Echocardiographic parameters as adjuncts to the Pulmonary Embolism Severity Index in predicting 30-day mortality in acute pulmonary embolism patients

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ABSTRACT

Background: The Pulmonary Embolism Severity Index (PESI) is a validated tool to predict 30-day all-cause mortality in patients with acute pulmonary embolism (PE) but includes only clinical variables.

Aims: We aimed to determine the effectiveness of PESI extended with an echocardiographic parameter.

Methods: This cross-sectional observational study included consecutive patients with acute PE diagnosed with computed tomography pulmonary angiography.

Results: Of 117 subjects (57 men, 48.7%), at a median age of 69 (59–80) years, 16 patients died during the 30-day follow-up. Six modified models of PESI with an additional single echocardiographic parameter were created, which increased the predictive value of PESI (area under the curve [AUC] 0.8608): tricuspid annular plane systolic excursion (TAPSE) <18 mm, right ventricular (RV) free wall longitudinal strain (RVFWLS) >–23%, 60/60 sign, RV global longitudinal strain (RVGLS) >–16%, pulmonary ejection acceleration time (AcT) <67 ms, and thrombus in right heart cavities (AUC 0.8657 to 0.8976, respectively, all markers P <0.001). TAPSE, AcT, RVFWLS, and RVGLS showed significant correlations with the PESI score, but not a thrombus in the right heart cavity or the 60/60 sign. As PESI adjuncts, they independently predicted fatal outcomes: thrombus with hazard ratio (HR) 10.04 (95% confidence interval [CI], 2.81–37.12; P <0.001) and the 60/60 sign with HR 4.07 (95% CI, 1.27–12.81; P <0.001).

Conclusions: The quantitative echocardiographic parameters of RV systolic function and pulmonary artery blood flow are associated with the PESI score and thus increase its predictive value to a limited extent. PE- specific findings: a thrombus in the right heart cavity and the 60/60 sign are effective adjuncts to the PESI score.

Key words: 60/60 sign, echocardiography, pulmonary embolism, pulmonary embolism severity index, thrombus

INTRODUCTION

Pulmonary embolism (PE) and deep vein thrombosis as clinical manifestations of venous thromboembolism are the third most frequent cardiovascular diseases worldwide [1]. Moreover, the prevalence of venous thromboembolism is steadily increasing while the estimated morbidity figures are underrepresented due to numerous clinically silent cases [2]. PE might be associated with various complications including severe disability related to subsequent chronic thromboembolic pulmonary hypertension and heart failure with decreased quality of life [3, 4].

Acute PE is associated with a different prognosis. Patients without hemodynamic impairment or myocardial injury have a mortality rate of under 3%, whereas those who

WHAT'S NEW?

The Pulmonary Embolism Severity Index (PESI) is a validated tool predicting 30-day all-cause mortality in patients with acute pulmonary embolism (PE). However, the PESI includes only clinical variables but none of transthoracic echocardiography (TTE) parameters. The results of our study show that the addition of TTE parameters to clinical evaluation of patients with acute PE helps to identify patients with right ventricular (RV) dysfunction and increases the prognostic power of PESI. The quantitative TTE parameters of RV systolic function and pulmonary artery blood flow based on measurements of tricuspid annular plane systolic excursion, RV longitudinal strain, and pulmonary ejection acceleration time correlate with the PESI score and thus increase its predictive value to a limited extent. The PE findings that are specific to PE but not correlated with PESI: a thrombus in the right heart cavity and the 60/60 sign are effective adjuncts to the PESI.

experience cardiopulmonary arrest — more than 90% [1, 5–7]. Thus, rapid diagnosis and early risk stratification with identification of individuals at high risk of hemodynamic deterioration and death is essential.

The contemporary mortality-risk appraisal in patients with acute PE advised by the European Society of Cardiology includes 2 scores validated in randomized trials: the Pulmonary Embolism Severity Index (PESI) and its simplified version (sPESI) [1, 8, 9]. The indexes combine clinical variables and vital signs but not biochemical parameters or imaging examination results. The PESI comprises age, male sex, cancer, chronic heart failure, chronic pulmonary disease, pulse rate ≥110 bpm, systolic blood pressure <100 mm Hg, respiratory rate >30 breaths per minute, body temperature <36°, altered mental status, arterial oxyhemoglobin saturation <90% with appropriately assigned points (10 to 60 and one point for each year of life) which are added together. The PESI score qualifies the patient into 1 of 5 (I–V) classes of 30-day all-cause mortality risk: very low, low, intermediate, high, and very high with corresponding threshold values of ≤65, 66–85, 86–105, 106–125, and ≥126 points, respectively, and fatal outcome risk from 0%–1.6% in class I to 10%–24.5% in class V [1].

Transthoracic echocardiography (TTE) is not routinely advised as part of the diagnostic path and risk stratification in hemodynamically stable patients with suspected or diagnosed PE [1, 10]. However, short-term prognosis in acute PE is conditioned by the hemodynamic status which is related to right ventricular (RV) failure. Moreover, RV dysfunction is also associated with increased risk of short-term mortality in normotensive patients [11]. Thus, TTE might detect RV dysfunction and help to identify patients at elevated risk of hemodynamic decompensation and early mortality [12, 13].

The question arises, if the addition of TTE results to the PESI, based on single simple reproducible markers, might improve fatal outcome prediction.

This study aimed to assess the usefulness of modifying PESI by adding a single TTE parameter reflecting RV dysfunction in predicting 30-day all-cause mortality in patients with acute PE and to estimate associations between different TTE parameters and the PESI score.

METHODS

This was a cross-sectional observational single-center study. The study group included consecutive patients of the Internal Medicine Department and the Special Care Cardiac Unit, with acute PE confirmed by computed tomography pulmonary angiography, enrolled between August 1, 2018 and April 30, 2021. The treatment regimen followed the guidelines on PE management of the European Society of Cardiology and was described thoroughly previously [1, 10, 14].

The exclusion criteria covered recurrent PE, chronic thromboembolic pulmonary hypertension, echocardiograms of inadequate quality (the ones in which not all parameters from the unified protocol could be evaluated), severe valvular defects, and tricuspid valve replacement.

A standard diagnostic protocol included measuring in all patients, on the day of admission to the ward, serum concentrations of troponin T, N-terminal pro B-type natriuretic peptide (NT-proBNP) and D-dimer levels, with laboratory methods summarized formerly [14]. TTE was performed within 24 hours after admission to the ward by an experienced sonographer cardiologist (JW) using echocardiographic systems of Vivid S60N or Vivid S6 (General Electric Company, Boston, MA, US) according to the unified protocol [14–16]. The measurements were made based on the current guidelines of the European Association of Cardiovascular Imaging with real-time electrocardiographic recording executed to accurately define the heart cycle phases [17]. The measurements of RV longitudinal strain by two-dimensional speckle-tracking echocardiography were performed within 6 segments of RV at the same time in the apical four-chamber view as described before [16, 18].

Simple and composite echocardiographic parameters, based on simple and reproducible measurements and quick calculations, indicating RV dysfunction including the ones with proven prognostic significance, were selected from the literature: RV transverse diameter (RVTD), RVTD/left ventricular (LV) transverse diameter (RVTD/LVTD, i.e., RV to LV ratio), tricuspid annular plane systolic excursion (TAPSE), pulmonary ejection acceleration time/right ventricular outflow Doppler acceleration time (AcT), pulmonary artery systolic pressure (PASP), the average values of

Table 1. Clinical characteristics and selected biochemical parameters of the study participants: all patients with acute pulmonary embolism, subgroups of survivors and deceased subjects within 30 days of observation

	All subjects (n = 117)	Survivors (n = 101)	Non-survivors (n = 16)	*P*-value
Male, n (%)	57 (48.72)	53 (52.48)	4 (25)	0.06
Age, years, median (IQR)	69 (59–80)	67 (57–79)	74 (68.75–84.5)	0.01
Body Mass Index, kg/m^2, median (IQR)	27.55 (25.19–31.17)	27.55 (25.19–31.07)	27.3 (25.24–31.82)	0.93
Arterial hypertension, n (%)	71 (60.68)	62 (61.39)	9 (56.25)	0.70
Diabetes, n (%)	26 (22.22)	20 (19.8)	6 (37.5)	0.11
Chronic heart failure, n (%)	30 (25.64)	25 (24.75)	5 (31.25)	0.60
Atrial fibrillation (present or prior), n (%)	15 (12.82)	13 (12.87)	2 (12.5)	0.95
Chronic lung disease, n (%)	8 (6.84)	7 (6.93)	1 (6.25)	0.92
Malignancy, n (%)	24 (20.51)	19 (18.81)	5 (31.25)	0.27
Infection, n (%)	39 (33.33)	32 (31.68)	7 (43.75)	0.34
Heart rate, beats per minute, median (IQR)	78 (71.5–99)	77 (70–90)	105 (97–114)	<0.001
Systolic blood pressure, mm Hg, median (IQR)	127.5 (115–139.75)	128 (115–139.5)	125 (101–138.5)	0.48
PESI, point, median (IQR)	97 (78.5–123)	93 (70–114.5)	141 (112.75–197.25)	<0.001
Troponin T, pg/ml, median (IQR)	22.09 (10.75–50.28)	19.8 (9.36–44.57)	72.81 (37.94–262.2)	<0.001
NT-proBNP, pg/ml, median (IQR)	597.5 (154.75–2948.5)	503 (139.25–2566.5)	3410.5 (1594–9739.5)	0.002
D-dimer, ng/ml, median (IQR)	4905 (2194.5–7811)	4474 (1949.25–7794.5)	5801.5 (4532.75–8857.75)	0.12
Creatinine clearance, ml/min, median (IQR)	82.2 (62.12–104.97)	83 (68.95– 104.72)	53.4 (25.85–103.33)	0.04

Abbreviations: NT-proBNP, N-terminal pro-B-type natriuretic peptide; PESI, Pulmonary Embolism Severity Index

longitudinal strain of 3 segments of RV free wall (RVFWLS) and of all 6 RV segments — RV global longitudinal strain (RVGLS), tricuspid peak regurgitation velocity, TAPSE/PASP, tricuspid valve peak systolic gradient /AcT, tricuspid valve peak systolic gradient/TAPSE, tricuspid annulus' peak systolic velocity measured with tissue Doppler imaging, PASP-TAPSE, 60/60 sign combining tricuspid regurgitation jet gradient of ≤60 mm Hg and AcT ≤60 ms, RVTD >41 mm, RVTD/LVTD >1, TAPSE <16 mm, McConnell sign (right ventricular free wall akinesis with sparing of the apex), RV hipokinesis or McConnell sign, PASP >35 mm Hg, RVFWLS >–20%, thrombus in right heart cavities, central PE, pulmonary artery mid-systolic notching, tricuspid annulus' peak systolic velocity measured with tissue Doppler imaging <9.5 cm/s, and paradoxical septal motion [1, 13, 18–22].

The study endpoint was 30-day overall mortality. Data collection during the follow-up of the study was described in detail in the earlier publication [14].

The study protocol was approved by the Bioethics Committee of the Regional Medical Chamber in Tarnów, Poland (No. 3/0177/2019). The study was performed in concordance with the ethical principles of clinical research based on the Declaration of Helsinki.

Statistical analysis

The Shapiro–Wilk test was applied to check the normality of distribution. Consequently, quantitative variables were expressed as medians with interquartile ranges while the Wilcoxon signed-rank test was utilized for their comparisons. Qualitative variables were expressed as numbers (percentage), and Fisher's test or the χ^2 test were used for their comparisons, when adequate. Hazard risk using univariate Cox proportional-hazards regression, and the corresponding 95% confidence intervals (CI) were calculated. The Spearman rank correlation coefficient was used to measure the strength and direction of associations between two numerical variables. Standard receiver-operating characteristic analysis was performed, and areas under the curves (AUC) were determined. The Youden index was used to calculate optimal cut-off values. We added extra points to the PESI scale when a TTE sign was present or TTE parameters exceeded the cut-off value with the number of points assigned according to the prediction strength of the given TTE marker. PESI modifications (scoring, cut-off points) were applied to maximize AUC. Two-sided *P*-values <0.05 were considered statistically significant. Statistical analysis was executed with the R Project for Statistical Computing version 4.2.1 (the R Foundation for Statistical Computing, Free Software Foundation Inc., Vienna, Austria).

RESULTS

The study group comprised 132 consecutive patients. Fifteen subjects had echocardiograms of poor quality. Eventually, 117 subjects (57 men, 48.7%), aged 69 (59–80) years were eligible for the analysis. The baseline characteristics and selected biochemical parameters are presented in Table 1. Six subjects (5.13%) had high-risk PE, 74 (63.24%) patients had intermediate-risk PE, and 37 (31.62%) had low-risk PE.

Sixteen patients died during the 30-day follow-up. Five patients required thrombolysis within 24 hours of admission to the ward — they received systemic thrombolysis with alteplase. Two of them died, and 3 survived. PE as a cause of refractory RV failure contributed to the death of a further 5 patients. PE contributed to the death of additional 9 subjects by aggravating other decompensated diseases: heart failure in 3, pneumonia in 3, kidney failure in 1, and disseminated neoplastic disease in 2. None of the

Table 2. Selected echocardiographic parameters

Echocardiographic parameter — quantitative variables	Survivors (n = 101)	Non-survivors (n = 16)	*P*-value	Echocardiographic parameter — qualitatitve variables	Survivors (n = 101)	Non-survivors (n = 16)	*P*-value
RVTD, mm, median (IQR)	41 (37–44)	37.5 (35–41.25)	0.07	60/60 sign, n (%)	16 (15.84)	7 (43.75)	0.009
RVTD/LVTD, median (IQR)	0.93 (0.83–1.05)	0.95 (0.88–1.06)	0.77	RVTD >41 mm, n (%)	48 (47.52)	4 (25)	0.25
TAPSE, mm, median (IQR)	21 (17–24)	17 (14–20)	0.02	RVTD/LVTD >1, n (%)	33 (32.67)	5 (31.25)	0.75
AcT, ms, median (IQR)	74 (59–99)	59 (46.5–65)	0.01	TAPSE <16 mm, n (%)	22 (21.78)	5 (31.25)	0.40
PASP, mm Hg, median (IQR)	34 (26–46)	43 (31.5–49)	0.32	McConnell sign, n (%)	9 (8.91)	1 (6.25)	0.86
RVFWLS, %, median (IQR)	–20 (–15.33 to –24.42)	–17.33 (–9.67 to –18.67)	0.04	RV hipokinesis or McConnell sign, n (%)	18 (17.82)	6 (37.5)	0.07
RVGLS, %, median (IQR)	–19 (–15.33 to –22)	–15.67 (–10.67 to –18.21)	0.03	PASP >35 mm Hg, n (%)	47 (46.53)	10 (62.5)	0.17
TRV, m/s, median (IQR)	2.7 (2.4–3.14)	2.9 (2.35–3.4)	0.63	RVFWLS > -20%, n (%)	29 (28.71)	6 (37.5)	0.49
TAPSE/PASP, mm/mm Hg, median (IQR)	0.64 (0.38–0.92)	0.46 (0.27–0.64)	0.07	Thrombus in right heart cavities, n (%)	4 (3.96)	7 (43.75)	<0.001
TRPG/AcT, mm Hg/ms, median (IQR)	0.42 (0.23–0.63)	0.53 (0.27–1.01)	0.25	Central PE, n (%)	40 (39.6)	10 (62.5)	0.09
TRPG/TAPSE, mm Hg/mm, median (IQR)	1.43 (1–2.33)	1.71 (1.21–2.99)	0.22	Pulmonary artery mid-systolic notching, n (%)	20 (19.8)	2 (12.5)	0.73
TASV TDI, cm/s, median (IQR)	15 (13–18)	16.5 (1319.75)	0.76	TASV TDI <9.5 cm/s, n (%)	99 (98.02)	14 (87.5)	0.13
PASP-TAPSE, mm Hg – mm, median (IQR)	12 (2–28)	21 (11.535.5)	0.15	Paradoxical septal motion, n (%)	4 (3.96)	1 (6.25)	0.53

Abbreviations: AcT, pulmonary ejection acceleration time; LVTD, left ventricular transverse diameter; PASP, pulmonary artery systolic pressure; RVFWLS, right ventricle free wall longitudinal strain; PE, pulmonary embolism; RVGLS, right ventricle global longitudinal strain; RVTD, right ventricular transverse diameter; TAPSE, tricuspid annular plane systolic excursion; TASV TDI, tricuspid annulus' peak systolic velocity measured with tissue Doppler imaging; TRPG, tricuspid valve peak systolic gradient; TRV, tricuspid peak regurgitation velocity

study participants required rescue thrombolysis during the follow-up.

Patients who died during the follow-up, compared to survivors, were older, had higher heart rates on admission to the ward, higher PESI scores, increased troponin T and NT-proBNP serum concentrations, but compromised creatinine clearance (Table 1).

Echocardiographic parameters

The deceased subjects, as compared to survivors, had diminished TAPSE, AcT, impaired RVFWLS, and RVGLS but presented more often with the 60/60 sign and a thrombus in right heart cavities (Table 2). There were no differences regarding LV parameters: LV end-diastolic diameter (LVEDd: 46 mm [42–52] vs. 42 mm [40.5–50]; $P = 0.25$), LV ejection fraction (LVEF: 57% [50–62] vs, 53.5% [32.25–60.25]; $P = 0.17$), and LV global longitudinal strain (LVGLS: –16.9% [–19.6 to –14.9] vs. –15.2% [–20.9 to –12.7]; $P = 0.67$), respectively.

Echocardiographic predictors of 30-day all-cause mortality

The presence of a thrombus in right heart cavities or the 60/60 sign strongly predicted a fatal outcome in the hazard-risk analysis — hazard ratio (HR) 10.04 (95% CI, 2.81–37.12; $P < 0.001$) and HR, 4.07 (95% CI, 1.27–12.81; $P < 0.001$), respectively. Cox models were built to predict HR for events during the first 30 days. The median time of follow-up was 30 days. Considering qualitative TTE parameters only AcT was a good predictor of death. TAPSE, RVFWLS, and RVGLS were weak predictors (AUC <0.7) (Figures 1 and 2). Considering the modified PESI models in which a single TTE parameter was added, the modification brought about only a small increase in the predictive power of AUC (Table 3). On the contrary, adding echocardiographic parameters to the PESI significantly increased their predictive values (Figure 1).

The association between echocardiographic parameters, predictors of 30-day all-cause mortality, and PESI scores

A mobile thrombus in right heart cavities and the 60/60 sign were not associated with the PESI score. To the contrary, AcT, RVFWLS, RVGLS, and TAPSE showed weak correlations with the PESI (with increasing correlation strength with Spearman rho coefficient of absolute values from 0.3 to 0.45, respectively, Table 4).

DISCUSSION

To date, the only study that has addressed the issue of extending the PESI to include TTE parameters is the one by Burgos et al. [21]. In a multicentric prospective study database, the analysis of the Argentinian CONAREC XX registry included consecutive PE patients admitted to hospitals with cardiology residency, reaching 75 sites altogether. Among 684 participants, 91% had TTE per-

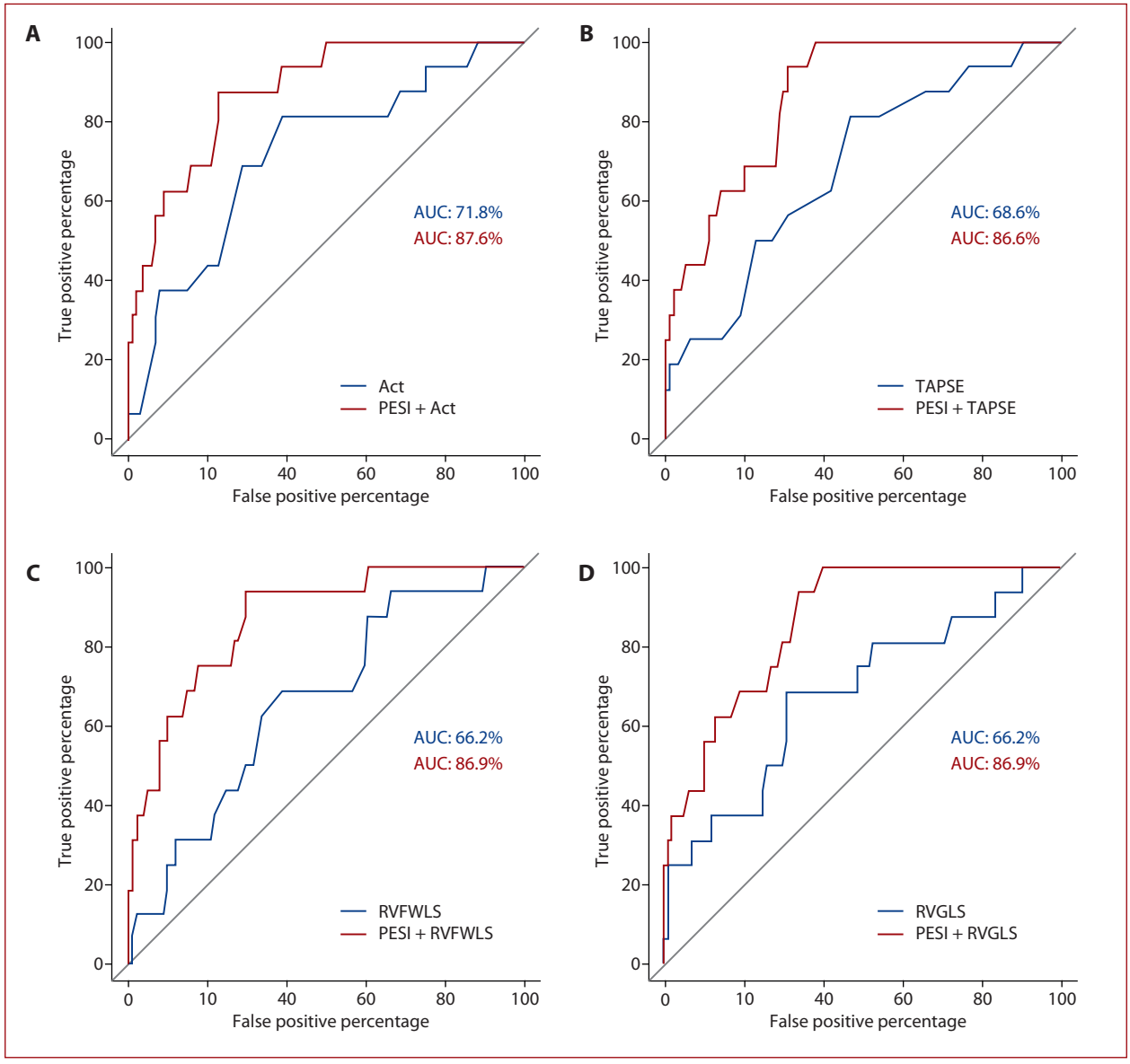

Figure 1. Comparison of receiver operating characteristic curves for echocardiographic parameters of predictive significance and models of Pulmonary Embolism Severity Index (PESI) score extended with each them

Abbreviations: AUC, area under the curve; other — see Table 2

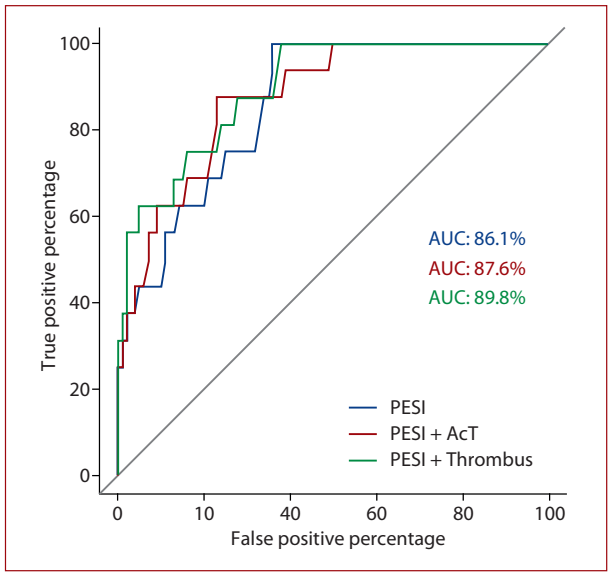

Figure 2. Comparison of receiver operating characteristic curves for PESI score and its modifications

Abbreviations: see Tables 1 and 2, and Figure 1

Table 3. Effectiveness of 6 different PESI modifications in prediction of 30-day all-cause mortality created by adding a single parameter to PESI (AUC 0.8608; *P* <0.001). Modified PESI score is obtained by adding a number of points provided in the table when a given sign is present or a given parameter exceeds the corresponding threshold value

Qualitative echocardiographic parameters Modified PESI = PESI + points if added parameter is positive				
Added parameter	**Points**	**AUC of modified PESI**	**AUC increase**	***P*-value**
Thrombus in right heart cavities	75	0.8976	0.0368	<0.001
60/60 sign	20	0.8704	0.0096	<0.001

Quantitative echocardiographic parameters Modified PESI = PESI + points if added parameter exceeds cut-off value					
Added parameter	**Cut-off**	**Points**	**AUC of modified with PESI**	**AUC increase**	***P*-value**
TAPSE, mm	18	20	0.8657	0.0049	<0.001
AcT, ms	67	30	0.8762	0.0154	<0.001
RVFWLS, %	–23	40	0.8685	0.0077	<0.001
RVGLS, %	–16	5	0.8645	0.0037	<0.001

Abbreviations: AUC, area under the curve; HR, hazard ratio; RVFWLS, right ventricle free wall longitudinal strain; TAPSE, tricuspid annular plane systolic excursion; other — see Tables 1 and 2

Table 4. The association between echocardiographic parameters and results of Pulmonary Embolism Severity Index (PESI) score

Qualitative echocardiographic parameters			
Sign	**PESI (sign present)**	**PESI (sign absent)**	***P*-value**
Thrombus in right heart cavities	95 (81–119)	78 (60.5–117.5)	0.69
60/60 sign	90 (69–117)	96 (79–119.5)	0.34
Quantitative echocardiographic parameters			
Parameter	**Spearman rho coefficient**		***P*-value**
TAPSE, mm	–0.45		<0.001
AcT, ms	–0.30		<0.001
RVFWLS, %	0.32		<0.001
RVGLS, %	0.33		<0.001

Abbreviations: See Tables 2 and 3

formed while both TAPSE and PASP could be estimated only in 355 patients (57%). PESI scores were combined with TTE parameters to produce the PESI-Echo score according to the formula: PESI + PASP – TAPSE, increasing the efficacy of mortality prediction of PESI, from AUC 0.75 to 0.82 (0.74–0.90; *P* = 0.007). The PESI-Echo score ≥128 points was the optimal cut-off for predicting mortality [21]. The PESI-Echo score has never been validated. The formula could not augment the predicting strength of PESI in our study — no differences regarding subtraction difference PASP-TAPSE between survivors and non-survivors were observed. It is noteworthy that TTE examinations in the survey by Burgos et al. [21] were conducted by numerous sonographers on various echocardiographic devices without a unified protocol, and the calculations on quite basic and reproducible TTE parameters of TAPSE and PASP could have been performed on a group slightly larger than half of the subjects. The study participants were recruited from academic centers, mainly secondary and tertiary care hospitals, and this is why the group did not represent the general PE patient population. Moreover, no diagnostic algorithm or guidelines for patient management were issued.

Assessment of RV systolic dysfunction plays an important role in predicting unfavorable outcomes in a broad array of cardiovascular disorders [23]. Unfortunately, complex RV geometry hinders determination of a universal parameter that could reliably represent RV size and function [1]. Different TTE parameters and their combinations reflecting RV dilation, RV systolic dysfunction, RV segmental cardiac contractility disorders, tricuspid valve insufficiency, and pulmonary artery blood flow related to elevated pulmonary vascular resistance have been applied to estimate prognosis in patients with acute PE (see also Table 4) [1, 13, 18–22]. Although different TTE markers show a consistent association with short-term mortality, their prognostic performance is rather poor to moderate. In our study, the AUC of TTE parameters with prognostic value (TAPSE, RVFWLS, RVGLS, and AcT) exceeded 0.7 only in the case of AcT AUC and showed only acceptable discrimination. Similar conclusions came from previous studies which included these echocardiographic markers [14, 16, 24–26]. Predominantly, TTE parameters have been shown to be inferior to composed clinical scores [27]. Importantly, what we have demonstrated is that all these 4 quantitative parameters potentially measured in all patients, i.e., TAPSE, RVFWLS, RVGLS, and AcT, correlate with PESI scores. In previous studies, the PESI score was also shown to correlate (apart from AcT) with LVEF and the pulmonary venous flow waves S/D

ratio (parameter related to clot burden and an independent mortality predictor) [28, 29]. Heart dysfunction, caused by PE and assessed with the above-described markers, might be also caused by some chronic conditions of the heart and lungs and translate into higher PESI scoring. But as opposed to TTE, PESI also includes clinical variables that have a huge impact on patient outcomes such as signs of hemodynamic incompetence, age, or chronic diseases with poor prognosis: cancer, chronic heart failure, or chronic pulmonary disease [30].

Notably, the predictive strength of PESI in our study was very high (AUC 0.86) compared to previous publications, e.g., in the aforementioned article on PESI-Echo by Burgos et al. [21], the predictive value equaled only 0.76. Moreover, lower predictive values of PESI are encountered in retrospective studies and venous thromboembolism registries (AUC 0.64–0.7), whereas single-center surveys report higher reaching even 0.925 [31–33]. These values mostly depend on study group population characteristics and data collection methods. Noteworthy, the higher value of AUC of PESI might affect the prediction effectiveness of TTE when PESI score is extended with additional TTE parameters. Analogically, the predictive value of TTE and its quality might vary among PE patients with different characteristics and can be affected by the study design [27]. Importantly, TTE assessment should be based on simple reproducible ultrasound modalities as more advanced ones, such as speckle-tracking longitudinal strain measurement, are highly operator and equipment-dependent [16, 34, 35].

The TTE findings with prognostic significance but not associated with PESI score were thrombi in right heart cavities and the 60/60 sign. Remarkably, they are the most specific ones for PE of the 6 studied. Mobile right-heart thrombi essentially confirm PE diagnosis, they might be detected by TTE, transesophageal echocardiography, or computed tomography pulmonary angiography in around 3%–5% of unselected PE patients and even in 18% of PE patients in the intensive care unit. A clot in transit within cardiac chambers is a potential source of recurrent embolism and has already been shown to be associated with higher short-term/30-day all-cause and PE-related mortality as well as 90-day mortality [36–38]. Moreover, it might indicate an increased amount of embolic material and is more often observed in patients with parallelly diagnosed deep vein thrombosis which itself is a predictor of a higher risk of in-hospital mortality of PE patients [39]. It also accompanies malignant neoplasms and COVID-19 — diseases with other pathological processes contributing to fatal outcomes [40, 41]. The 60/60 sign — combining a tricuspid regurgitation jet gradient of ≤60 mm Hg and AcT ≤60 ms has been introduced by Torbicki and Kurzyna and their colleagues [42, 43] at the turn of the century as a marker of elevated pulmonary arterial pressure related to the presence of embolic obstacles within pulmonary arteries, increased pulmonary vascular resistance as well as elevated RV strain in acute PE. In principle, a normal RV, in patients without pulmonary or left heart diseases evoking chronic pulmonary hypertension, is usually insufficient to maintain PASP >60 mm Hg [44]. The 60/60 sign has been found to be highly specific to PE diagnosis but shows poor sensitivity [43]. Its prevalence varied from 12.9% to 70.8% in different studies [45, 46]. Similarly to right heart thrombi, as those signs are present in only a few subjects, they are rarely included in prognosis assessment after PE. Nevertheless, in a recent study by Shah et al. [46], the 60/60 sign was shown to be an independent predictor of short-term mortality in patients with acute PE (odds ratio 8.13; 95% CI, 1.11–59.21; $P = 0.034$).

To conclude, as we have demonstrated, addition of TTE parameters to clinical evaluation of patients with acute PE brings benefits regarding identification of patients with RV dysfunction and helps to increase the prognostic power of clinical variables combined in the PESI score. The abnormalities concerning RV systolic dysfunction (TAPSE, TAPSE, RVFWLS, RVGLS), non-specific to PE, and elevated pulmonary artery pressure (AcT) are associated with PESI score, whereas specific ones — a mobile thrombus in right heart cavities and the 60/60 sign are not related to the PESI and act as independent predictors and valuable adjuncts to the PESI. The PESI divides patients into five categories of 30-day mortality risk. Due to the the low number of fatal events in our study, we did not try to provide such division for PESI modifications. Identification of ideal criteria for RV dysfunction is still under investigation [35, 47]. Moreover, we did not incorporate biochemical parameters in the analysis as that exceeds the scope of this article. Their inclusion and novel approach to prognosis in PE subjects, using developing technologies and artificial intelligence, are in the pipeline [27].

Study limitation

This study had a relatively low number of participants. Echocardiograms were not repeated, and thus variability of echocardiographic parameters could not be assessed. The significance of multiple echocardiographic parameters was not examined. The prognostic role of biomarkers was not investigated.

CONCLUSIONS

The addition of TTE parameters to clinical evaluation of patients with acute PE helps to identify patients with RV dysfunction and increases the prognostic power of clinical variables combined in the PESI score. The quantitative TTE parameters of RV systolic function and pulmonary artery blood flow are associated with the PESI and thus increase its predictive value to a limited extent. The presence of findings specific to PE such as a thrombus in the right heart cavity and the 60/60 sign are effective adjuncts to the PESI score.

Article information

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REFERENCES

1. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020; 41(4): 543–603, doi: 10.1093/eurheartj/ehz405, indexed in Pubmed: 31504429.
2. Meignan M, Rosso J, Gauthier H, et al. Systematic lung scans reveal a high frequency of silent pulmonary embolism in patients with proximal deep venous thrombosis. Arch Intern Med. 2000; 160(2): 159–164, doi: 10.1001/archinte.160.2.159, indexed in Pubmed: 10647753.
3. Wiliński J, Chukwu O, Ciuk K, et al. Clinical and linguistic validation of a Polish version of the Pulmonary Embolism Quality of Life Questionnaire: a disease-specific quality of life questionnaire for patients after acute pulmonary embolism. Kardiol Pol. 2021; 79(9): 1019–1021, doi: 10.33963/KP.a2021.0074, indexed in Pubmed: 34331310.
4. Pruszczyk P, Torbicki A. Pulmonary embolism. In: Szczeklik A, Gajewski P. ed. Szczeklik's Internal Medicine. Medycyna Praktyczna, Kraków 2023: 579–591.
5. Bělohlávek J, Dytrych V, Linhart A. Pulmonary embolism, part I: Epidemiology, risk factors and risk stratification, pathophysiology, clinical presentation, diagnosis and nonthrombotic pulmonary embolism. Exp Clin Cardiol. 2013; 18(2): 129–138, indexed in Pubmed: 23940438.
6. Goldhaber SZ. Assessing the prognosis of acute pulmonary embolism: tricks of the trade. Chest. 2008; 133(2): 334–336, doi: 10.1378/chest.07-2464, indexed in Pubmed: 18252908.
7. Kürkciyan I, Meron G, Sterz F, et al. Pulmonary embolism as a cause of cardiac arrest: presentation and outcome. Arch Intern Med. 2000; 160(10): 1529–1535, doi: 10.1001/archinte.160.10.1529, indexed in Pubmed: 10826469.
8. Aujesky D, Obrosky DS, Stone RA, et al. Derivation and validation of a prognostic model for pulmonary embolism. Am J Respir Crit Care Med. 2005; 172(8): 1041–1046, doi: 10.1164/rccm.200506-862OC, indexed in Pubmed: 16020800.
9. Jiménez D, Aujesky D, Moores L, et al. Simplification of the pulmonary embolism severity index for prognostication in patients with acute symptomatic pulmonary embolism. Arch Intern Med. 2010; 170(15): 1383–1389, doi: 10.1001/archinternmed.2010.199, indexed in Pubmed: 20696966.
10. Konstantinides SV, Torbicki A, Agnelli G, et al. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J. 2014; 35(43): 3033–3069, doi: 10.1093/eurheartj/ehu283, indexed in Pubmed: 25173341.
11. Barco S, Mahmoudpour SH, Planquette B, et al. Prognostic value of right ventricular dysfunction or elevated cardiac biomarkers in patients with low-risk pulmonary embolism: a systematic review and meta-analysis. Eur Heart J. 2019; 40(11): 902–910, doi: 10.1093/eurheartj/ehy873, indexed in Pubmed: 30590531.
12. Pruszczyk P, Skowrońska M, Ciurzyński M, et al. Assessment of pulmonary embolism severity and the risk of early death. Pol Arch Intern Med. 2021; 131(12): 16134, doi: 10.20452/pamw.16134, indexed in Pubmed: 34775739.
13. Cimini LA, Candeloro M, Pływaczewska M, et al. Prognostic role of different findings at echocardiography in acute pulmonary embolism: a critical review and meta-analysis. ERJ Open Res. 2023; 9(2): 00641-2022, doi: 10.1183/23120541.00641-2022, indexed in Pubmed: 37009027.
14. Wiliński J, Skwarek A, Borek R, et al. Subcostal echocardiographic assessment of tricuspid annular kick (SEATAK): A novel independent predictor of 30-day mortality in patients with acute pulmonary embolism. Kardiol Pol. 2022; 80(11): 1127–1135, doi: 10.33963/KP.a2022.0213, indexed in Pubmed: 36088580.
15. Wiliński J, Skwarek A, Borek R, et al. Right ventricular wall thickness indexed to body surface area as an echocardiographic predictor of acute pulmonary embolism in high-risk patients. Kardiol Pol. 2022; 80(2): 205–207, doi: 10.33963/KP.a2021.0180, indexed in Pubmed: 34904219.
16. Wiliński J, Skwarek A, Borek R, et al. Indexing of speckle tracking longitudinal strain of right ventricle to body surface area does not improve its efficiency in diagnosis and mortality risk stratification in patients with acute pulmonary embolism. Healthcare (Basel). 2023; 11(11): 1629, doi: 10.3390/healthcare11111629, indexed in Pubmed: 37297770.
17. Recommended Reading on Echocardiography - European Association of Cardiovascular Imaging (EACVI). https://www.escardio.org/Guidelines/Recommended-Reading/Cardiovascular-Imaging/Echocardiography (accessed: December 31, 2023).
18. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2015; 16(3): 233–270, doi: 10.1093/ehjci/jev014, indexed in Pubmed: 25712077.
19. Dzikowska-Diduch O, Kurnicka K, Lichodziejewska B, et al. A novel doppler trpg/act index improves echocardiographic diagnosis of pulmonary hypertension after pulmonary embolism. J Clin Med. 2022; 11(4): 1072, doi: 10.3390/jcm11041072, indexed in Pubmed: 35207345.
20. Alerhand S, Sundaram T, Gottlieb M. What are the echocardiographic findings of acute right ventricular strain that suggest pulmonary embolism? Anaesth Crit Care Pain Med. 2021; 40(2): 100852, doi: 10.1016/j.accpm.2021.100852, indexed in Pubmed: 33781986.
21. Burgos LM, Scatularo CE, Cigalini IM, et al. The addition of echocardiographic parameters to PESI risk score improves mortality prediction in patients with acute pulmonary embolism: PESI-Echo score. Eur Heart J Acute Cardiovasc Care. 2021; 10(3): 250–257, doi: 10.1093/ehjacc/zuaa007, indexed in Pubmed: 33620435.
22. Ciurzyński M, Kurnicka K, Lichodziejewska B, et al. Tricuspid Regurgitation Peak Gradient (TRPG)/Tricuspid Annulus Plane Systolic Excursion (TAPSE): A novel parameter for stepwise echocardiographic risk stratification in normotensive patients with acute pulmonary embolism. Circ J. 2018; 82(4): 1179–1185, doi: 10.1253/circj.CJ-17-0940, indexed in Pubmed: 29375106.
23. Cavigli L, Focardi M, Cameli M, et al. The right ventricle in "left-sided" cardiomyopathies: The dark side of the moon. Trends Cardiovasc Med. 2021; 31(8): 476–484, doi: 10.1016/j.tcm.2020.10.003, indexed in Pubmed: 33065314.
24. Kurnicka K, Lichodziejewska B, Ciurzyński M, et al. Peak systolic velocity of tricuspid annulus is inferior to tricuspid annular plane systolic excursion for 30 days prediction of adverse outcome in acute pulmonary embolism. Cardiol J. 2020; 27(5): 558–565, doi: 10.5603/CJ.a2018.0145, indexed in Pubmed: 30484266.
25. Dahhan T, Siddiqui I, Tapson VF, et al. Clinical and echocardiographic predictors of mortality in acute pulmonary embolism. Cardiovasc Ultrasound. 2016; 14(1): 44, doi: 10.1186/s12947-016-0087-y, indexed in Pubmed: 27793158.
26. Shmueli H, Steinvil A, Aviram G, et al. Re-appraisal of echocardiographic assessment in patients with pulmonary embolism: prospective blinded long-term follow-up. Isr Med Assoc J. 2020; 11(22): 688–695, indexed in Pubmed: 33249789.
27. Silva BV, Calé R, Menezes MN, et al. How to predict prognosis in patients with acute pulmonary embolism? Recent advances. Kardiol Pol. 2023; 81(7-8): 684–691, doi: 10.33963/KP.a2023.0143, indexed in Pubmed: 37366261.
28. Klasnja S, Manojlovic A, Popadic V, et al. Point-of-care echocardiographic characteristics of COVID-19 patients with pulmonary embolism. Diagnostics (Basel). 2022; 12(10): 2380, doi: 10.3390/diagnostics12102380, indexed in Pubmed: 36292069.
29. Aydınyılmaz F, Özbeyaz NB, Algül E, et al. The relationship between pesi score and pulmonary venous flow parameters in patients with acute

pulmonary embolism. Echocardiography. 2022; 39(12): 1532–1539, doi: 10.1111/echo.15483, indexed in Pubmed: 36348259.
30. Eckelt J, Hobohm L, Merten MC, et al. Long-term mortality in patients with pulmonary embolism: results in a single-center registry. Res Pract Thromb Haemost. 2023; 7(5): 100280, doi: 10.1016/j.rpth.2023.100280, indexed in Pubmed: 37601025.
31. Gerardo F, Faria D, Silvério António P, et al. PrOgnosis in Pulmonary Embolism (PoPE): 30-Day mortality risk score based on five admission parameters. Rev Port Cardiol. 2024; 43(1): 1–8, doi: 10.1016/j.repc.2023.04.011, indexed in Pubmed: 37423312.
32. El-Bouri WK, Sanders A, Lip GYH, et al. Predicting acute and long-term mortality in a cohort of pulmonary embolism patients using machine learning. Eur J Intern Med. 2023; 118: 42–48, doi: 10.1016/j.ejim.2023.07.012, indexed in Pubmed: 37487827.
33. Duarte F, Barradas MI, Oliveira L, et al. Poster No. 027 Clinical, echocardiographic, analytic and anatomical parameters: which are the main prognostic factors in hospitalized patients with acute pulmonary embolism? Cardiovascular Research. 2022; 118(Suppl 2): ii49, doi: 10.1093/cvr/cvac157.041.
34. Lee JH, Park JH, Park KI, et al. A comparison of different techniques of two-dimensional speckle-tracking strain measurements of right ventricular systolic function in patients with acute pulmonary embolism. J Cardiovasc Ultrasound. 2014; 22(2): 65–71, doi: 10.4250/jcu.2014.22.2.65, indexed in Pubmed: 25031796.
35. Pruszczyk P, Kurnicka K, Ciurzyński M, et al. Defining right ventricular dysfunction by the use of echocardiography in normotensive patients with pulmonary embolism. Pol Arch Intern Med. 2020; 130(9): 741–747, doi: 10.20452/pamw.15459, indexed in Pubmed: 32579314.
36. Barrios D, Rosa-Salazar V, Morillo R, et al. Prognostic significance of right heart thrombi in patients with acute symptomatic pulmonary embolism: systematic review and meta-analysis. Chest. 2017; 151(2): 409–416, doi: 10.1016/j.chest.2016.09.038, indexed in Pubmed: 27746202.
37. Li W, Liu ZY, Chen XX, et al. Right heart thrombus in acute pulmonary embolism: A single center experience in China. Pulm Circ. 2023; 13(3): e12291, doi: 10.1002/pul2.12291, indexed in Pubmed: 37744669.
38. Casazza F, Bongarzoni A, Centonze F, et al. Prevalence and prognostic significance of right-sided cardiac mobile thrombi in acute massive pulmonary embolism. Am J Cardiol. 1997; 79(10): 1433–1435, doi: 10.1016/s0002-9149(97)00162-8, indexed in Pubmed: 9165180.
39. Pagano T, Fabbri IS, Benedetto M, et al. Predicting in-hospital mortality in patients admitted from the emergency department for pulmonary embolism: Incidence and prognostic value of deep vein thrombosis. A retrospective study. Clin Respir J. 2024; 18(1): e13697, doi: 10.1111/crj.13697, indexed in Pubmed: 37726801.
40. Gaspar V, Silva B, Ambrioso I, et al. Right ventricle thrombus in a massive pulmonary embolism COVID-19 patient. Cureus. 2023; 15(8): e43937, doi: 10.7759/cureus.43937, indexed in Pubmed: 37746420.
41. Amin S, Shahab A, Qazi AR, et al. A rare incidence of hepatocellular carcinoma with tumor thrombus extending to the right heart. Cureus. 2023; 15(8): e43965, doi: 10.7759/cureus.43965, indexed in Pubmed: 37746383.
42. Torbicki A, Kurzyna M, Ciurzynski M, et al. Proximal pulmonary emboli modify right ventricular ejection pattern. Eur Respir J. 1999; 13(3): 616–621, doi: 10.1183/09031936.99.13361699, indexed in Pubmed: 10232436.
43. Kurzyna M, Torbicki A, Pruszczyk P, et al. Disturbed right ventricular ejection pattern as a new Doppler echocardiographic sign of acute pulmonary embolism. Am J Cardiol. 2002; 90(5): 507–511, doi: 10.1016/s0002-9149(02)02523-7, indexed in Pubmed: 12208411.
44. Goldhaber SZ, Elliott CG. Acute pulmonary embolism: part I: epidemiology, pathophysiology, and diagnosis. Circulation. 2003; 108(22): 2726–2729, doi: 10.1161/01.CIR.0000097829.89204.0C, indexed in Pubmed: 14656907.
45. Kurnicka K, Lichodziejewska B, Goliszek S, et al. Echocardiographic pattern of acute pulmonary embolism: Analysis of 511 consecutive patients. J Am Soc Echocardiogr. 2016; 29(9): 907–913, doi: 10.1016/j.echo.2016.05.016, indexed in Pubmed: 27427291.
46. Shah BR, Velamakanni SM, Patel A, et al. Analysis of the 60/60 Sign and Other Right Ventricular Parameters by 2D Transthoracic Echocardiography as Adjuncts to Diagnosis of Acute Pulmonary Embolism. Cureus. 2021; 13(3): e13800, doi: 10.7759/cureus.13800, indexed in Pubmed: 33842172.
47. Bova C, Vanni S, Prandoni P, et al. A prospective validation of the Bova score in normotensive patients with acute pulmonary embolism. Thromb Res. 2018; 165: 107–111, doi: 10.1016/j.thromres.2018.04.002, indexed in Pubmed: 29631073.