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Relationship Between Left Atrial Spontaneous Echo Contrast and the MAPH Score in Patients With Severe Rheumatic Mitral Stenosis

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Abstract

Objective

Left atrial spontaneous echo contrast (SEC) is an echocardiographic finding in which blood—normally non-contrasting—appears as a swirling, smoke-like echogenic pattern. The presence of SEC in the left atrium is associated with an increased risk of thromboembolism, and this risk increases with higher SEC grades. The MAPH score has recently been defined as a simple index of whole-blood viscosity. In this study, we aimed to evaluate the relationship between the MAPH score and the presence and grade of SEC in patients with severe rheumatic mitral stenosis in sinus rhythm.

Methods

This single-center, retrospective study included 96 patients in sinus rhythm who underwent percutaneous mitral balloon valvuloplasty for severe mitral stenosis. SEC presence was assessed by transesophageal echocardiography in all patients. Patients were grouped according to SEC presence (SEC+/SEC−) and SEC grade. The MAPH score (age, MPV, hematocrit, total protein) was calculated for each patient.

Results

Among 96 patients, 75 (78.1%) were SEC(+) and 21 (21.9%) were SEC(−). The MAPH score was higher in the SEC(+) group (Mann–Whitney U = 389.5; $p < 0.001$). No significant association was found between SEC severity and the MAPH score (Kruskal–Wallis $p = 0.487$). In ROC curve analysis, MAPH showed a significant ability to discriminate between SEC presence and absence (AUC = 0.753; 95% CI 0.639–0.866; $p < 0.001$). According to the Youden index, the optimal cut-off was MAPH ≥ 3, with a sensitivity of 56.0% and a specificity of 90.5%. In multivariable analysis, the MAPH score, left atrial diameter, and mitral valve area were identified as independent predictors of SEC presence. The AUC of the model built using continuous component values was 0.766 (95% CI 0.655–0.877; $p < 0.001$).

Conclusion

The MAPH score showed significant predictive performance for SEC presence but limited ability to discriminate SEC grade.

INTRODUCTION

Left atrial spontaneous echo contrast (SEC) is the smoke-like, swirling echogenicity of blood that is usually non-echogenic on echocardiography and is most commonly observed in patients with mitral stenosis (MS) and atrial fibrillation (AF). SEC is most easily visualized with transesophageal

echocardiography (TEE) and is frequently detected within the left atrium(LA) and left atrial appendage(LAA). [1, 2] Clinically, SEC increases the risk of left atrial thrombus formation and thromboembolic events, and greater SEC severity further increases embolic risk [3–5]. Therefore, improving our understanding of the mechanisms underlying SEC and identifying predictors of its presence may help reduce adverse events in patients with MS.

Studies have found that SEC in the LA is influenced not only by low blood flow velocity but also by factors such as blood viscosity, erythrocyte aggregation, hematocrit, and plasma protein levels. The correlation between SEC, hematocrit, and fibrinogen levels indicates that the phenomenon is attributable to erythrocyte aggregation and elevated blood viscosity [5–7]. The MAPH score (mean platelet volume–age–total protein–hematocrit), developed in recent years, is a straightforward index reflecting whole-blood viscosity and correlates with coronary slow flow, thrombus burden in acute coronary syndromes, and the severity of ischemic stroke [8–10]. In our study, we aimed to evaluate the relationship between the MAPH score and the presence of left atrial SEC in patients with MS.

MATERIALS AND METHODS

Study Population

This is a retrospective, single-center study of patients with severe mitral stenosis who underwent percutaneous mitral balloon valvuloplasty at our institution between October 2022 and November 2025. The study analyzed data from 156 participants. Before percutaneous mitral balloon valvuloplasty, all patients underwent TEE and transthoracic echocardiography (TTE) to rule out left atrial thrombus. The SEC in the LA was assessed using TEE. The study group was divided into two subgroups: those with SEC detected in the left atrium (SEC(+)) and those without SEC (SEC(-)).

The study excluded patients with hematologic disorders, active malignancies, chronic inflammatory or autoimmune diseases, clinical or laboratory evidence of acute infection or sepsis, advanced renal or hepatic insufficiency, significant thyroid dysfunction, a history of blood transfusion in the previous three months, severe anemia (Hb < 10 g/dL), diagnosed polycythemia, or pregnancy. Additionally, patients with prior valve surgery or mitral balloon valvuloplasty, intrinsic cardiomyopathy, severe aortic stenosis or regurgitation, severe mitral regurgitation, or serious extravalvular disease were excluded.

After applying these exclusion criteria, data from the remaining 96 patients were examined. Detailed records were maintained for all patients, including age, gender, diabetes, hypertension, smoking status, cerebrovascular disease, coronary artery disease, peripheral vascular disease, comorbidity history, and laboratory findings at admission. The ethics committee of our hospital approved the trial.

Laboratory measurements

Blood samples were drawn from the antecubital vein into EDTA tubes for a complete blood count performed on a Sysmex K-1000 (Kobe, Japan) and for biochemical analysis performed on a Roche Diagnostics Cobas 8000 c502 (Indianapolis, IN, USA). Samples were analyzed immediately to prevent platelet swelling. The MAPH score was calculated as a combination of mean platelet volume (MPV), age, total protein, and hematocrit, as defined in the literature. Cutoff points were determined using the Youden index from ROC curves that evaluated the effects of MPV, age, total protein, and hematocrit on the target outcome. 1 point was given for each parameter above the cut-off value, and an MAPH score ranging from 0 to 4 was created [6]. Glucose, urea, creatinine, liver function tests, and lipid profile were obtained using standard methods.

Echocardiography

All echocardiographic examinations were performed after at least 10–15 minutes of rest, using two-dimensional, M-mode, color Doppler, and spectral Doppler echocardiography (Vivid S70, GE Healthcare, USA). TTE and TEE were performed in the same session whenever possible. All measurements were performed in accordance with the American Society of Echocardiography guidelines [7]. The left ventricular ejection fraction(LVEF) was measured from the apical four-chamber view using the modified Simpson method. The mitral valve area (MVA) was measured directly from the parasternal short-axis view using planimetry. The mean mitral gradient was calculated as the average of the pressure differences obtained from transmitral flow measured by continuous-wave Doppler. Continuous-wave Doppler measured the maximum velocity of the tricuspid regurgitation jet, and the resulting trans-tricuspid gradient was added to right atrial pressure to estimate systolic pulmonary artery pressure (SPAP). The diameters of the left atrium, left ventricule and right heart chambers were measured according to standard guidelines. For TEE, after local anesthesia was applied to the pharyngeal region with topical 10% lidocaine spray, the multiplane TEE probe was advanced into the esophagus approximately 25–35 cm, and the LA and left atrial appendage (LAA) were evaluated in detail at the level where the best image was obtained. A pattern of slowly swirling, smoke-like echo densities was considered SEC. The SEC severity was graded from 0 to 4 + according to the Fatkin et al criteria [7]. All transthoracic and transesophageal echocardiographic assessments were performed by a cardiologist experienced in echocardiography.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics (Mac version, v21.0). Data showing normal distribution were presented as mean ± standard deviation, while data not showing normal distribution were presented as median (interquartile range, IQR). Categorical variables were expressed as numbers (percentages).

Comparisons between SEC groups were performed using the independent-samples t-test or Mann–Whitney U test for continuous variables, depending on data distribution. The Chi-square test or Fisher's

exact test was applied for categorical variables, particularly when expected cell counts were low. MAPH scores among SEC severity groups within SEC(+) patients were compared using the Kruskal–Wallis test.

The ability of the MAPH score and other parameters to distinguish SEC presence was assessed using receiver operating characteristic (ROC) analysis. Area under the curve (AUC) values were reported with 95% confidence intervals. Optimal cut-off values were identified using the Youden index, and sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated at the relevant thresholds.

Logistic regression was performed to identify independent determinants of SEC status. First, univariate analyses were performed; then, clinically significant variables and/or variables found to be significant or borderline significant in the univariate analyses were included in the same multivariate model. The results were reported with an odds ratio (OR) and a 95% confidence interval. Additionally, ROC analysis was performed on the predicted probabilities from a logistic model trained on continuous values of MPV, age, total protein, and hematocrit to evaluate the potential impact of dividing into two groups based on the cutoff, and the AUC was reported. p values lower than 0.05 were considered to demonstrate statistical significance.

RESULTS

Of the 96 patients, 21 (21.9%) were SEC(-) and 75 (78.1%) were SEC(+). In the SEC(+) group, the distribution was as follows: Grade 1: 42 (56.0%); Grade 2: 17 (22.7%); Grade 3: 9 (12.0%); and Grade 4: 7 (9.3%). Due to the small number of samples in subgroup analyses, Grade 3 and 4 cases were grouped as 'high-grade SEC (Grade 3–4)' (n = 16, 21.3%). Age was significantly higher in the SEC(+) group. The prevalence of gender, hypertension, and other comorbidities did not differ significantly between the groups (Table 1).

Table 1
Demographic characteristics of the study populations.

Variables	SEC (−) (n = 21)	SEC (+) (n = 75)	p value
Age (years), mean ± SD	45.29 ± 7.48	51.77 ± 11.29	0.003
Female sex, n (%)	14 (66.7)	59 (78.7)	0.255
Hypertension, n (%)	4 (19.0)	24 (32.0)	0.248
Diabetes mellitus, n (%)	2 (9.5)	12 (16.0)	0.728
CAD, n (%)	1 (4.8)	3 (4.0)	1.000
CVD (stroke/TIA), n (%)	1 (4.8)	8 (10.7)	0.679
Current smoker, n (%)	6 (28.6)	8 (10.7)	0.073
CAD, coronary artery disease; CVD, cerebrovascular disease			

Table 2 displays the differences in laboratory results between the two groups. In the comparison between SEC (−) and SEC (+) groups, creatinine, albumin, AST, and platelet count differed significantly ($p < 0.05$). The SEC (+) group had higher creatinine, AST, and platelet count, whereas albumin levels were lower. All other laboratory parameters were similar between groups ($p > 0.05$).

Table 2
Laboratory findings of the study populations.

Variables	SEC (−) (n = 21)	SEC (+) (n = 75)	p value
Creatinine (mg/dl)	0.73 ± 0.19	0.83 ± 0.21	0.044
Sodium (mmol/L)	138.67 ± 3.40	139.13 ± 2.79	0.521
Potassium (mmol/L)	4.10 ± 0.33	4.25 ± 0.38	0.119
Albumin (g/L)	42.73 ± 2.74	40.03 ± 5.17	0.023
AST (U/L)	16.81 ± 5.49	28.33 ± 20.61	< 0.001
ALT(U/L)	17.00 ± 8.68	24.73 ± 18.21	0.063
Glucose (mg/dl)	89.38 ± 12.83	105.96 ± 38.42	0.055
LDL cholesterol (mg/dl)	105.05 ± 40.28	118.40 ± 32.38	0.124
Triglycerides (mg/dl)	100.50 ± 54.88	125.14 ± 56.65	0.087
HDL cholesterol (mg/dl)	46.90 ± 8.19	44.14 ± 13.75	0.394
Hemoglobin (g/dL)	13.25 ± 1.25	12.65 ± 1.52	0.099
Platelet count (×10³/μL)	215.00 ± 44.88	254.13 ± 71.78	0.004
Neutrophils (×10³/μL)	5.06 ± 2.01	5.11 ± 1.80	0.926
Lymphocytes (×10³/μL)	2.20 ± 0.72	2.24 ± 1.35	0.901
MPV (fL)	11.33 ± 1.42	11.21 ± 1.02	0.660
Total protein (g/L)	66.28 ± 6.06	68.74 ± 6.05	0.103
Hematocrit (%)	37.93 ± 4.20	38.59 ± 3.71	0.514

AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDL, low-density lipoprotein; HDL, high-density lipoprotein; MPV, mean platelet volume; SEC, spontaneous echo contrast.

In the echocardiographic evaluation, the left atrial diameter, Left ventricular end-diastolic diameter, and systolic pulmonary artery pressure were higher in the SEC(+) group compared to the SEC(−) group, although the mitral valve area was diminished. The mean transmitral gradient, ejection fraction, and left ventricular end-systolic diameter showed no significant difference across the groups. (Table 3)

Table 3
Echocardiographic Characteristics of the Patients

Variables	SEC (−) (n = 21)	SEC (+) (n = 75)	p value
LA (cm)	4.16 ± 0.23	4.71 ± 0.70	< 0.001
LVEF (%)	63.9 ± 5.8	62 ± 4.6	0.339
LVEDD (cm)	4.40 ± 0.23	4.61 ± 0.56	0.011
LVESD (cm)	2.73 ± 0.29	2.87 ± 0.51	0.222
sPAP (mmHg)	33.52 ± 9.78	43.32 ± 18.32	0.002
Mean TMG (mmHg)	11.81 ± 2.18	11.80 ± 3.43	0.988
MVA (cm^2)	1.22 ± 0.14	1.12 ± 0.17	0.014

SEC, spontaneous echo contrast; LA, left atrial diameter; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; sPAP, systolic pulmonary artery pressure; TMG, transmitral gradient ; MVA, mitral valve area.

The MAPH score was significantly higher in the SEC(+) group compared to the SEC(−) group (Mann–Whitney U = 389.5, Z = − 3.676, $p < 0.001$, $r \approx 0.38$). No significant differences in MAPH score were observed across SEC severity grades among SEC(+) patients. (Kruskal–Wallis H = 1.440, df = 2, p = 0.487). ROC analysis showed that MAPH discriminated the presence of SEC (AUC = 0.753; 95% CI 0.639–0.866; $p < 0.001$). In a sensitivity analysis, the predicted probability from a logistic regression model using continuous MPV, age, total protein, and hematocrit values showed similar discriminative performance (AUC = 0.766; 95% CI 0.655–0.877; $p < 0.001$). (Fig. 1)

Based on the Youden index, the optimal cut-off value was MAPH ≥ 3, yielding a sensitivity of 56.0% and specificity of 90.5% (PPV 95.5%, NPV 36.5%). The cut-off values for MPV, age, total protein, and hematocrit were derived using the ROC–Youden method. Among these parameters, only age showed significant discrimination for SEC presence (p = 0.008), whereas MPV, total protein, and hematocrit showed no significant discrimination (p = 0.922, p = 0.203, and p = 0.787). (Table 4)

Table 4
ROC–Youden-derived cut-off values

Variables	Cut-off (ROC–Youden)	p value
Age (years)	≥ 46.5	0.008
MPV (fL)	≥ 10.15	0.922
Total protein (g/L)	≥ 65.55	0.203
Hematocrit (%)	≥ 39.15	0.787
MPV, mean platelet volume; ROC, receiver operating characteristic.		

In multivariate logistic regression analysis, the MAPH score, left atrial diameter, and mitral valve area were independent predictors of SEC (Table 5)

Table 5
Logistic regression analyses for the presence of spontaneous echo contrast

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	p value	OR	95% CI	p value
MAPH score	2.400	1.328–4.338	0.004	2.103	1.047–4.223	0.037
Left atrial diameter (cm)	1.200	1.074–1.341	0.001	1.207	1.062–1.372	0.004
Mitral valve area (cm²)	0.648	0.501–0.930	0.019	0.576	0.501–0.895	0.015
sPAP (mmHg)	1.053	1.007–1.100	0.023	1.009	0.958–1.062	0.742
Platelet count (×10³/μL)	1.010	1.001–1.018	0.024	1.007	0.996–1.018	0.232
OR: odds ratio (Exp(B)); CI: confidence interval; SEC, spontaneous echo contrast. Odds ratios for left atrial diameter and mitral valve area are expressed per 0.1 cm and 0.1 cm², respectively. Multivariable model: all variables listed in the table were entered simultaneously into the same model. p values were calculated using the Wald test.						

DISCUSSION

This study investigated the correlation between the MAPH score and the presence of left atrial spontaneous echo contrast in patients with severe rheumatic mitral stenosis in sinus rhythm. To our knowledge, this relationship has not been well characterized previously. MAPH was significantly higher in patients with SEC than in those without SEC. In SEC(+) patients, MAPH showed no significant variation across severity grades. These findings indicate that MAPH may be effective at detecting the presence of SEC but less useful for differentiating between levels of SEC severity.

Rheumatic MS remains a major public health problem in developing countries. The incidence of AF and related thromboembolic events increases in patients with MS [8]. Studies show that thromboembolic events occur more frequently in patients with MS than in those without MS, independent of AF [1]. SEC is defined by dynamic, smoke-like echogenicity in the LA or LAA. Although LA-SEC is only occasionally detected on TTE, TEE is superior for detecting LA thrombus and SEC. Studies have also reported a higher prevalence of LA thrombus in the presence of SEC [9]. Sigel et al. demonstrated that SEC severity correlated positively with hematocrit and fibrinogen levels and negatively with shear stress, suggesting that SEC reflects red blood cell aggregation[10, 11]. Black et al. similarly demonstrated that SEC correlated with hematocrit, fibrinogen concentration, and left atrial diameter, but showed no association with platelet count [12]. Fatkin et al. observed reduced LAA emptying velocity and lower shear rates in patients with AF and SEC [13]. A study showed that fibrinogen and gamma-globulin levels, as well as plasma/serum viscosity, were higher in patients with SEC than in those without SEC, underscoring the role of plasma proteins in SEC pathogenesis [14]. Rastegar et al. showed in vitro that fibrinogen-mediated erythrocyte aggregation may contribute to SEC formation. The strongest SEC occurred at fibrinogen 400–500 mg/dL and hematocrit 39–47%, similar to acute coronary syndrome levels [15]. The role of platelets in the pathophysiology of SEC remains incompletely understood, and existing findings are inconsistent. Chen et al. showed that patients with MS had higher P-selectin (CD62P) expression in the LA than in the right atrium and peripheral samples, and that this expression correlated with the severity of stenosis [16]. Studies investigating the source of SEC directly in left atrial blood samples found that platelet and leukocyte aggregates contribute to SEC [17]. The correlation between platelet indices, such as MPV and SEC, is also heterogeneous in the literature, with some studies reporting a positive association and others not. Therefore, platelet activation may be a more meaningful component in terms of the prothrombotic milieu accompanying SEC and thrombus formation, rather than in the formation of SEC itself [18–20]. In summary, SEC is a complex issue that, in stasis, is linked to blood parameters such as hematocrit, fibrinogen/total protein, viscosity, and platelet activation. Routine, readily available parameters may help identify patients at a higher likelihood of SEC and related thrombus formation. The MAPH score—age, MPV, hematocrit, and total protein—is an accessible way to assess blood viscosity and risk of thrombosis. Previous studies have shown that the MAPH score is associated with coronary thrombus burden in patients with acute coronary syndrome and may predict high thrombus burden [6, 21]. Akhan et al. showed that the MAPH score was an independent predictor of coronary slow flow [22]. Yurdam et al. found a negative correlation between TIMI flow grade and MAPH score [23]. Based on these findings, MAPH components are likely to overlap with the pathophysiology of SEC. In our investigation, the MAPH score was associated with SEC presence; however, it did not differ significantly across SEC grades among SEC-positive individuals. These findings suggest that the severity of SEC may be linked to left atrial stasis/flow dynamics, the hemodynamic effects of mitral stenosis, and blood rheology. In addition, the small number of cases with high SEC grades in our study may have reduced the statistical power to detect differences between grades. Therefore, in larger studies, especially in cohorts with sufficient numbers of Grade 3–4, the relationship between the MAPH score and SEC severity levels can be more clearly evaluated. In our investigation, when the components of the MAPH score were examined individually, each parameter showed limited discriminative ability; however,

the composite MAPH score was significantly associated with the presence of SEC. The fact that MAPH demonstrated substantial discrimination as a 'composite' in our data supports the theory that more than one factor related to blood flow characteristics and thrombosis tendency may be effective in the pathogenesis of SEC, rather than a single parameter. The restricted discriminability of each parameter in analyses where components are assessed separately can be attributed to the composite score more effectively encapsulating the overall effect.

Our echocardiographic results are also consistent with the literature. Beppu, et al. found that in individuals with MS, left atrial SEC was associated with lower cardiac output, higher LA size, and a smaller mitral valve area [24]. Other studies in patients with MS have found that LA SEC is associated with more severe stenosis, AF, older age, and the absence of moderate-to-severe mitral regurgitation [1, 12, 25]. In our study, the LA diameter was larger, and the MVA was smaller in patients with SEC. This finding supports the prominent role of key hemodynamic factors, such as stasis and stenosis severity, in SEC. Therefore, when evaluating SEC, it may be useful to consider echocardiographic indicators alongside composite scores that reflect blood flow characteristics and thrombotic tendency.

Our study identified the MAPH score, LA diameter, and MVA as independent predictors of SEC in multivariate logistic regression. This suggests that the MAPH score is not merely a surrogate for echocardiographic severity markers and may provide additional information related to blood flow characteristics and thrombotic tendency associated with SEC. Conversely, SPAP and platelet count were not significant in the multivariate model, possibly due to overlap with key hemodynamic determinants or sample-related factors. Since the cutoff values were derived from our sample, it is important to confirm their generalizability to future studies across different patient populations. Additionally, finding similar discrimination to MAPH when using continuous component values supports the conclusion that our results are not solely dependent on the cutoff selection.

According to our study, MAPH can be used clinically to risk-classify patients with a high probability of SEC and to prioritize them for further evaluation, rather than as a diagnostic test on its own, especially in settings with limited access to TEE.

Study Limitations

The most important limitation of our study is the relatively small sample size. Additionally, because the study had a single-center, retrospective design, the selected patient population may not be representative of the entire mitral stenosis cohort, and the generalizability of the findings may be limited. In subgroup analyses, the small number of patients with SEC(−) and, especially, high-grade SEC (Grade 3–4) may have reduced statistical power in group comparisons, making it difficult to detect potential differences. In addition, TEE parameters such as LAA emptying velocities, which reflect LAA function, could not be evaluated in our study. Because cutoff values were derived from the study cohort, their performance should be confirmed in independent populations.

Conclusions

In conclusion, the MAPH score, in conjunction with echocardiographic parameters, may be a simple and practical tool for estimating the likelihood of SEC in patients with rheumatic mitral stenosis in sinus rhythm. Larger, multicenter studies validating these findings in diverse patient groups are needed before clinical application.

Abbreviations

MS mitral stenosis

AF atrial fibrillation

SEC spontaneous echo contrast

TEE transesophageal echocardiography

TTE transthoracic echocardiography

EDTA ethylenediaminetetraacetic acid

Hb hemoglobin

MPV mean platelet volume

LVEF left ventricular ejection fraction

MVA mitral valve area

SPAP systolic pulmonary artery pressure

LA left atrium

LAA left atrial appendage

AUC area under the curve

ROC receiver operating characteristic

NPV negative predictive value

PPV positive predictive value

CI confidence interval

df degrees of freedom

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Ankara Etlik City Hospital. (AEŞH-BADEK2-2025-613) The study was conducted in accordance with the principles of the Declaration of Helsinki. Patient data were anonymized prior to analysis, and the ethics committee waived the requirement for informed consent. Clinical trial number: not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to patient confidentiality and ethical restrictions but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

T.K.A., N.T.Ş., B.Y. and F.B. planned the research together. T.K.A., B.E., and M.A ensured the collection of data. T.K.A and F.B. performed statistical analysis of the data. All authors contributed to the writing of the article and approved the final version of the article.

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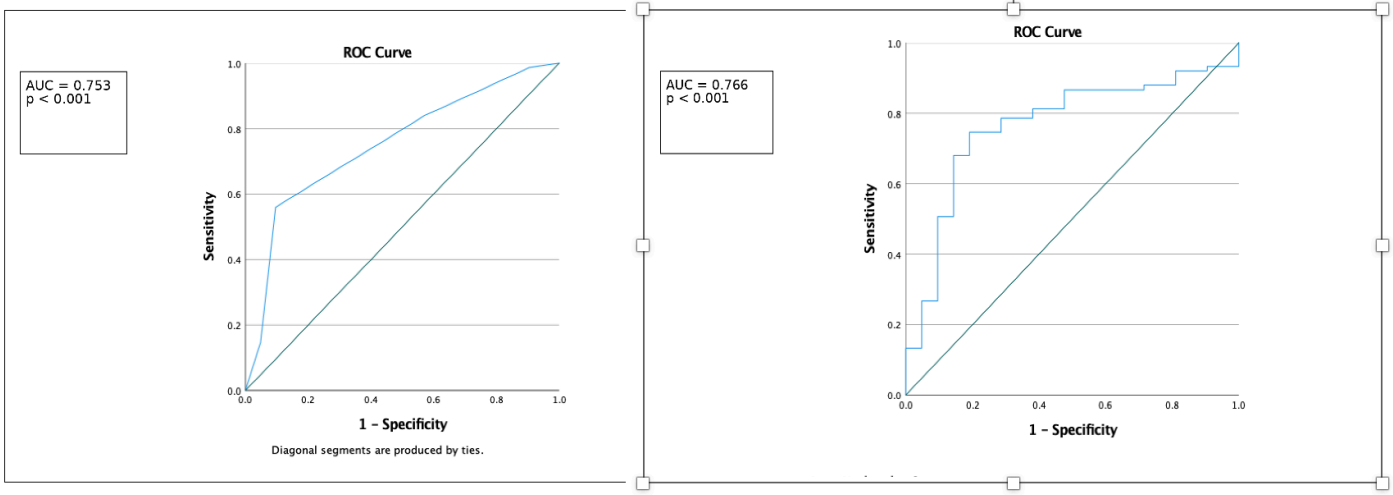
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Figures

Figure 1. ROC curves



A: MAPH total score (0–4).

B: Predicted probability from the logistic model using continuous components (MPV, age, total protein, hematocrit) (sensitivity analysis).

Figure 1

See image above for figure legend.