The association between mean platelet volume and spontaneous echocardiographic contrast or left atrial thrombus in patients with mitral stenosis

Kevser Gülcihan Balcı, Orhan Maden, Mustafa Mücahit Balcı, Fatih Şen, Sefa Ünal, Serdar Kuyumcu, Meryem Kara, Hatice Selçuk, Mehmet Timur Selcuk, Ahmet Temizhan

Department of Cardiology, Türkiye Yüksek İhtisas Research and Education Hospital; Ankara-*Turkey*

Abstract

Objective: Although the role of platelet activation has been debated in patients with mitral stenosis (MS) and spontaneous echocardiographic contrast (SEC), data on differences in mean platelet volume (MPV) according to the presence of SEC/left atrial thrombus and the rhythm status are lacking. In this study, MPV was analyzed in patients with MS according to the presence of SEC/left atrial thrombus.

Methods: Between January 2005 and March 2014, 188 symptomatic patients having moderate or severe MS (mean age, 45.0±11.7 years; female, 81.4%) with favorable valve morphology for percutaneous mitral balloon valvuloplasty (PMBV) and underwent a transesophageal echocardiogram to assess the eligibility for PMBV were retrospectively enrolled in the study. The relation between MPV and echocardiographic thromboembolic risk factors were evaluated. Independent predictors of SEC/left atrial thrombus presence were determined by multiple logistic regression analyses.

Results: Among all patients, MPV did not differ according to the rhythm status or the presence of SEC/left atrial thrombus ($p>0.05$). Also, MPV did not vary according to the gender and presence of prior stroke in both atrial fibrillation and sinus rhythm groups ($p>0.05$). In correlation analysis, MPV did not show any significant correlation with the echocardiographic thrombus predictors ($p>0.05$).

Conclusion: Using MPV with echocardiographic and clinical thrombus risk determinants for predicting individual thromboembolism risk in MS is debatable according to our results. *(Anatol J Cardiol 2016; 16: 863-7)*

Keywords: mitral stenosis, thrombus, mean platelet volume

Introduction

Mitral stenosis (MS), which is commonly a sequela of rheumatic fever, causes significant morbidity and mortality in disadvantaged populations. The most serious complication of rheumatic MS is systemic thromboembolism. Blood stasis and low bloodstream velocity, which occurs in the left atrium (LA), play a major role in thromboembolism (1). Despite treatment with an oral anticoagulant, patients may experience thromboembolic events attributed to a hypercoagulable state in the course of the disease (2). In MS, increased platelet activity has therefore been addressed in thromboembolic events (3). Platelets have an important role in the coagulation system, through the activation of intrinsic pathway factors, and also in the hemostatic system. The restricted mitral valve orifice area leads to a shear stress (4–6) that results in platelet activation in both the peripheral and left atrial blood (7, 8) of patients with MS. Mean platelet volume (MPV), which reflects platelet size, is useful in predicting platelet function and activity. Large platelets are more active than small ones, show greater aggregation, and release more thromboxane A2 and β-thromboglobulin, which in turn result in high prothrombotic potential. In the literature, few studies have investigated the relation between MPV and the presence of spontaneous echocardiographic contrast (SEC) in MS (9–11). Akpek et al. (10) found a high MPV among SEC+ patients; similar to this finding, the presence of SEC was regarded as an independent predictor of a high MPV in another study (11). However, previous studies did not evaluate the differences in MPV according to SEC and thrombus presence. Furthermore, MPV values were not investigated according to rhythm status, and data on the relation between rhythm status and MPV are lacking. Therefore, we aimed to examine the relationship of both echocardiographic and clinical thromboembolic risk factors with MPV among patients with MS and determine the differences in MPV

Address for correspondence: Dr. Kevser G. Balcı, Türkiye Yüksek Ihtisas Eğitim ve Araştırma Hastanesi Kardiyoloji Bölümü, 06810 Ankara-*Türkiye*
Phone: +90 530 328 38 69 Fax: +90 312 306 10 00 E-mail: kevs84@gmail.com

Accepted Date: 16.12.2015 **Available Online Date:** 25.04.2016

DOI:10.14744/AnatolJCardiol.2015.6675

according to the left atrial thrombus or SEC. We also aimed to determine whether rhythm status influences MPV according to the presence of SEC and LA thrombus.

Methods

Between January 2005 and March 2014, 188 symptomatic patients having moderate or severe MS (mean age, 45.0±11.7 years; female, 81.4%) with favorable valve morphology for percutaneous mitral balloon valvuloplasty (PMBV) and underwent a transesophageal echocardiogram (TEE) for the assessment of the eligibility for PMBV were retrospectively enrolled in the study. The patients with MS were divided into three groups—without LA thrombus or SEC, complicated with SEC, and complicated with LA thrombus—and analyzed according to the rhythm status. Exclusion criteria were as follows: chronic inflammatory disease, hematological disorders, history of malignancy, connective tissue disease, thyroid disease, immune thrombocytopenic purpura, renal or hepatic disorders, and other hematological diseases. All patients underwent a comprehensive transthoracic echocardiogram, and TEE was performed on all MS patients to determine the eligibility for PMBV. Electronic medical records were used to obtain participants' medical histories. The study protocol was approved by the local institutional Ethics Committee.

Echocardiographic assessment

The transthoracic studies were done by a standard technique using a commercially available device (Vivid 7 Ultrasound System; GE, Horten, Norway). LA diameter was measured in the parasternal long-axis view by M-mode echocardiography at the end-systole. Mitral valve area was measured with pressure half-time method. Continuous-wave Doppler was used to determine transmitral gradient. Valve morphology was assessed by using Wilkins' (12) echo scoring system (leaflet mobility, thickness, calcification, and subvalvular lesions). Doppler was used to calculate the peak pressure gradient of the tricuspid regurgitation jet velocity according to Bernoulli equation, and systolic pulmonary artery pressure was calculated by adding the right atrial pressure (10 mm Hg) to this value. Under local pharyngeal anesthesia (1% lidocaine spray) and intravenous diazepam; TEE assessment was obtained using the same system with a 5-MHz transducer. An experienced cardiologist determined the presence of a thrombus (either attached to the left atrial wall or within the left atrial appendix) and SEC. A thrombus was defined as intracavitary echo-dense mass attaching to an atrial wall that visualized by at least two different planes with different degrees of mobility and echogenicity compared to adjacent structures. Multiple images were taken to detect thrombus in the LA appendix by placing the probe at the level of the mid-esophagus and then cineloops were obtained. The severity of left atrial spontaneous echo contrast was graded from 0 to 4+ according to previously reported criteria (13): 0 (none), absence of echogenicity; 1+ (mild), minimal echogenicity located in the left atrial appendage or sparsely distributed in the main cavity of the left atrium detectable only transiently during the cardiac cycle and not visible at low gain settings; 2+ (mild to moderate), more dense swirling pattern than 1+ having similar distribution pattern and detectable without increased gain settings; 3+ (moderate), dense swirling pattern distributed throughout both the left atrium and the left atrial appendage and may fluctuate in intensity but was detectable throughout the cardiac cycle; and 4+ (severe), more intense echo density and very slow swirling pattern than 3+.

Blood sampling

After 8 h of fasting, blood samples were drawn from the antecubital vein by careful venipuncture without stasis at 8:00 to 10:00 AM in both groups on admission and collected in dipotassium ethylenediaminetetraacetic acid (EDTA) tubes. An automated blood cell counter (Siemens ADVIA 2120i Hematology System; Siemens Healthcare, Malvern, PA, United States) was used to measure hematologic indices. MPV was recorded within an hour after sampling to prevent EDTA-induced platelet swelling.

Statistical analyses

Data analysis was performed by using SPSS for Windows, version IBM11.5 (SPSS Inc., Chicago, IL, United States). Kolmogorov–Smirnov test was used to determine the distributions of continuous variables; Levene test was used to evaluate the homogeneity of variances. Continuous variables were displayed as the mean±standard deviation (SD) and median (25^{th}–75^{th}) percentiles, where applicable.

Whether the differences in medians between two independent groups were statistically significant or not was compared by Mann–Whitney U test, while the mean differences among more than two independent groups were analyzed by one-way ANOVA; otherwise, Kruskal–Wallis test was used for comparisons of the medians. When the p value from one-way ANOVA or Kruskal–Wallis test is statistically significant, posthoc Tukey HSD or Conover's multiple comparison test was used to compare intergroup differences. Pearson's chi-square test was used to analyze categorical data.

Multiple logistic regression analyzes were used to determine the best predictors that affect the presence of SEC/left atrial thrombus. Odds ratios and 95% confidence intervals for each independent variable were also calculated.

A p value <0.05 was considered statistically significant.

Results

The baseline clinical and echocardiographic characteristics of the study population are shown in Table 1. Of the 188 patients, 105 (55.8%) patients were in sinus rhythm (SR). LA thrombus was detected in 31 (16.4%) patients, and all of them were located in the LA appendix. SEC was found in 142 (75.5%) patients. Among thrombus-detected patients, 10 (32.2%) were in SR; and in the SEC-detected group, 82 (57.7%) were in SR. When patients were divided according to the rhythm status, among patients

Table 1. Clinical and echocardiographic features of the study population

Variables	SEC+ (n=142)	Thrombus+ (n=31)	SEC/Thrombus– (n=15)	*P*
Age, years	44.5±11.4	52.5±9.6	34.5±9.6	0.003
Female	119 (83.8%)	21 (67.7%)	13 (86.7%)	0.099
MVG, mm Hg	11 (9–13)	10 (7–13)	11 (9–15)	0.059
MVA, cm^2	1.2 (1.0–1.3)	1.2 (0.9–1.2)	1.1 (1.1–1.3)	0.268
sPAP, mm Hg	47 (40–55)	45 (38–46)	45 (38–50)	0.813
LA, cm	4.6 (4.2–5.0)	4.9 (4.4–5.3)	4.4 (4.0–4.6)	0.002
MR	1 (1–1)	1 (1–1.2)	1 (1–1)	0.005
Valvular score	8 (7–8)	9 (8–10)	8 (6–8)	<0.001
MPV, fL	9.0 (8.3–9.8)	9.1 (8.3–9.6)	9.0 (8.6–9.6)	0.516
Warfarin+	73 (51.4%)	21 (67.7%)	2 (13.3%)	0.003
Aspirin+	46 (32.4%)	11 (35.5%)	5 (33.3%)	0.946

LA - left atrium; MPV - mean platelet volume; MR - mitral regurgitation; MVA - mitral valve area; MVG - mean valvular gradient; SEC - spontaneous echocardiographic contrast; sPAP - systolic pulmonary artery pressure
Age: Thrombus+ and SEC/thrombus–, *P*<0.001; SEC+ and thrombus+, *P*=0.037; SEC/Thrombus– and SEC+, *P*=0.001. LA: Thrombus+ and SEC/thrombus–, *P*=0.012; SEC+ and thrombus+, *P*=0.229; SEC/Thrombus– and SEC+, *P*=0.003. MR: Thrombus+ and SEC/thrombus–, *P*=0.002; SEC+ and thrombus+, *P*=0.010; SEC/Thrombus– and SEC+, *P*=0.566. Valvular score: Thrombus+ and SEC/thrombus–, *P*=0.020; SEC+ and thrombus+, *P*=0.008; SEC/Thrombus– and SEC+, *P*=0.493. Warfarin: Thrombus+ and SEC/thrombus–, *P*=0.001; SEC+ and thrombus+, *P*=0.099; SEC/Thrombus– and SEC+, *P*=0.005

with SR, 9.5% had LA thrombus, and 78% of them had SEC. In the SR group, thrombus+ patients were older than those without thrombus (p=0.007) and the percentage of male patients was significantly higher in the thrombus+ group than in the thrombus– group (p=0.008). Also, the LA size was significantly greater in the thrombus+ group than in the thrombus– group (p=0.035). In the AF group; the degree of MR was significantly higher in the SEC-positive group than in the thrombus-positive group (p=0.008). According to the rhythm status, aspirin and warfarin usage were significantly higher in the AF group (aspirin; SR 24.8% vs. AF 42.2%, p=0.011, and warfarin; SR 13.3% vs. AF 98.8% p<0.001). All patients in the AF group had either SEC or LA thrombus.

Among all patients, there was no significant difference according to the SEC/LA thrombus presence regarding MPV (Table 1). In the SR group, there were no significant differences between the groups with respect to MPV [SEC/thrombus–, 8.8 (8.6– 9.6) fL; SEC+, 9.1 (8.3–9.8) fL; thrombus+, 8.6 (8.4–9.5) fL; p=0.263]; and similarly in the AF group, MPV did not vary between the groups [SEC/thrombus–, 9.6 (8.6–9.6) fL; SEC+, 8.9 (8.2–9.7) fL; thrombus+, 9.3 (8.6–9.6) fL; p=0.282] (Fig. 1). Among all patients, MPV did not vary according to the grade of SEC between the groups (Table 2). When patients were divided into SR and AF groups, MPV did not show any significant difference according to the grade of SEC (SR: grade 1, 9.0 (8.7–9.9) fL; grade 2, 9.2 (8.3–9.7) fL; and grade 3–4, 8.9 (8.3–9.9) fL; p=0.774 and AF: grade 1, 9.9 (8.7–9.9) fL; grade 2, 8.5 (8.0–9.3) fL; and grade 3–4, 9.2 (8.3–9.9) fL; p=0.142). Also, MPV did not vary according to the gender and presence of prior stroke in both AF and sinus rhythm groups (Table 3).

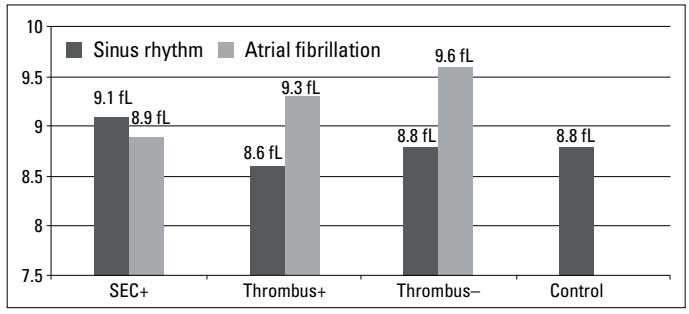

Figure 1. Comparison of mean platelet volumes between the study groups according to the rhythm status

Table 2. Comparison of the variables according to the grade of SEC

Variables	Grade 1 (n=27)	Grade 2 (n=71)	Grade 3–4 (n=44)	*P*
Age, years	42.1±9.7	42.3±10.5	49.7±12.2	0.713
Female	25 (92.6%)	60 (84.7%)	34 (76.7%)	0.189
Warfarin+	9 (33.3%)	32 (45.0%)	33 (75.0%)	<0.001
Aspirin+	6 (22.2%)	25 (35.2)	15 (34%)	0.236
MPV, fL	9.1 (8.7–9.9)	8.9 (8.2–9.7)	9.1 (8.3–10.0)	0.540
LA, cm	4.3 (4.0–4.8)	4.5 (4.2–4.8)	5.0 (4.6–5.6)	<0.001
MR	1 (1–2)	1 (1–1)	1 (1–1)	0.068
MVA, cm^2	1.2 (1.1–1.3)	1.2 (1.1–1.3)	1.1 (1.0–1.3)	0.640
MVG, mm Hg	11 (10–13)	11 (9–13)	11 (8–13)	0.595
sPAP, mm Hg	45 (38–52)	48 (40–55)	48 (40–60)	0.325

LA - left atrium; MPV - mean platelet volume; MR - mitral regurgitation; MVA - mitral valve area; MVG - mean valvular gradient; sPAP - systolic pulmonary artery pressure.
LA: Grade 1 and Grade 2, *P*=0.51; Grade 1 and Grade 3–4, *P*<0.001; Grade 2 and Grade 3–4, *P*<0.001. Warfarin: Grade 1 and Grade 2, *P*=0.011; Grade 1 and Grade 3–4, *P*<0.001; Grade 2 and Grade 3–4, *P*=0.002

Table 3. Comparison of MPV values according to the gender, rhythm, and prior history of CVA

Variables	n	MPV	*P*
Sinus rhythm+			
Male	17	8.7 (8.0–9.2)	0.146
Female	88	8.9 (8.5–9.7)	
Sinus rhythm–			
Male	18	9.4 (8.4–10.0)	0.314
Female	65	8.9 (8.3–9.5)	
CVA			
+	178	9.0 (8.3–9.6)	0.542
–	10	8.8 (9.2–10.1)	

CVA - cerebrovascular accident; MPV - mean platelet volume

In correlation analysis, there were no significant correlations between MPV and echocardiographic thrombus predictors (p>0.05) (Table 4).

Multiple logistic regression analysis of factors related to SEC/LA thrombus presence showed that only age was related

Table 4. Correlation analyses between MPV and the other variables

	Sinus rhythm		Atrial fibrillation	
	Correlation coefficient	*P*†	Correlation coefficient	*P*†
Age	-0.021	0.805	0.156	0.159
LA	0.099	0.248	0.132	0.236
MR	0.112	0.188	0.182	0.099
MVA	-0.064	0.455	0.014	0.903
MVG	0.084	0.352	-0.114	0.303
sPAP	0.102	0.256	0.047	0.676
Hemoglobin	-0.056	0.532	0.212	0.055
WBC count	0.025	0.781	0.171	0.122
Platelet count	-0.365	<0.001	-0.213	0.053

LA - left atrium; MPV - mean platelet volume; MR - mitral regurgitation; MVA - mitral valve area; MVG - mean valvular gradient; sPAP - systolic pulmonary artery pressure; WBC - white blood cell

Table 5. Multiple logistic regression analysis of factors related to SEC/LA thrombus presence according to the rhythm status

Variables	Odds ratio	95% CI	*P*
Sinus rhythm			
Age	1.070	1.006–1.138	0.031
LA diameter	2.497	0.603–10.351	0.207
Atrial fibrillation			
Age	1.216	0.955–1.549	0.112
LA diameter	3.002	0.639–14.093	0.164
sPAP	1.099	0.907–1.331	0.336

CI - Confidence interval; LA - left atrium; sPAP - systolic pulmonary artery pressure

to the presence of SEC/LA thrombus in the sinus rhythm group (p=0.031) (Table 5).

Discussion

In this study, we did not observe any significant differences in MPV according to SEC and thrombus presence and rhythm status between the study groups. In addition, no significant correlation was observed between MPV and echocardiographic thrombus predictors.

Despite proper anticoagulative or antiplatelet treatment, a risk for thromboembolism among patients with MS is known (14). Therefore, many efforts have been made to detect the risk factors for thromboembolism in MS. The presence of AF, increasing age, LA dilatation, dense SEC, and severe MS have been proposed to determine individual risk for LA clot formation and consequent thromboembolism in mitral stenosis (15–17). In addition to echocardiographic and clinical determinants, the role of hematologic indices that are inexpensive and derived from routine blood counts have been debated in several reports (9, 10, 18). Together with coagulation factors, platelets play an important role in thromboembolism, and increased platelet activity has been reported in MS patients (14, 19). Platelet size, reflected as MPV, was found to be elevated in SEC-complicated patients with MS; elevated MPV values were therefore concluded to indicate a high risk of systemic thromboembolism (3). Platelet activation caused by a restricted mitral valve area and shear stress was reported in previous studies (4, 5).

In the present study, we did not observe any significant differences in MPV between the SEC-positive, thrombus-positive, and thrombus-negative groups. When patients were divided according to SEC grade, MPV did not vary between the groups, and no significant correlations were found between MPV and echocardiographic thrombus predictors. Furthermore, in both SR and AF groups, MPV did not vary according to rhythm status. Similarly, Peverill et al. (9) reported no significant differences in MPV between AF and sinus rhythm groups and among SEC+ patients according to SEC grade. Other than hematologic indices, echocardiographic variables showed significant differences according to rhythm status in the study of Peverill et al. (9). Only hematocrit and red cell concentration showed a significant correlation with SEC grade in the sinus rhythm group. Similarly, Alyan et al. (20) reported that MPV did not differ according to the rhythm status in patients with MS. However, the authors found a high MPV among SEC+ patients. Similar to this, Akpek et al. (10) and Ileri et al. (11) reported a relation between a high MPV and left atrial SEC in MS. These varying degrees of results may be explained by the lack of a standardized MPV measure (21). Therefore, a careful interpretation of MPV results is needed (22). Different properties of the selected study populations may also affect the results. Instead of hematologic indices, echocardiographic measures in conjunction with clinical thromboembolic risk factors may enable precise determination during assessment of thromboembolism risk.

Study limitations

The retrospective design and modest size of this study are its possible limitations. Another is the method of hematologic index measurement. Platelet swelling may occur in tripotassium EDTA-based anticoagulated blood samples. In addition, other markers of platelet activation, such as soluble p-selectin or soluble CD40L, were not evaluated. Finally, the absence of left atrial functions may be another limitation because these parameters were not studied routinely in our study population.

Conclusions

Our study showed that among patients with MS, MPV is not associated with the presence of SEC/LA thrombus. The results indicated that using MPV with echocardiographic and clinical thrombus risk determinants to predict individual thromboembolism risk in MS is debatable.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept – O. M., K.G. B., M.M. B.; Design – K.G.B., M.M.B., O. M., T.S., H.S.; Supervision – O.M., T.S., H.S.; Resource – S.Ü., S. K., K.G.B., F.Ş., M.K.; Data collection &/or processing – F. Ş., K.G.B., M.K., S.K.; Analysis &/or interpretation – A.T., M.M.B., S.K., O.M., F.Ş., K.G.B., M.K.; Literature search – M.M.B., O.M., F.Ş., K.G.B., M.K., S.K.; Writing – K. G. B., M.M. B.; Critical review – O. M., T.S., H.S., A. T.

References

1. Black IW, Hopkins AP, Lee LC, Walsh WF. Left atrial spontaneous echo contrast: a clinical and echocardiographic analysis. J Am Coll Cardiol 1991; 18: 398-404. Crossref
2. Yavuz B, Ertuğrul DT, Yalçın AA, Küçükazman M, Ata N, Dal K. Increased mean platelet volume in rheumatic mitral stenosis: a possible factor for thromboembolic events. J Cardiol 2009; 53: 204-7.
3. Varol E, Özaydın M, Türker Y, Alaca S. Mean platelet volume, an indicator of platelet activation, is increased in patients with mitral stenosis and sinus rhythm. Scand J Clin Lab Invest 2009; 69: 708-12.
4. Smith RL, Blick EF, Coalson J, Stein PD. Thrombus production by turbulence. J Appl Physiol 1972; 32: 261-4.
5. Stein PD, Sabbah HN. Measured turbulence and its effect on thrombus formation. Circ Res 1974; 35: 608-14. Crossref
6. Yu SK, Latour JG, Marchandise B, Bois M. Shear stress-induced changes in platelet reactivity. Thromb Haemost 1978; 40: 551-600.
7. Chen MC, Wu CJ, Yip HK, Chang HW, Fang CY, Yu TH, et al. Left atrial platelet activity with rheumatic mitral stenosis: correlation study of severity and platelet P-selectin expression by flow cytometry. Chest 2003; 124: 1663-9. Crossref
8. Kunishima S, Hattori M, Kobayashi S, Hattori H, Iwama Y, Imai Y, et al. Activation and destruction platelets in patients with rheumatic heart disease. Eur Heart J 1994; 15: 335-8.
9. Peverill RE, Graham R, Gelman J, Yates LA, Harper RW, Smolich JJ. Haematologic determinants of left atrial spontaneous echo contrast in mitral stenosis. Int J Cardiol 2001; 81: 235-42. Crossref
10. Akpek M, Kaya MG, Yarlioglues M, Doğdu O, Ardıç I, Şahin O, et al. Relationship between platelet indices and spontaneous echo contrast in patients with mitral stenosis. Eur J Echocardiogr 2011; 12: 865-70. Crossref
11. İleri M, Kanat S, Gürsoy HT, Şahin D, Bayır PT, Şahin G, et al. Increased mean platelet volume in rheumatic mitral stenosis: assessment of clinical and echocardiographic determinants. Kardiol Pol 2015; 73: 46-53. Crossref
12. Wilkins GT, Weyman AE, Abascal WM, Block PC, Palacios IF. Percutaneous balloon dilatation of the mitral valve: an analysis of echocardiographic variables related to outcome and the mechanism of dilatation. Br Heart J 1988; 60: 299-308. Crossref
13. Fatkin D, Kelly RP, Feneley MP. Relations between left atrial appendage blood flow velocity, spontaneous echocardiographic contrast and thromboembolic risk in vivo. J Am Coll Cardiol 1994; 23: 961-9.
14. Zotz RJ, Pinnau U, Genth S, Erbel R, Meyer J. Left atrial thrombi despite anticoagulant and antiplatelet therapy. Clin Cardiol 1994; 17: 375-82. Crossref
15. Manjunath CN, Srinivasa KH, Panneerselvam A, Prabhavathi B, Ravindranath KS, Rangan K, et al. Incidence and predictors of left atrial thrombus in patients with rheumatic mitral stenosis and sinus rhythm: a transesophageal echocardiographic study. Echocardiography 2011; 28: 457-60. Crossref
16. Kronzon I, Tunick PA, Glassman E, Slater J, Schwinger M, Freedberg RS. Transesophageal echocardiography to detect atrial clots in candidates for percutaneous transseptal mitral balloon valvuloplasty. J Am Coll Cardiol 1990; 16: 1320-2. Crossref
17. Goswami KC, Yadav R, Rao MB, Bahl VK, Talwar KK, Manchanda SC. Clinical and echocardiographic predictors of left atrial clot and spontaneous echo contrast in patients with severe rheumatic mitral stenosis: a prospective study in 200 patients by transesophageal echocardiography. Int J Cardiol 2000; 73: 273-9. Crossref
18. Öztürk D, Ertürk M, Çelik O, Özyılmaz S, Aktürk F, Çakmak HA, et al. The role of the neutrophil/lymphocyte ratio in patients with rheumatic mitral stenosis as an indicator of spontaneous echocardıographic contrast. Kardiol Pol 2014; 72: 969-76. Crossref
19. Hasan-Ali H, Mosad E. Changes in platelet, coagulation, and fibrinolytic activities in mitral stenosis after percutaneous mitral valvotomy: role of hemodynamic changes and systemic inflammation. Clin Appl Thromb Hemost 2015; 21: 339-47. Crossref
20. Alyan O, Metin F, Kaçmaz F, Özdemir O, Maden O, Topaloğlu S, et al. High levels of high sensitivity C-reactive protein predict the progression of chronic rheumatic mitral stenosis. J Thromb Thrombolysis 2009; 28: 63-9. Crossref
21. Lancé MD, Sloep M, Henskens YM, Marcus MA. Mean platelet volume as a diagnostic marker for cardiovascular disease: drawbacks of preanalytical conditions and measuring techniques. Clin Appl Thromb Hemost 2012; 18: 561-8. Crossref
22. Lancé MD. Mean platelet size: looking at the chicken or the egg? Anatol J Cardiol 2015; 15: 113-4. Crossref