.456
Pomp		81.51±23.16	81.28±24.05	0.839
ICU stay time		4.25±2.05	4.11±1.47	0.967
Postop service stay		10.72±4.92	9.4±3.57	0.089

EF: Ejection Fraction , ICU: Intensive Care Unit

Postoperative platelet to lymphocyte ratio and mean platelet volume values (280.3+/-112.3; 9.9+/-1.7) were also significantly higher in those with atrial fibrillation group than preoperative values (129.2+/-49.3; 9.6+/-1.6, p<0.0001, p<0.0009) (Figure 1-2). There was no difference between the preoperative and postoperative platelet to lymphocyte ratio and mean platelet volume in the group without atrial fibrillation (p>0.05) (Table 4).

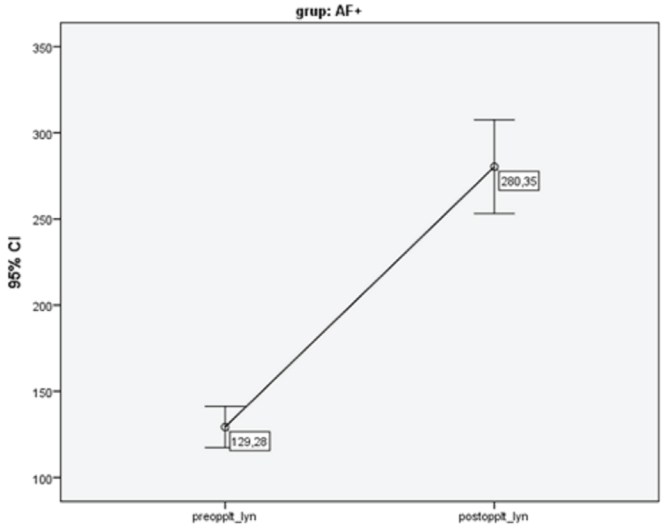

Figure 1. Preoperative and postoperative plt/lym ratio in AF+ group AF: Atrial Fibrillation, Lym: Lymphocyte, Plt: Platelet

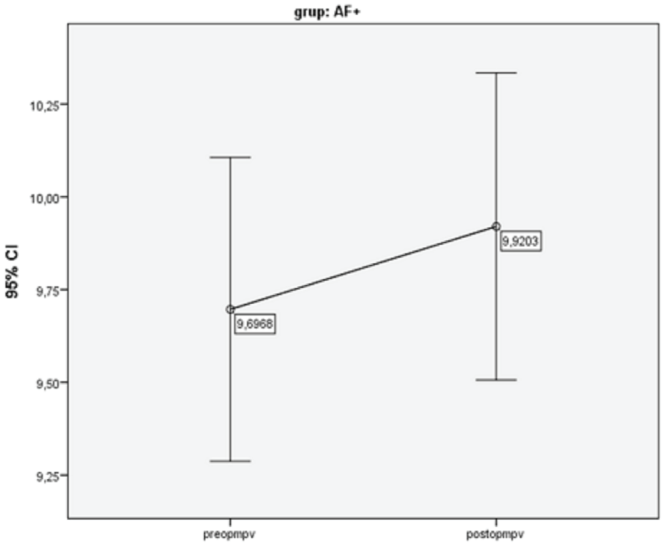

Figure 2. Preoperative and postoperative MPV values in AF+ Group AF: Atrial Fibrillation, MPV: Mean Platelet Volume

Table 4. Pre and Postop PLR and MPV Measurements in AF Detail

AF	Preop	Postop	
	Average ± SS		P
Plt/lym (PLR)	129.27±49.39	280.35±112,35	<0.001*
MPV	9.69±1.69	9.92±1.70	0.009*
AF-			
Plt/lyn (PLR)	123.34±49.24	131.00±46.35	0.062
MPV	10.20±1.07	10.25±1.28	0.227

AF: Atrial Fibrillation, Lym: Lymphocyte MPV: Mean Platelet Volume PLR: Platelet to Lymphocyte Ratio, Plt: Platelet

DISCUSSION

The most common arrhythmia after coronary artery bypass graft surgery is atrial fibrillation (5). Atrial fibrillation can cause complications such as heart failure, thromboebolism, renal insufficiency, morbidity, mortality and prolonged hospitalization which increases the cost per patient (6). A variety of risk factors have been identified for atrial fibrillation; Advanced age, male sex, diabetes mellitus, hypertension, valve disease, myocardial infarction, heart failure, obesity, increased inflammatory marker concentrations and prolonged PR interval (7). Changes in the atria associated with age such as dilatation, loss of nodal fibers, muscle atrophy, increased fibrous tissue and fat tissue in the sinus node, local interstitial amyloid deposits at the atrium, and advanced age have been recognized as risk factors for the development of atrial fibrillation after CABG (8). In our study it was seen that average age was higher in the patients with atrial fibrillation than without atrial fibrillation.

A study by Benjamin and colleagues investigating the effect of atrial fibrillation on mortality showed a significantly higher mortality rate in patients with atrial fibrillation (9). The mortality rate of patients with atrial fibrillation in our study is 4.4%, which is 1.5% in non-developing patients, which supports the negative effect of atrial fibrillation on mortality.

The study by Çiçekçioğlu and his colleagues showed that patients with atrial fibrillation after coronary artery bypass surgery had a longer intubation time (10). In our current study, the duration of intubation was significantly longer in patients with postoperative atrial fibrillation than in those without atrial fibrillation.

In a study that Frustaci and colleagues conducted, it was first suggested that there is a relationship between atrial fibrillation and inflammation (11). There is also an association between newborn atrial fibrillation and inflammatory response after CABG operation.Studies of the correlation between neutrophil / lymphocyte ratio and development of atrial fibrillation by Gibson et al. have shown that the rate of atrial fibrillation development is higher in patients with a high neutrophil / lymphocyte ratio that is used as an inflammatory marker (12). Inflammation may play a role in the pathogenesis of atrial fibrillation and may be explained by the high CRP levels, which are indicative of systemic inflammation, and the incidence of atrial fibrillation.Cardiac surgery triggers inflammatory response resulting in activation of the complex system and release of the inflammatory mediator (13). Ronnier and his colleagues concluded an average follow-up of 7.8 years on 5806 people that the patients with high CRP values were 1.3 times more likely to develop atrial fibrillation (14).

The relationship between the development of atrial fibrillation and inflammation in patients undergoing CABG operation was first demonstrated by Lo et al. (15). Serum levels of CRP, IL-6, IL-8, TNF alpha and platelet activation were the most frequent on the second and third days after CABG, and 70% of the atrial fibrillation developed in this period (16).

In recent years, the platelet / lymphocyte ratio has been used as a new marker to predict possible cardiovascular morbidities (17).

Inflammatory mediators such as Interleukin 1 and Interleukin 6 induce thrombocytosis by stimulating megakaryocytic proliferation. Therefore, the number of platelets can be regarded as a sign of inflammation. In addition, lymphopenia is a sign of physiological stress and generalized impairment (18). Recent studies suggest that platelet / lymphocyte ratio is a marker of micro-inflammation (19). It has been shown that increased platelet / lymphocyte ratio is associated with coronary slow flow (20). There are studies showing effects of platelet / lymphocyte ratio on hospital stay and mortality in myocardial infarction with ST elevation or not (21,22). In a study of 2121 patients Gary and colleagues have performed, it is suggested that patients with high platelet/ lymphocyte rates are at risk for critical limb ischemia (23). In another study include 388 patients, a high platelet / lymphocyte ratio was reported as an important risk factor for predicting severe atherosclerosis (24). Beside the evidences supporting the use of platelet to lymphocyte ratio in cardiovascular diseases ,Seropian et al described that higher platelet to lymphocyte ratio is associated with worse outcome after heart transplantation (25).

A limited number of studies are available in the literature on the association between platelet / lymphocyte ratio and atrial fibrillation after CABG surgery. In a study conducted by Gungor and colleagues, the relationship between preoperative platelet / lymphocyte ratio and postoperative atrial fibrillation was investigated and it was reported that patients with higher pre-operative platelet / lymphocyte levels had a higher risk of developing atrial fibrillation (26). In our study, the preoperative and postoperative platelet/ lymphocyte rates of patients with atrial fibrillation after isolated coronary artery bypass grafting were compared with the control group and this ratio was found to be significantly higher in the atrial fibrillation group ($p<0.001$). Thus, in the light of the relationship between atrial fibrillation and inflammation and the platelet / lymphocyte ratio as an indicator of inflammation, the platelet / lymphocyte ratio can be used as an inexpensive and easily applicable marker, unlike other inflammatory markers predictive of atrial fibrillation after isolated CABG.

Mean platelet volume (MPV) indicates platelet dimensions and is an indication of platelet function activation. A study comparing the MPV levels of patients with normal sinus rhythm in patients with non-valvular atrial fibrillation rhythm performed by Tekin et al., MPV values of atrial fibrillation patients was found to be higher (27). Similar findings were found in the study performed by Xu et al. that MPV levels are associated with atrial fibrillation and thromboembolic events (28). Early detection of stroke patients with high-risk atrial fibrillation is important. High MPV values have been shown to be significantly

associated with stroke formation (29). In a similar study, there was a correlation between stroke and high MPV levels after CABG (30).

Studies have shown that there is a correlation between levels of inflammation and increased MPV levels in some chronic inflammatory diseases and is associated with other inflammatory markers such as CRP and erythrocyte sedimentation rate (31). Numerous studies have been conducted on the pathogenesis of thrombosis and inflammation in relation to numerous platelet markers, including MPV (32). The results of these studies have found significant results between inflammation and MPV levels. As already mentioned studies have shown that there is a link between inflammation and atrial fibrillation. In our study, MPV levels as an indicator of inflammation were found to be statistically significant in cases with atrial fibrillation after isolated CABGO than without atrial fibrillation (p=0.009). MPV is an inexpensive and effective laboratory test that is easy to implement and results in a short time and in our current study has yielded meaningful predictions for newly developed atrial fibrillation after isolated CABG operations.

As a result PLR and MPV values are cheap and statistically reliable laboratory tests that are easy to apply and gives fast results in predicting atrial fibrillation after isolated CABGO. There is a need for extensive studies involving large patient populations to support this view and we believe that when used routinely, is a valuable parameters in terms of prophylactic treatment of AF that can develop after CABG.

Competing interests: The authors declare that they have no competing interest.
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REFERENCES

1. Takeshi O, Yuichi K. Management of postoperative atrial fibrillation. J Anesth 2012;26:429-37.
2. Yutao G, Gregory YH, Stavros A. Inflammation in atrial fibrillation. J Am Coll Cardiol 2012;60:2263-70.
3. Akboga MK, Canpolat U, Yayla C, et al. Association of platelet to lymphocyte ratio with inflammation and severity of coronary atherosclerosis in patients with stable coronary artery disease. Angiology 2016;67:89-95.
4. Xue-Feng X, Feng-Lin J, Mei-Jun O, et al. The association between mean platelet volume and chronic atrial fibrillation and the presence of thrombotic events. Biomed Rep 2015;3:388-94.
5. Gungor H, Eryılmaz U, Akgullu C, et al. Preoperative poor coronary collateral circultion can predict the development of atrial fibrillation after coronary artery bypass graft surgery. Coronary Artery Disease 2013;24:572-6.
6. Gungor H, Ayik MF, Kirilmaz B, et al. Serum resistin level: as a predictor of atrial fibrillation after coronary artery bypass graft surgery.Coronary Artery Disease 2011;22:484-90.
7. Rienstra M, McManus DD, Benjamin EJ. Novel risk factors for atrial fibrillation.Circulation 2012;125:941-6.
8. Zangrillo A, Landoni G, Sparicio D et al. Predictors of atrial fibrillation after off-pump coronary artery bypass graft surgery.J Cardiothorac Vasc Anesth 2004;18:704-8.
9. Benjamin E.J, Wolf P.A, D'Agostino R.B et al. Impact of atrial fibrillation on the risk of death:the Framingham heart study. Circulation 1998;98:946-52.
10. Çiçekçioğlu F, Kervan Ü, Parlar Aİ, et al. Koroner bypass cerrahisinden sonra gelişen atriyal fibrilasyon tedavisinde amiodaronun etkinliği. Türk Kalp Damar Cerrahi Derg 2009;17:077-82.
11. Frustaci A, Chimenti C, Bellocci F, et al. Histological substrate of atrial biopsies in patients with lone atrial fibrillation. Circulation 1997;96:1180-4.
12. Gibson PH, Cuthbertson BH, Croal BL et al. Usefulness of neutrophil/lymphocyte ratio as predictor of new-onset atrial fibrillation after coronary artery bypass grafting. Am J Cardiol 2010;105:186-91.
13. Abdelhadi RH, Gurm HS, Wagoner DR, et al. Relation of an exaggerated rise in white blood cells after coronary bypass or cardiac valve surgery to development of atrial fibrillation postoperatively. Am J Cardiol 2004;93:1176-8.
14. Aviles RJ, Martin DO, Apperson HC, et al. Inflammation as a risk factor for atrial fibrillation. Circulation 2003;108:3006-10.
15. Lo B, Fijnheer R, Nierich AP, et al. C-reactive protein is a risk indicator for atrial fibrillation after myocardial revascularization. Ann Thorac Surg 2005;79:1530-5.
16. Paparella D, Yau T M, Young E. Cardiopulmaonary bypass induced inflammation:pathophysiology and treatment.An update. Eur J Cardiothorac Surg 2002;21:232-44.
17. Sari I, Sunbul M, Mammadov C, 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.
18. Varim C, Varim P, Acar BA, et al. Usefulness of the platelet-to-lymphocyte ratio in predicting the severity of carotid artery stenosis in patients undergoing carotid angiography. Kao J of Med Scis 2016;32:86-90.
19. Altintas Ö, Tasal A, Niftaliyev E, et al. Association of platelet-to-lymphocyte ratio with silent brain infarcts in patients with paroxysmal atrial fibrillation. A J Progress in Neurosurgery, Neurology and Neurosciences 2016;38:753-8.
20. Akboga MK, Canpolat U, Balci KG et al. Increased platelet to lymphocyte ratio is related to slow coronary flow. Angiology 2016;67:21-6.
21. Ozcan Cetin EH, Cetin MS, Aras D, et al. Platelet to lymphocyte ratio as a prognostic marker of in-hospital and long-term major adverse cardiovascular events in ST-segment elevation myocardial infarction. Angiology 2016;67:336-45.
22. Azab B, Shah N, Akerman M, et al. Value of platelet/lymphocyte ratio as a predictor of all-cause mortality after non-ST-elevation myocardial infarction. J Thromb Thrombolysis 2012;34:326-34.
23. Gary T, Picher M, Belaj K et al. Platelet-to-lymphocyte ratio:a novel marker for critical limb ischemia in peripheral arterial occlusive disease patients. PLos One 2013;8:e67688.
24. Yüksel M, Yıldız A, Oylumlu M, et al. The association between platelet/lymphocyte ratio and coronary artery disease severity. Anatol J Cardiol 2015;15:640-7.
25. Ignacio MS, Francisco JR, Rodolfo P, et al. Neutrophil-to-lymphocyte ratio and platelet-tolymphocyte ratio as predictors of survival after heart transplantation. ESC Heart Failure 2018;5:149-56.

26. Gungor H, Babu AS, Zencir C, et al. Association of preoperative platelet-to-lymphocyte ratio with atrial fibrillation after coronary artery bypass graft surgery. Med Princ Pract 2017;26:164-8.
27. Tekin G, Tekin YK, Sivri N, et al. Mean platelet volume in patients with nonvalvular atrial fibrillation. Blood Coagul Fibrinolysis 2013;24:537-9.
28. Xu X.F, Jiang F.L, Ou M.J, Zhang Z.H. The association between mean platelet volume and chronic atrialfibrillation and the presence of thrombotic events. Biomed Rep 2015;3:388-94.
29. Turfan M, Erdogan E, Ertas G et al. Usefulness of mean platelet volume for predicting stroke risk in atrial fibrillation patients. Blood Coagul Fibrinolysis 2013;24:55-8.
30. Aygün F, Özülkü M, Günday M. Preoperatif MPV,KABGO sonrası serebrovasküler olay için prediktör olabilir mi? Cumhuriyet Tıp Derg 2014;36:540-7.
31. Gunluoglu G, Yazar EE, Veske NS, et al. Mean platelet volume as an inflammtion marker in active pulmonary tuberculosis. Multidiscip Respir Med 2014;28:11.
32. Gasparyan AY, Ayvazyan L, Mikhailidis DP, et al. Mean platelet volume:a link between thrombosis and inflammation? Curr Pharm Des 2011;17:47-58.