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Case report

Relationship between spontaneous echo contrast and hematological markers in patients with rheumatic mitral stenosis

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ABSTRACT

Introduction: Systemic thromboembolism is a serious morbidity and mortality cause for patients with rheumatic mitral stenosis (RMS). Previously conducted researches showed that spontaneous echo contrast (SEC) found in the left atrium can constitute a risk factor for thrombus formation. The aim of this study is to evaluate the role of echocardiographic and hematologic parameters in anticipating the presence of SEC in the left atrium of patients with moderate–severe RMS.

Methods: This retrospective study includes all patients who were diagnosed with moderate–severe RMS and underwent a transesophageal echocardiography between 2011 and 2014. They were then divided in two groups depending on SEC presence; a SEC negative group and a SEC positive group.

Results: There were 33 patients (32%) in the SEC negative group and 71 patients (68%) in the SEC positive group. The mean platelet volume was found to be significantly higher in the SEC positive group (10.0 ± 1.3 vs. 11.6 ± 1.4 , $p < 0.001$). To identify the factors affecting the presence of SEC, a multivariate analysis of the hematologic parameters was conducted and the mean platelet volume was found to be an independent predictor (odds ratio 1.913, 95% confidence interval 1.300–2.814; $p = 0.001$). In the receiver operating characteristics curve analysis, a mean platelet volume > 11.8 fl had a 55% sensitivity and 92% specificity in predicting SEC in patients with mitral stenosis.

Conclusion: Mean platelet volume constitutes an independent risk factor for the presence of left atrial SEC in patients with moderate–severe mitral valve stenosis.

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Introduction

Especially in developing countries, rheumatic mitral stenosis (RMS) is still a major health concern.¹ Patients with RMS show an elevated risk for systemic thromboembolism, which becomes a primary mortality and morbidity cause.² Among the suggested mechanisms leading to the disease are autoimmunity, inflammation and increased thrombotic activity.^{3–5}

Spontaneous echo contrast (SEC) is the presence of smoke – like echoes with a characteristic swirling motion of blood found during echocardiography.⁶ Previously conducted researches showed that presence of SEC in the left atrium can constitute a risk factor for thrombus formation.⁷ In patients with RMS the risk of thrombosis and left atrial SEC development is eventually higher.⁸ The aim of this study is

to investigate the relationship between the presence of SEC and related hematologic parameters in patients with moderate–severe RMS.

Methods

In this retrospective study all moderate–severe RMS patients, who had a percutaneous mitral balloon valvuloplasty between 2011 and 2014 in our clinic were included (mitral valve area < 1.5 cm²). Their respective electrocardiograms were inspected and the rhythm defined.

The exclusion criteria for the present study were left atrial thrombus formation, significant mitral regurgitation (grade > 1), other moderate or severe valve disease, history of malignancy, history of inflammatory disease, current therapy with corticosteroids, connective tissue disease, thyroid disease, other hematological disease and acute infectious disease. A medical history was recorded from patient anamnesis form.

Transesophageal echocardiography (TEE) and transthoracic echocardiography (TTE) records were also investigated (EPIQ 7 Ultrasound System, Philips, Heide, Netherlands). All the echocardiographic findings were carefully evaluated by two separate cardiologists. All measurements were taken according to the recommendations of the American Society of Echocardiography.⁹ The mean value of 3 measurements was

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taken from patients with sinus rhythm and the mean value of 7 measurements from patients with atrial fibrillation. Routine echocardiographic measurements were also recorded. The planimetric measurements of the mitral valve area were also conducted. The mitral valve was assessed by TEE. The Wilkins score was determined by rating the severity of leaflet mobility, leaflet thickening, leaflet calcification and subvalvular thickening with a score of 0–4 and then adding the results together.¹⁰ Left atrial SEC presence and degree was assessed by TEE according to the criteria laid down by Fatkin et al.¹¹ The patients were then divided into two groups; a SEC positive group and a SEC negative one.

On the TEE day, the patients had blood drawn from the antecubital vein and underwent routine biochemistry and complete blood count (CBC) tests, after a 12 hour fast. CBC including white blood cell (WBC), neutrophil and lymphocyte counts, mean platelet volume (MPV, normal range: 7.4–10.4 fl) were done using an automatized CBC count device (Abott Cell Dyn, Illinois USA). The C-reactive protein (CRP) levels (normal range: 0–5 mg/L) were analyzed with a Beckman Coulter Inc. (Image 800, California, USA).

Statistical analysis

Data were analyzed with the SPSS software version 21.0 for Windows (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean + SD, and categorical variables are expressed as percent. The χ^2 test and Fisher's exact test were used to compare categorical variables. The Shapiro–Wilk test was used to assess the distribution of continuous variables. Student's t-test was used for variables with normal distribution and the values were presented as mean \pm SD. Continuous variables without normal distribution were analyzed using Mann–Whitney U test. Receiver operating characteristic (ROC) curve analysis was performed to identify optimal cutoff values for MPV. The effects of different variables on SEC were calculated in univariate analysis for each. The variables for which the unadjusted P-value was 0.10 in logistic regression analysis were identified as potential risk markers and included in the full model. The odds ratios (OR) and 95% confidence intervals (CI) were calculated. A two-tailed p-value of <0.05 was considered statistically significant.

Results

104 patients were included in this study of which 80 (77%) were female. 33 of them (32%) were in the SEC negative group (mean age 43.6 + 14.5) and 71 (68%) in the SEC positive group (mean age 47.0 + 11.3). Mean age, diabetes mellitus, hypertension, hyperlipidemia presence and aspirin or warfarin usage was similar among the groups. Atrial fibrillation (AF) was detected in 11 (33%) of the SEC negative group patients and 28 (40%) in the SEC positive one ($p = 0.634$). Also, in 31 of the 39 patients who had AF (79%) and in 48 of the 65 patients who did not have AF (73%), SEC presence was detected ($p = 0.632$). The groups' baseline characteristics are shown in Table 1.

The Wilkins score (9.6 ± 2.8 vs. 7.0 ± 2.2 , $p < 0.001$) and the left atrial diameter (46.3 ± 2.7 mm vs. 44.7 ± 2.2 mm, $p = 0.010$) were found to be significantly higher in the SEC positive group. There was no significant difference among groups with regard to the mitral valve area ($1.0 + 0.2$ vs. $1.1 + 0.2$, $p = 0.423$). TTE and TEE findings are shown in Table 2.

There was no significant difference among the groups with respect to some hematologic parameters like WBC count, platelet count, red cell distribution width and CRP (Table 3). However, MPV (11.6 ± 1.4 vs 10.0 ± 1.3 , $p < 0.001$) was found to be significantly higher in the SEC positive group (Fig. 1). A univariate logistic regression analysis was performed in order to determine the factors leading to SEC presence and MPV (OR = 1.972, 95% CI: 1.411–2.758; $p < 0.001$), Wilkins score (OR = 1.409, 95% CI: 1.172–1.693, $p < 0.001$) and left atrial diameter (OR = 1.265, 95% CI: 1.051–1.522; $p = 0.013$) were

Table 1
Demographic characteristics of the groups according to the SEC presence.

Variable	SEC negative (n = 33)	SEC positive (n = 71)	P value
Age, years	43.6 \pm 14.5	47.0 \pm 11.3	0.286
Female, n (%)	28 (84%)	52 (73%)	0.062
DM, n (%)	3 (11.5%)	13 (16.7%)	0.755
Hypertension, n (%)	11 (42.3%)	37 (47.4%)	0.650
TC, mg/dl	189.0 \pm 42.9	184.3 \pm 36.5	0.417
LDL, mg/dl	125.5 \pm 34.5	115.0 \pm 34.6	0.106
HDL, mg/dl	45.0 \pm 9.3	42.2 \pm 8.3	0.119
Trygliceride, mg/dl	98.9 \pm 43.3	122.2 \pm 59.1	0.072
AF, n (%)	11 (33%)	28 (40%)	0.634
Aspirin, n (%)	17 (51%)	38 (53%)	0.248
Warfarin, n (%)	12 (38%)	29 (41%)	0.228
Beta blocker, n (%)	16 (48%)	36 (51%)	0.728

(Data are expressed as mean \pm standard deviation for normally distributed data and percentage for categorical variables).

(AF: atrial fibrillation, DM: diabetes mellitus, HDL: high density lipoprotein, LDL: low density lipoprotein, TC: total cholesterol).

shown to be risk factors. Also, a multivariate logistic regression analysis was performed in order to determine the factors leading to SEC presence and MPV value was found to be an independent predictor (OR = 1.913, 95% CI: 1.300–2.814, $p = 0.001$) (Table 4). In the ROC curve analysis, a MPV > 11.8 fl had a 55% sensitivity and 92% specificity in predicting SEC in patients with mitral stenosis (area under the curve 0.780, $p < 0.001$) (Fig. 2).

Discussion

Patients with moderate–severe RMS were included in this study and 23% of them were found to have SEC presence in their left atrium. Univariate and multivariate analysis showed that Wilkins echo score, MPV and left atrium diameter were risk factors related to left atrial SEC presence. In addition to that, MPV > 11.8 fl was found to have a 55% sensitivity and 92% specificity in predicting SEC presence in patients with mitral stenosis.

SEC is a dynamic smoke-like echo with a characteristic swirling motion of blood detected by echocardiography.¹² In RMS patients there is an increase in general inflammatory and prothrombotic state and therefore the risk of stasis in the left atrium that will eventually lead to left atrial SEC or thrombus, is significantly higher than the normal population.^{13,14} In previous studies SEC was found to have a frequency of 21–67% in RMS patients and systemic thromboembolism was reported as an independent predictor of SEC presence.^{6,15,16} Some

Table 2
Echocardiographic characteristics of the groups according to the SEC presence (variables with normal distribution were expressed as mean \pm SD).

Variable	SEC negative (n = 33)	SEC positive (n = 71)	P value
LVEF, %	62.1 \pm 4.2	62.0 \pm 4.4	0.682
LA diameter, mm	44.7 \pm 2.2	46.3 \pm 2.7	0.010
LAVI, ml/m ²	32.1 \pm 8.2	33.4 \pm 7.2	0.378
LVEDD, mm	44.0 \pm 4.0	46.1 \pm 5.0	0.128
LVESD, mm	28.3 \pm 4.4	30.1 \pm 5.0	0.090
MVA, cm ²	1.1 \pm 0.2	1.0 \pm 0.2	0.423
Peak gradient, mm Hg	24.5 \pm 9.2	21.9 \pm 7.7	0.679
Mean gradient, mm Hg	14.5 \pm 6.2	13.1 \pm 6.2	0.317
WS	7.0 \pm 2.2	9.6 \pm 2.8	<0.001
Valve mobility	1.7 \pm 0.6	2.4 \pm 0.7	<0.001
Subvalvular	1.6 \pm 0.6	2.4 \pm 0.9	<0.001
Valve thickness	1.9 \pm 0.7	2.5 \pm 0.8	0.004
Calcification	1.7 \pm 0.9	2.3 \pm 0.9	0.010
sPAP, mm Hg	43.9 \pm 13.4	40.7 \pm 8.7	0.365

(LA: left atrium, LAVI: left atrial volume index, LVEF: left ventricular ejection fraction, LVEDD: left ventricular end diastolic diameter, LVESD: left ventricular end systolic diameter, MVA: mitral valve area, SEC: spontaneous echo contrast, WS: Wilkins score).

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