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Is it possible to estimate the mortality risk in acute pulmonary embolism by means of novel predictors? A retrospective study

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ABSTRACT

Objectives: This study aims to evaluate the relationship of echocardiographic measurements, whole blood viscosity, and other hematological markers with short-term (0-30 days after the diagnosis) and long-term (31st day -12th month after the diagnosis) mortality in acute pulmonary embolism (APE).

Patients and methods: This retrospective study included a total of 80 patients (35 males, 45 females; mean age 68.0±17.1 years; range, 22 to 92 years) with the definitive diagnosis of APE between January 2015 and December 2017. The patients were divided into three study groups as follows: short-term mortality group (n=20; 25.0%), long-term mortality group (n=15; 18.8%), and alive group (n=45; 56.2%) surviving beyond one year during follow-up. The demographic data, Pulmonary Embolism Severity Index, simplified Pulmonary Embolism Severity Index, complete blood count, N-terminal pro-brain natriuretic peptide (NT-proBNP), D-dimer, C-reactive protein, whole blood viscosity values, and echocardiographic measurements of the patients were recorded.

Results: The increased levels of high shear rate-whole blood viscosity, low shear rate-whole blood viscosity, and the decreased levels of tricuspid annular plane systolic excursion were found to be associated with short-term mortality in APE. The red blood cell distribution width and NT-proBNP levels and pulmonary artery and right ventricular diameters were found to be associated with early and late mortality.

Conclusion: Whole blood viscosity levels appear to estimate the patients susceptible to early mortality in APE, while late mortality seems to be predictable in the presence of increased red cell distribution width. Echocardiographic measurements seem to be applicable indicators of increased early and late mortality in APE.

Keywords: Acute pulmonary embolism, long-term mortality, short-term mortality, whole blood viscosity.

Acute pulmonary embolism (APE) is a medical condition associated with high mortality rates. Initial risk assessment in APE is essential for an effective management strategy. Clinical scoring systems, imaging modalities, and biochemical analyses are used to estimate the short-term prognosis of the patients diagnosed with APE.[1] The Pulmonary Embolism Severity Index (PESI) and its simplified form (sPESI) are the most widely used clinical scoring systems.[2,3] Echocardiography and laboratory markers such as N-terminal pro-brain natriuretic peptide (NT-proBNP) and troponin are other parameters to estimate the risk of short-term mortality.[4] It has been reported that the increased mortality rates due to APE compared to the healthy population are not limited to short-term, but also persist in the long-term. Since

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there are few studies on the long-term mortality rate in the literature, the identification of new prognostic factors may facilitate a decline in the mortality rates of APE.[5,6]

Whole blood viscosity is a principal determinant of blood flow and is supposed to have a role in atherosclerosis and thrombosis formations. The association between the increased whole blood viscosity and unfavorable clinical outcomes including mortality has been described previously.[7] Furthermore, several studies reported an increased blood viscosity in deep venous thrombosis and APE.[8,9]

In the literature, the prognostic role of whole blood viscosity in APE has not been reported to date. In the present study, we aimed to evaluate the markers to be used in predicting short-term and long-term mortality in patients hospitalized due to APE.

PATIENTS AND METHODS

This retrospective, causal-comparative study was conducted at Kahramanmaraş Sütçü Imam University, Faculty of Medicine between January 2015 and December 2017. The database of the institution was retrospectively screened. Based on the computed tomography pulmonary angiograms, the patients with the definitive diagnosis of APE were included in this study. Exclusion criteria were as follows: the presence of liver and/or kidney failure, sepsis, malignancy, severe anemia or any hematological disorder on admission, and the history of acute coronary syndrome or the use of any immunosuppressive agent within 30 days before the admission. Finally, a total of 80 consecutive patients (35 males, 45 females; mean age 68.0±17.1 years; range, 22 to 92 years) were included in this study. The records of the patients were assessed to determine the mortality rates by the end of December 2018. Thus, a minimum of one-year follow-up was accomplished in the study population. A written informed consent was obtained from each patient. The study protocol was approved by the Institutional Review Board of Kahramanmaraş Sütçü Imam University, Faculty of Medicine (03.01.2018-2018/01-22). The study was conducted in accordance with the principles of the Declaration of Helsinki.

The patients were divided into three study groups as follows: short-term mortality group (STMG; n=20; 25.0%), long-term mortality group (LTMG; n=15; 18.8%), and alive group (AG; n=45; 56.2%) surviving beyond one-year during follow-up. Death events within the first 30 days of the disease were assigned to the STMG, while those within the period from 31st day to the end of the 12th month of the disease were assigned to the LTMG. The mortality rates of the patients were determined according to the death reports registered to the National Death Reporting System, an official database of the Republic of Turkey, Ministry of Health.

Clinical and laboratory analysis

The demographic data, hemodynamic parameters, and calculated PESI and sPESI scores of the patients were recorded. The values of biochemical and hematological biomarkers, including complete blood count, NT-proBNP, D-dimer, C-reactive protein (CRP), and partial oxygen pressure (PaO_2) were also noted. The whole blood viscosity values were determined both as low shear rate (LSR, 0.5/s) and high shear rate (HSR, 208/s), based on the levels of total plasma protein and hematocrit, using the following validated:[10]

High shear rate: Whole blood viscosity (208/sec) = (0.12 × hematocrit + (0.17 × total plasma protein) -2.07

Low shear rate: Whole blood viscosity (0.5/sec) = (1.89 × hematocrit) + (3.76 × total plasma protein) -78.42

Standard echocardiography

The standard echocardiographic assessments were performed in all patients using the GE Vivid 7® ultrasound system, equipped with a 2.5 to 5 MHz probe (GE VingMed Ultrasound AS; Horten, Norway). The dimensions of the right and left ventricles, thicknesses of the right ventricular and left ventricular walls, diameters of the right and left atria, left ventricular ejection fraction (LVEF), diameter of the pulmonary artery, and tricuspid annular plane systolic excursion (TAPSE) were measured during the assessment for each patient. Systolic pulmonary artery pressure was calculated using the modified Bernoulli's equation which is based on peak velocities of tricuspid regurgitation. The primary outcome measure was the relationship between the mortality rates, based on the period of the disease, and the laboratory and echocardiographic variables.

Statistical analysis

Study power analysis and sample size calculation were performed using the Microsoft R Open version 3.3.2 software (Microsoft Corp., WA, USA). Statistical analysis was performed using the IBM SPSS for Windows 64-bit, version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation (SD), median

(25^{th} to 75^{th} percentile) or number and percentage. The compliance of the variables with normal distribution was analyzed using the Shapiro-Wilk test. The Kruskal Wallis H test was used for the non-normally distributed variables. The Dunn-Sidak test was applied as a post-hoc test. The chi-square test and Fisher's exact test were used to assess the distribution of the categorical variables. A multinomial logistic regression analysis was performed to identify the predictive value of the variables. A p value of <0.05 was considered statistically significant.

RESULTS

The median follow-up was 10.5 (range, 2.5 to 17.5) days in the STMG, 188.0 (range, 38.0 to 433.0) days in the LTMG, and 474.5 (range, 369.0 to 596.0) days in the AG, while the overall median follow-up was 574.5 (range, 468.5 to 699.7) days. The median age of AG was significantly lower compared to the STMG and LTMG (p<0.001) (Table 1). The median value of systolic blood pressure in the STMG was significantly lower than the AG and LTMG (p<0.001). On the other hand, there was no significant difference among the study groups in terms of comorbidities. The median value of PESI was significantly higher in the STMG than the AG (p<0.001), while the median value of sPESI in the STMG was significantly higher compared to the other two groups (p=0.005). The median PESI and sPESI values indicated a high risk for all study groups.

The study groups were also compared considering the laboratory test results. The median values of lactate dehydrogenase (p=0.289), CRP (p=0.14), and D-dimer (p=0.061) demonstrated no significant difference among the study groups. The median value of NT-proBNP in the AG was 147.00 (range, 102.00 to 280.00) ng/L, while the median value in the LTMG was 350.00 (range, 168.00 to 880.00) ng/L, showing significantly high levels in the latter group compared to the former group (p=0.031) (Table 2). The median values of HSR-whole blood viscosity and LSR-whole blood viscosity were significantly higher in the STMG (HSR-whole blood viscosity: 3.47 [3.08 to 3.99] and LSR-whole blood viscosity: 14.47 [8.78 to 23.8]) than the AG (HSR-whole blood viscosity: 3.0 [2.62 to 3.6] and LSR-whole blood viscosity: 8.76 [1.97 to 17.85]; p=0.012 for HSR-whole blood viscosity and p=0.015 for LSR-whole blood viscosity).

Table 1. Demographic data of patient groups

	Alive group (n=45)				Short-term mortality group (n=20)				Long-term mortality group (n=15)				
	n	%	Median	Q1-Q3	n	%	Median	Q1-Q3	n	%	Median	Q1-Q3	*p*
Age (year)†			67.00	51.00-76.00[b,c]			80.00	67.50-85.50[a]			78.00	71.00-85.00[a]	**0.001***
Sex†													0.243
Female	28	62.22			8	40.00			9	60.00			
Heart rate (beats/m)†			120.00	110.00-136.00			120.50	108.00-129.50			112.00	100.00-125.00	0.218
Oxygen saturation (%)†			81.00	76.00-85.00			74.5	70.50-83.00			83.00	80.00-85.00	0.053
Systolic BP (mmHg)†			95.00	90.00-105.00[b]			80.0	75.00-87.50[a,c]			90.00	85.00-100.0[b]	**0.001***
Diastolic BP (mmHg)†			60.00	50.0-65.00[b]			45.00	45.00-60.00[a]			58.00	50.00-65.00	**0.026***
PESI†			121.00	111.00-138.00[b]			155.00	138.50-164.00[a]			135.00	123.00-157.00	**0.001***
sPESI†			2.00	2.00-3.00[b]			3.00	2.00-4.00[a,c]			2.00	2.00-3.00[b]	**0.005***
Hypertension‡	18	40.00			11	55.00			10	66.67			0.186
Hyperlipidemia‡	8	17.78			5	25.00			3	20.00			0.928
Diabetes mellitus‡	9	20.00			3	15.00			5	33.33			0.460
Coronary artery disease‡	6	13.33			5	25.00			6	40.00			0.082
Congestive heart failure‡	3	6.67			5	25.00			4	26.67			0.052
Chronic obstructive pulmonary disease‡	9	20.45			5	25.00			5	33.33			0.637
CVD‡	7	15.56			8	40.00			4	26.67			0.098
Chronic kidney disease‡	3	6.67			1	5.00			1	6.67			1.00
Smoking‡	6	13.33			5	25.00			5	33.33			0.186

BP: Blood pressure; PESI: Pulmonary Embolism Severity Index; sPESI: Simplified Pulmonary Embolism Severity Index; CVD: Cerebrovascular disease; † Kruskal-Wallis H test, Post-hoc:Dunn-Sidak test; ‡ Chi-square test, α: 0.05; * The difference is statistically significant; a The difference with alive group is significant; b The difference with the short-term mortality group is significant; c The difference with the long-term mortality group is significant.

Table 2. Laboratory data of patient groups

	Alive group (n=40)		Short-term mortality group (n=20)		Long-term mortality group (n=15)		
	Median	Q1-Q3	Median	Q1-Q3	Median	Q1-Q3	*p*
NT- proBNP (ng/L)	147.00	102.00-280.00[c]	265.00	135.50-400.00	350.00	168.00-880.00[a]	0.031*
D-dimer (mg/L)	3.80	2.10-9.10	8.10	5.30-10.80	7.30	3.90-16.50	0.061
Protein (mg/dL)	6.20	5.80-6.50	6.05	5.50-6.80	6.20	6.10-6.60	0. 956
Leukocyte (1000×mL)	8.67	7.54-9.94[b]	11.77	9.81-13.31[a]	10.17	7.23-14.00	0.005*
Hematocrite (%)	33.90	31.00-38.40[b]	37.50	33.90-42.30[a]	37.80	35.30-41.70	0.010*
RDW (%)	14.50	12.90-16.20[b,c]	18.35	14.80-22.65[a]	18.10	14.500-19.40[a]	0.001*
Thrombocyte (1000×mL)	236.00	174.00-331.00	312.50	227.50-362.50[c]	175.00	138.00-226.00[b]	0.004*
HSR-WBV	3.00	2.62-3.60[b]	3.47	3.08-3.99[a]	3.50	3.13-3.99	0.012*
LSR-WBV	8.76	1.97-17.85[b]	14.47	8.78-23.80[a]	15.96	9.34-23.71	0.015*

NT-proBNP: N-terminal pro-brain natriuretic peptide; RDW: Red blood cell distribution width; HSR-WBV: High shear rate-whole blood viscosity; LSR-WBV: Low shear rate-whole blood viscosity; * The difference is statistically significant; a The difference with alive group is significant; b The difference with the short-term mortality group is significant; c The difference with the long-term mortality group is significant.

There were significant differences in the several parameters of the complete blood counts among the groups. The median values of hematocrit level and leukocyte count were significantly high in the STMG compared to the AG (p=0.01 and p=0.005, respectively). The median value of the red blood cell distribution width (RDW) was 14.5% (range, 12.9 to 16.2%) in the AG, while the median values in the STMG and LTMG were 18.35% (range, 14.8 to 22.65%) and 18.1% (range, 14.5 to 19.4%), respectively. The RDW was significantly lower in the AG than the other two groups (p=0.001). The median platelet count of the LTMG was significantly lower than the STMG (p=0.004). The median values of the remaining laboratory tests showed no significant differences among the study groups.

The median right ventricular diameters in the AG, STMG, and LTMG were 38.0 (range, 36.0 to 41.0) mm, 44.0 (range, 40.0 to 45.5) mm, and 42.0 (range, 40.0 to 45.0) mm, respectively. The median pulmonary diameters were measured as 28.0 (range, 26.0 to 29.0) mm in the AG, 33.5 (range, 28.0 to 35.0) mm in the STMG, and 32.0 (range, 29.0 to 35.0) mm in the LTMG. The right ventricular and pulmonary artery diameters were significantly lower in the AG than the other two groups (p=0.001 for both), while there was no significant difference between the STMG and LTMG.

The median TAPSE values in the AG were significantly higher (18.0 mm [17.0 to 20.0 mm]) compared to the STMG (14.0 mm [13.0 to 17.0 mm]), and LTMG (14.0 mm [13.0 to 18.0 mm]) (p=0.001). On the other hand, the difference between the STMG and LTMG was not significant in terms of the median TAPSE values. The median values of systolic pulmonary artery pressure in the AG were significantly lower (42.0 mmHg [36.0 to 50.0 mmHg]) to the STMG (59.0 mmHg [43.50 to 65.0 mmHg]) and LTMG (52.0 mmHg [45.0 to 61.0 mmHg]) (p=0.006). The median values of the LVEF (p=0.602) and right atrium diameter (p=0.319) demonstrated no significant difference among the study groups (Table 3).

Table 3. Echocardiographic data of patient groups

	Alive group (n=40)		Short-term mortality group (n=20)		Long-term mortality group (n=15)		
	Median	Q1-Q3	Median	Q1-Q3	Median	Q1-Q3	*p*
RV diameter (mm)	38.0	36.00-41.00[b,c]	44.00	40.00-45.50[a]	42.00	40.00-45.00[a]	0.001*
PA diameter (mm)	28.00	26.00-29.00[b,c]	33.50	28.00-35.00[a]	32.00	29.00-35.00[a]	0.001*
TAPSE (mm)	18.00	17.00-20.00[b,c]	14.00	13.00-17.00[a]	14.00	13.00-18.00[a]	0.001*
SPAP (mmHg)	42.00	36.00-50.00[b]	59.00	43.50-65.00[a]	52.00	45.00-61.00	0.006*

RV: Right ventricular; PA: Pulmonary artery; TAPSE: Tricuspid annular plane systolic excursion; SPAP: Systolic pulmonary artery pressure; * The difference is statistically significant; a The difference with alive group is significant; b The difference with the short-term mortality group is significant; c The difference with the long-term mortality group is significant.

Table 4. Logistic regression analysis results for early and late mortality predictors of acute pulmonary embolism

					95% CI OR	
	B	Wald	*p*	OR	Lower	Upper
Early mortality						
Age	0.340	1.645	0.200	1.405	0.836	2.361
Systolic BP	-0.041	0.016	0.899	0.960	0.508	1.813
Diastolic BP	-0.287	0.889	0.346	0.751	0.414	1.363
PESI	0.230	1.649	0.199	1.258	0.886	1.787
sPESI	-1.526	0.259	0.611	0.217	0.001	77,464
NT-proBNP	-0.012	4.238	0.040*	0.988	0.977	0.999
Leukocyte	0.066	0.049	0.824	1.068	0.596	1.916
Hematocrite	1.806	0.488	0.485	6.084	0.038	966,240
RDW	1.443	3.294	0.070	4.234	0.891	20,121
Platelet	0.064	4.315	0.038*	1.067	1.004	1.134
HSR-WBV	-0.562	0.001	0.979	-	-	-
RV diameter	-0.157	0.041	0.840	0.855	0.186	3.933
PA diameter	-0.345	0.166	0.684	0.708	0.134	3.730
TAPSE	-2.059	1.729	0.189	0.128	0.006	2.746
SPAP	0.050	0.065	0.799	1.051	0.717	1.540
Late mortality						
Age	0.367	1.629	0.202	1.443	0.822	2.533
Systolic BP	-0.079	0.225	0.636	0.924	0.666	1.282
Diastolic BP	0.048	0.103	0.748	1.050	0.781	1.411
PESI	0.111	1.122	0.289	1.117	0.910	1.372
sPESI	-3.671	2.854	0.091	0.025	0.000	1.801
NT-proBNP	-0.003	0.777	0.378	0.997	0.989	1.004
Leukocyte	-0.417	1.799	0.180	0.659	0.358	1.212
Hematocrite	2.313	1.020	0.313	-	-	-
RDW	1.469	6.101	0.014*	4.344	1.354	13,932
Platelet	0.028	2.214	0.137	1.028	0.991	1.067
HSR-WBV	-8.154	0.234	0.628	-	-	-
RV diameter	0.858	2.012	0.156	2.358	0.721	7.715
PA diameter	0.666	2.505	0.114	1.946	0.853	4.440
TAPSE	0.368	0.214	0.644	1.444	0.304	6.858
SPAP	-0.210	1.810	0.179	0.811	0.598	1.100

CI: confidence interval; OR: Odds ratio; BP: Blood pressure; PESI: Pulmonary Embolism Severity Index; sPESI; Simplified Pulmonary Embolism Severity Index; NT-proBNP: N-terminal pro-brain natriuretic peptide; RDW: Red blood cell distribution width; HSR-WBV: High shear rate-whole blood viscosity; RV: Right ventricular; PA: Pulmonary artery; TAPSE: Tricuspid annular plane systolic excursion; SPAP: Systolic pulmonary artery pressure; * Statistical significance; Significant Predictor for Early mortality.

The parameters which showed a significant correlation in the univariate analysis were included in the multivariate analysis to identify their predictive values. Based on the multivariate analysis, high NT-proBNP levels (p=0.040, odds ratio [OR]: 0.988, confidence interval [CI]: 0.977-0.999) and the high median platelet counts (p=0.038, OR: 1.067, CI: 1.004-1.134) predicted early mortality, whereas high RDW values (p=0.014, OR: 4.344, CI: 1.354-13.932) predicted late mortality. The results of logistic regression analysis are shown in Table 4.

DISCUSSION

Acute pulmonary embolism has been shown to be associated with a high risk of mortality within the first 30 days of the disease.[2,3] Deaths occurring within this period, also called short-term, are mostly attributed to thromboembolic events. The likelihood of increased mortality due to APE is not limited to short-term, but also exists in long-term.[6] Despite the persistent risk of mortality throughout the first year of the disease, morbidities including malignancy, cardiovascular diseases, and infections such as pneumonia are commonly accused of long-term mortality.[6,11]

In addition to the relationship between APE and cardiovascular diseases, there is a significant increase in the mortality rates of APE patients with concomitant cardiovascular problems.[12] Although comorbidities were more common in the mortality groups in our study, the difference among the groups

was insignificant, which is contradictory to the common opinion.

The PESI and sPESI, calculated using the demographic and clinical data of the patients, are the clinical scoring systems to identify the high mortality risk in APE.[5] Although the scores in the STMG were significantly higher compared to the AG in our study, multivariate analysis was unable to confirm the association between the scores and mortality rates.

Transthoracic echocardiography is an accessible and a non-invasive screening test, frequently used to diagnose APE and to predict the prognosis. It is also crucial in the immediate recognition of right ventricular dysfunction and increase in the right ventricular afterload, the factors that increase morbidity and mortality in APE.[13] Acute pulmonary embolism induces thrombotic cascade manifested by platelet activation in liver and kidney. The thrombotic cascade, a potentially fatal condition, develops due to impaired perfusion which is triggered by right ventricular systolic dysfunction.[14] Although the relationship between cardiac function impairment and the increased mortality rate in the early period of APE was demonstrated in previous researches, few studies investigated the link between consequent cardiac impairment and both short-term and long-term mortality.[13]

The relationship between the mortality rates and values of TAPSE, right ventricular diameter, pulmonary artery diameter, and systolic pulmonary artery pressure - the main parameters measured in APE using transthoracic echocardiography - were also investigated in our study. The TAPSE measurement, which is commonly used owing to its practicality and low variability between the operators, provides more precise results than the overall assessment of right ventricular function. Besides, the TAPSE is reported to be a reliable parameter to predict the short-term mortality in APE.[15] The TAPSE values in the mortality groups of this study were significantly lower to the AG. Conversely, the diameters of the right ventricle and pulmonary artery were significantly higher in the mortality groups than the AG. These findings appear to support the capability of right ventricle and pulmonary artery diameter measurements and TAPSE measurement in the prediction of early and late mortality caused by APE. In addition, the detection of high systolic pulmonary arterial pressure levels may facilitate the identification of patients with a high risk of mortality in the early period of APE. Of note, significantly lower values of the right ventricular diameter, systolic pulmonary artery pressure level, and pulmonary artery diameter in the AG, compared to the mortality groups, support the use of these parameters in the assessment of the prognosis.

The NT-proBNP and troponin levels are also among the mortality predictors of APE. An increase in the NT-proBNP levels, a marker of right ventricular dysfunction, has been reported to be associated with early mortality in low-to-intermediate risk groups, diagnosed with APE.[16] The results of our study indicated the association between elevated NT-proBNP levels and late mortality, while the multivariate analysis demonstrated that the former could predict the latter.

In the literature, the association between erythrocyte count and the occurrence of venous thrombosis has been also described.[17] An elevation in RDW, a semi-quantitative measurement of erythrocyte anisocytosis, indicates an increased heterogeneity of the erythrocyte volume. High RDW values, caused by inflammatory processes, have been shown to be associated with many cardiovascular and cerebrovascular diseases.[18,19] Besides, the elevation in RDW values has been suggested to predict early and late mortality in APE.[20,21] In our study, the mean RDW values of the mortality groups were significantly higher than the mean RDW value of AG. However, the multivariate analysis only indicated a relationship in the LTMG, a four-fold increase in the mortality rate with elevated RDW levels. These results suggest the RDW value elevation as a useful marker to identify the patients with a high risk for early and late mortality due to APE.

Blood flow to the tissues, tissue perfusion, is mainly affected by the whole blood viscosity. The determinants of the whole blood viscosity include plasma viscosity, hematocrit level, erythrocyte-specific factors, and body temperature.[22] Previous studies have shown that impairment in the blood viscosity is associated with an increased risk of cardiovascular events and mortality.[7,8,23] Similarly, whole blood viscosity has been shown to be associated with an increased risk of venous thromboembolic disease, such as deep vein thrombosis and APE.[8,9] However, to the best of our knowledge, the relationship between the whole blood viscosity and mortality rates of APE in short-term and long-term has not been investigated, yet.

The whole blood viscosity measurement is not routinely performed. However, blood viscosity can

be quantified using a validated equation for low and HSRs, as described by de Simone et al.[10] Despite significantly higher values of LSR-whole blood viscosity and HSR-whole blood viscosity in the STMG compared to the AG, multivariate analysis was unable to confirm a significant correlation. The failure to demonstrate this relationship is attributable to the relatively small size of the study groups and the strict exclusion criteria to produce homogenous patient population.

The main limitations to the present study include its single-center, retrospective design with a relatively small sample size. Due to its retrospective design, there were missing data for some variables such as troponin level, which was previously shown to be correlated to the severity of clinical course in APE.[24] In addition, this study included only high-risk APE cases and, thus, the results cannot be applied to low- and intermediate-risk groups.

In conclusion, increased levels of systolic pulmonary artery pressure, LSR-whole blood viscosity, and HSR-whole blood viscosity appear to differentiate the patients susceptible to early mortality due to APE. A decreased tricuspid annular plane systolic excursion level, increased right ventricular diameter, increased pulmonary artery diameter, and increased RDW can be also suggested as the indicators of an increased risk of early and late mortality. Besides, late mortality in APE seems to be predictable in the presence of an increased RDW. Further large-scale, prospective studies are needed to provide a better insight into this issue.

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