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Role of echocardiographic indicators of right ventricular dysfunction in prediction of 30-day mortality in non-high-risk patients with acute pulmonary embolism within different variants of Bova score

Short title: Bova score and echocardiographic parameters

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WHAT'S NEW?

Bova score is a validated tool of early mortality risk stratification in normotensive patients with acute pulmonary embolism and apart from clinical and biochemical variables includes echocardiographic parameters of right ventricular dysfunction. As prognostic value of echocardiographic markers of right ventricular dysfunction in this group of patients remains controversial, we have demonstrated that an appropriate selection of such parameters might

augment the prediction capability of Bova score. The most efficient echocardiographic criteria comprised the 60/60 sign and right ventricular free wall longitudinal strain >–19%.

ABSTRACT

Background: Bova score is a validated tool of short-term mortality risk stratification in normotensive patients with acute pulmonary embolism (PE). The prognostic value of echocardiographic parameters in this group of patients remains controversial.

Aims: To assess the role of echocardiographic indicators of right ventricular dysfunction in different variants of Bova score.

Methods: Patients with PE confirmed in computed tomography pulmonary angiography had transthoracic echocardiogram performed during first day of hospitalization and 30-day follow-up.

Results: One hundred eleven consecutive subjects with non-high-risk PE entered the analysis — 55 men (49.6%), with median age 69 (58–79) years; 12 patients died during the 30-day follow-up. Among 3 Bova score variants with different echocardiographic criteria used in practice the original one AD 2014 had the best but objectively poor predictive strength — area under the curve (AUC) 0.679. Bova score with right to left ventricle ratio >1 and tricuspid annular plane systolic excursion <16 mm was even poorer indicator (AUC 0.652), whereas Bova score with free wall longitudinal strain >–19% and Bova score with 60/60 sign were of fair predictability (AUC 0.701 and 0.731, respectively) but still inferior to simplified Pulmonary Embolism Severity Index (sPESI, AUC — 0.815). The subjects with Bova score variants with points >4 had higher risk of death (hazard risk of 1.43–1.59) and sPESI with ≥1 point — hazard risk of 2.02.

Conclusions: Various echocardiographic markers of right ventricular dysfunction within divergent variants of Bova score yield different prediction strength but are all inferior to sPESI score.

Key words: 60/60 sign, Bova score, echocardiography, pulmonary embolism, simplified Pulmonary Embolism Severity Index

INTRODUCTION

Venous thromboembolic disease with its clinical manifestations of pulmonary embolism (PE) and deep vein thrombosis is on the last step of the podium of the most frequent cardiovascular

diseases globally [1]. Its prevalence continues to increase and poses a serious burden to healthcare system [2]. Acute PE is associated not only with different clinical presentations, but also with diverse prognosis. The patients of low-risk PE have a mortality rate of marginal under 3%, while the ones of high-risk PE who faced cardiopulmonary arrest of dramatic more than 90% [1, 3, 4]. Furthermore, the survivors of acute PE might suffer from complications concerning various fields of life, not only related to health with heart failure or chronic thromboembolic pulmonary hypertension, but also to different aspects of wealth: employment, the environment, mental health, education, recreation and leisure time and social belonging [5, 6]. Consequently, early diagnosis and accurate risk stratification for determining the appropriate therapeutic management approach is pivotal.

According to the European Society of Cardiology (ESC) guidelines, the PE patients who present without hemodynamic instability are to be stratified according to two sets of prognostic criteria: clinical, imaging, and laboratory indicators of PE severity that are related to the presence of right ventricle's (RV) dysfunction and comorbidities and other aggravating conditions that could adversely affect early prognosis. Noteworthy, transthoracic echocardiography (TTE), non-invasive, widely available tool is not recommended in a routine work-up in hemodynamically stable patients with suspected or diagnosed PE [1]. However, the use of TTE helps to diagnose the dysfunction of RV, even clinically silent, and thus help to identify patients at increased risk of hemodynamic deterioration and early mortality since short-term outcome in those patients is closely related to RV failure. Therefore, TTE seems to be an underestimated and underutilized tool in this field [7, 8].

As stand-alone parameters may not suffice to classify PE severity, various combinations of clinical, imaging and laboratory parameters were used to build prognostic scores which allow at least a semi-quantitative assessment of short-term mortality risk in non-high-risk PE patients. The scores such as Pulmonary Embolism Severity Index (PESI) and its simplified version (sPESI), Bova score and FAST score based on heart-type fatty acid-binding protein (H-FABP) or high-sensitivity troponin T have been validated in randomized trials [9–15].

Importantly, it is sPESI that shows the highest discriminatory performance concerning 30-day all-cause mortality in low to intermediate risk PE [16]. Interestingly, the only one of them which incorporates TTE parameters is Bova score which is intended for non-high risk PE patients. Noteworthy, various constellations of TTE parameters of RV dysfunction were included in the different variants of this score. In principle, the Bova prognostic model includes elevated cardiac troponin (2 points), RV dysfunction (detected in TTE or computed tomography pulmonary angiography with different criteria, 2 points), heart rate ≥110 bpm (1 point), systolic

blood pressure 90–100 mm Hg (2 points), with the result of ≤4 points for low risk and >4 points for intermediate-high risk [1]. It is an open question, to what extent TTE might augment the prognostic stratification as a part of Bova score?

The aim of the study is to assess different echocardiographic indicators of RV dysfunction in prediction of 30-day mortality in non-high-risk patients with acute pulmonary embolism within different variants of Bova score.

MATERIAL AND METHODS

Methodology

This was a cross-sectional observational single-center study. The study group consisted of consecutive patients of the Internal Medicine Department and the Special Care Cardiac Unit with acute PE, of low to intermediate risk according to ESC, confirmed in computed tomography pulmonary angiography between August 1, 2018 and April 30, 2021. The treatment regimen followed the guidelines on PE management of ESC and was described thoroughly previously [1, 17, 18].

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

A standard diagnostic protocol comprised determination in all patients on the day of admission to the ward the laboratory parameters including i.e. serum concentrations of troponin T, N-terminal pro-B-type natriuretic peptide (NT-proBNP) and D-dimer with laboratory methods summarized formerly [18]. 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 [18–21]. The measurements were made based on the current guidelines of European Association of Cardiovascular Imaging with real-time electrocardiographic recording performed to precisely define the phases of the heart cycle [22]. The measurements of RV longitudinal strain by two-dimensional speckle-tracking echocardiography were executed within six segments of RV at the same time in the apical 4-chamber view as described before [20, 23]. RV free wall longitudinal strain (RVFWLS) as the average value of the strain of 3 RV free wall segments and RV global longitudinal strain (RVGLS) as the average value of the strain of all 6 RV segments (free wall and septal ones) were calculated. Based on previous

studies results, the TTE parameters whose abnormal values indicate RV dysfunction were included in the analysis [8, 18–21].

Three different Bova score variants with various RV dysfunction criteria used in practice were included: (1) AD 2014: the one with original RV dysfunction criteria: end-diastolic diameter >30 mm from the parasternal view or the RV appearing larger than the left ventricle (LV) from the subcostal or apical view (RV:LV >1), hypokinesis of the RV free wall (any view), or peak tricuspid regurgitation velocity 2.6 m/s from the apical or subcostal 4-chamber view [11, 13] and its modified versions: (2) AD 2016: RV dysfunction considered when at least two of the following were present: dilatation of the RV (end-diastolic diameter >30 mm from the parasternal view or the RV appearing larger than the LV from the subcostal or apical view — RV:LV >1), hypokinesis of the RV free wall (any view), and estimated systolic pulmonary artery pressure over 30 mm Hg [24] and (3) AD 2018: at least one of the following criteria was fulfilled: RV end-diastolic diameter >30 mm (parasternal long-axis or short-axis view), RV/LV end-diastolic diameter — RV:LV >0.9 (apical or subcostal 4-chamber view), RV free wall hypokinesis from any view, tricuspid systolic velocity > 2.6 m/s from the apical or subcostal 4-chamber view [25].

For comparisons also other models of Bova score were created in which the echocardiographic criteria with TTE parameters indicating RV dysfunction that differed the groups of survivors and non-survivors in our analysis with *P*-value of ≤0.2 were considered (Table 2). Their predictive efficiency was tested along with the one of sPESI score. The dichotomous approach to scores interpretation was adopted from ESC guidelines along with cut-off values of Bova (≤4 vs. >4 points) and sPESI (0 vs. ≥1 point) scores [1].

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 [18].

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

Statistical analysis

With the Shapiro–Wilk test the normality of distribution was disproved. Subsequently, quantitative variables are expressed as median with interquartile range whereas Mann–Whitney U-test was utilized for their comparisons. Qualitative variables are expressed as numbers (percentage) and the Fisher test or χ^2 test were used for their comparisons, when adequate. Standard receiver operating characteristic analysis was performed, area under the curve (AUC)

was calculated for quantitative parameters and scores' points. Sensitivity, specificity and accuracy and the corresponding 95% confidence interval (CI) were determined. Youden index was used to calculate optimal cut-off values. Cox-proportional hazard models were built; only univariate models were created due to low number of fatal events. We calculated the hazard risk (HR) for the event of death during the 30-day observation.

Two-sided *P*-values <0.05 were considered statistically significant. Statistical analysis was executed with the R Project for Statistical Computing version 4.3.0 (The R Foundation for Statistical Computing, Free Software Foundation Inc., Vienna, Austria).

RESULTS

The study group comprised 132 consecutive patients with confirmed PE. Six patients had high risk PE. Fifteen subjects had echocardiograms of poor quality. In effect, 111 subjects — 55 men (49.6%), with median age 69 (58–79) years — were eligible to enter the analysis. Baseline characteristics and selected biochemical parameters are presented in Table 1.

During 30-day follow-up 12 patients died. Six patients died due to heart failure. In the next 6 subjects PE contributed to death by aggravating other decompensated diseases: pneumonia in 3, kidney failure in 1 and disseminated neoplastic disease in 2. None of the study participants required rescue thrombolysis in the observational period.

The patients who died during the follow-up compared to survivors were older and had increased troponin T and NT-proBNP serum concentrations (Table 1).

Echocardiographic parameters

The deceased patients as compared to survivors presented more often with 60/60 sign. In the comparisons between subjects of opposite prognosis 3 other TTE parameters reached the assumed statistical probability value: RV:LV >1 and tricuspid annular plane systolic excursion(TAPSE) <16 mm, RVFWLS, RVGLS (Table 2).

Prediction efficiency

All these TTE markers were then used to build 4 separate Bova score variants and along with the 3 variants of Bova score used previously in the literature were altogether tested for their prediction efficiency compared to sPESI. The optimal estimated cut-off value for RVFWLS was –19% and for RVGLS was –17%. All scores but not Bova 2016 version had predictive value in our analysis. The only score with good predictive value (exceeding 0.8) measured with AUC was sPESI and with fair strength (exceeding 0.7) — Bova score with 60/60 sign and Bova

score with RVFWS >–19% [26]. Bova scores showed lower sensitivity and higher specificity while sPESI "*vice-versa*". All the scores showed high negative predictive value and low positive predictive value. The share of correctly classified patients was low in Bova AD 2014, 2016 and 2018 score variants and definitely higher in sPESI, Bova scores with 60/60 sign, with RVFWS >–19% and with RVGLS >–17% (Table 3).

The subjects with Bova score variants with points >4 had higher risk of death (HR of 1.43–1.59), apart from Bova score AD 2016 version which did not show significant association, and sPESI with ≥1 point had higher mortality rate with HR of 2.02 (Table 4).

DISCUSSION

Short-term outcome in acute PE is mainly determined by the hemodynamic status. Not surprisingly, RV dysfunction specified as the presence of signs of RV pressure overload on imaging examinations (echocardiography or computed tomography) among low-risk patients, or alternatively as myocardial injury based on elevated cardiac troponins or natriuretic peptides has been shown to be associated with an increased risk of mortality [27]. As for echocardiography, numerous studies have shown consistent associations between various TTE parameters and short-term mortality in unselected patients with acute PE [18, 20, 28–30].

Interestingly, RV dysfunction has no generally accepted definition. In the paper by Pruszczyk et al. [31] on 490 normotensive individuals with PE the combined RV dysfunction criterion of RV to LV ratio >1 with TAPSE <16 mm showed a positive predictive value of 23.3% with a high negative predictive value of 95.6% regarding the composite end-point of PE-related mortality, hemodynamic collapse or rescue thrombolysis with significant HR 6.5 (95% CI, 3.2–13.3; P <0.001). Importantly, the recent meta-analysis performed to assess the role of different definitions of RV dysfunction and of its individual parameters as predictors of death demonstrated that at TTE RV dysfunction, regardless of its criteria, was associated with increased risk of death (risk ratio 1.49; 95% CI, 1.24–1.79; $I^2 = 64\%$) and PE-related death (risk ratio 3.77; 95% CI, 1.61–8.80; $I^2 = 0\%$) in all-comers with PE, and with death in hemodynamically stable patients (risk ratio 1.52; 95% CI, 1.15–2.00; $I^2 = 73\%$). In patients with PE, increased RV to LV ratio and TAPSE but not increased RV diameter were associated with death, whereas in hemodynamically stable patients RV to LV ratio and TAPSE were not significantly associated with mortality. The authors of this meta-analysis concluded that as the appraisal of RV dysfunction with TTE is a useful tool for risk stratification in all-comers with acute PE and in hemodynamically stable patients, the prognostic value of individual parameters of RV dysfunction in hemodynamically stable patients remains controversial [8]. Noteworthy,

those studies focused only on the parameters of classic TTE including ventricles' diameters, interventricular septum flattening, RV hypokinesis, TAPSE and tricuspid valve peak systolic gradient's appraisal and their combinations. Neither the discussed analyses incorporated 60/60 sign nor longitudinal strain assessment of RV.

The 60/60 sign which combines a tricuspid regurgitation jet gradient of ≤60 mm Hg and pulmonary ejection acceleration time ≤60 ms serves as a marker of elevated pulmonary arterial pressure related to the presence of embolic obstacles within pulmonary arteries with subsequent increased pulmonary vascular resistance along with elevated RV wall strain in acute PE [32, 33]. A healthy RV in patients without chronic pulmonary or left heart diseases evoking pulmonary hypertension is usually insufficient to maintain pulmonary artery systolic pressure >60 mm Hg [34]. The prevalence of 60/60 sign in acute PE ranged from 12.9% to 70.8% in various studies [35, 36]. The sign is highly specific to PE diagnosis but is characterized by poor sensitivity [32]. It is also a useful TTE finding to differentiate acute PE and chronic pulmonary hypertension [37]. Since 60/60 sign is observed in a small percentage of all-comers with PE, it is seldom included in prognosis assessment after PE. Interestingly, in a recent survey the 60/60 sign was an independent predictor of short-term mortality in patients with acute PE (odds ratio 8.13; 95% CI, 1.11–59.21; $P = 0.034$) [36].

In an Australian study difference in RVFWLS between PE subjects and healthy individuals was a great discriminator for PE. In comparative multiple logistic regression models for PE, RVFWLS produced a powerful classifier (AUC 0.966; sample entropy 0.013; $P < 0.022$) with significantly better performance than the model which included traditional measures of RV size and function but without RVFWLS [38]. Moreover, in a recent prospective study RVFWLS was found to be the most common abnormal echocardiographic marker of RV dysfunction in patients with acute PE. RVFWLS correlated with D-dimer and NT-proBNP concentrations and differed significantly between patients with a sPESI of low risk and those of high risk ($P < 0.001$) [39]. In the publication by Dahhan et al. [29] RVFWLS and RVGLS, in addition to Tei index, were the only TTE predictors of mortality after acute PE, whereas in the paper by Lee et al [40] RVFWLS and RVGLS independently predicted in-hospital events: all-cause death, need of additive treatments such as thrombolysis or pulmonary artery thromboembolectomy, and need of inotropic agents due to unstable hemodynamic status. RVFWLS was also a predictor of mortality after acute PE in one-year follow-up [41]. Importantly, the value of RVGLS is more than RVFWLS affected by the disorders of LV and especially conditions influencing the performance of interventricular septum, including coronary artery diseases and chronic heart failure, thus RVFWLS appears to be more accurate

in PE. On the other hand, despite growing clinical usefulness of longitudinal strain of myocardium appraisal, it is currently not the part of a routine TTE examination in many echocardiographic laboratories [38, 42].

Nevertheless, considering predictive value, generally the performance of TTE parameters is moderate at best when compared to composed clinical scores and their incorporation into clinical scores does not bring the expected benefits [21, 43]. First, RV dysfunction might be also evoked by some preexisting chronic conditions of the heart and lungs not only by acute PE. Second, composed scores include clinical variables that can hugely impact the outcome such as signs of hemodynamic incompetence, age or chronic diseases with poor prognosis: cancer, chronic heart failure, or chronic pulmonary disease, etc. [44]. Third, what has been recently demonstrated in the example of PESI, quantitative TTE parameters whose incorrect values reflect RV dysfunction like TAPSE, RVFWLS, RVGLS correlated with PESI scores and therefore augmented its predictive value to the limited extent when added to PESI scale. On the contrary, thrombus in the right heart cavity and the 60/60 sign did not correlate with PESI score and as PESI adjuncts they independently predicted fatal outcomes: thrombus with HR 10.04 (95% CI, 2.81–37.12; P <0.001) and 60/60 sign with HR 4.07 (95% CI, 1.27–12.81; P <0.001) [21].

To summarize, various TTE markers of RV dysfunction within divergent variants of Bova score models in non-high-risk patients with PE yield different prediction strength but are all inferior to sPESI score. Among Bova score TTE variants the most efficient ones include Bova with 60/60 sign and Bova with RVFWLS >–19%. The holistic approach to assessment of prognosis including clinical characteristics, diagnostic imaging but also biochemical markers is reasonable. Additional clinical information could improve predictability that is not provided by a single scoring system [45].

CONCLUSIONS

Different criteria of RV dysfunction as components of the Bova score in hemodynamically stable patients with acute pulmonary embolism affect its prognostic efficacy but to a limited extent. The assessment of tricuspid regurgitation jet gradient with pulmonary ejection acceleration time and the longitudinal strain of the free wall of RV provides the most valuable markers of RV dysfunction in prognostic value of Bova score. However, they are of less strength than sPESI score.

Study limitation

The study has a relatively low number of participants. Variability of echocardiographic parameters could not be assessed as echocardiograms were not repeated. The prognostic role of biomarkers was not investigated.

Article information

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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 = 111)	**Survivors (n = 99)**	**Non-survivors (n = 12)**	***P*-value**
Male, n (%)	55 (49.55)	52 (52.53)	3 (25)	0.12
Age, years, median (IQR)	69 (58–79)	67 (57–79)	74 (68.75–83.75)	0.02
Body mass index, kg/m^2, median (IQR)	27.55 (25.09–31.22)	27.55 (25.09–31.12)	27.3 (25.24–32.64)	0.98
Arterial hypertension, n (%)	68 (61.26)	61 (61.62)	7 (58.33)	0.83
Hyperlipidemia, n (%)	40 (36.04)	37 (37.37)	3 (25)	0.53
Diebetes, n (%)	24 (21.62)	20 (20.2)	4 (33.33)	0.29
Coronary artery disease, n (%)	24 (21.62)	22 (22.22)	2 (16.67)	0.87
Chronic heart failure, n (%)	29 (26.13)	24 (24.24)	5 (41.67)	0.24
Atrial fibrillation (present or prior), n (%)	14 (12.61)	12 (12.12)	2 (16.67)	0.65
Stroke, n (%)	2 (1.8)	2 (2.02)	0 (0)	0.81
Smoking, n (%)	10 (9.01)	9 (9.09)	1 (8.33)	0.96
Chronic lung disease, n (%)	8 (7.21)	7 (7.07)	1 (8.33)	0.93
Malignancy, n (%)	22 (19.82)	18 (18.18)	4 (33.33)	0.21
Infection, n (%)	36 (32.43)	31 (31.31)	5 (41.67)	0.47
Troponin T, pg/ml, median (IQR)	22 (10.78–44.78)	19.9 (9.94–44.08)	35.56 (19.75–79.66)	0.04
NT-proBNP, pg/ml, median (IQR)	589 (155.5–2913)	529 (141.5–2630.5)	2476 (1212.25–6106.25)	0.02

D-dimer, ng/ml, median (IQR)	4701 (2226.5–7817)	4701 (2168–8142.5)	4737 (3913–6348.75)	0.91
Creatinine clearance, mL/min, median (IQR)	82.4 (65.5–105.7)	83 (69.2–104.97)	65.5 (45.1–125.6)	0.34
sPESI, points, median (IQR)	1 (0–2)	1 (0–2)	3 (1.75–3.25)	<0.001
Bova score AD 2014, points, median (IQR)	4 (2–4)	4 (2–4)	4 (3.75–5)	0.03

Abbreviations: IQR, interquartile range; NT-proBNP, N-terminal pro-B-type natriuretic peptide; sPESI, Simplified Pulmonary Embolism Severity Index

Table 2. Selected echocardiographic parameters in patients with acute pulmonary embolism

	All subjects (n = 111)	**Survivors (n = 99)**	**Non-survivors (n = 12)**	***P*-value**
LVTD, mm, median (IQR)	44 (39–48)	44 (40–48)	40 (37.75–46.25)	0.22
LVEF, %, median (IQR)	56 (50.5–62)	57 (50.5–62)	55.5 (48.5–60.25)	0.52
RVTD/LVTD, median (IQR)	0.92 (0.83–1.05)	0.92 (0.83–1.05)	0.94 (0.85–1.03)	0.96
TAPSE, mm, median (IQR)	21 (17–24)	21 (17–24)	19.5 (16–20.5)	0.24
RVTD/LVTD>1 and TAPSE<16 mm, n (%)	8 (7.21)	6 (6.06)	2 (16.67)	0.18
60/60 sign, n (%)	21 (18.92)	16 (16.16)	5 (41.67)	0.03
TRPG, mm Hg, median (IQR)	31.36 (25–43.56)	31.36 (25–43.56)	31.4 (23.59–42.28)	0.79
McConnell sign or RV hipokinesis, n (%)	21 (18.92)	18 (18.18)	3 (25)	0.70
RV FAC, %, median (IQR)	39.09 (30.48–46.38)	39.09 (29.41–47.36)	39.13 (37.16–41.1)	0.97
RVFWLS, %, median (IQR)	–20 (–15 to –24.33)	–20 (–15.33 to –24.33)	–17.83 (–12.75 to –21.58)	0.19
RVGLS, %, median (IQR)	–19 (–15.33 to –22)	–19.08 (–15.46 to –22.04)	–16.17 (–13.75 to –20.08)	0.16

Abbreviations: LVTD, left ventricular transverse diameter; RV FAC, right ventricle fraction area change; RVFWLS, right ventricle free wall longitudinal strain; RVGLS, right ventricle global longitudinal strain; RVTD, right ventricular transverse diameter; TAPSE, tricuspid annular plane systolic excursion; TRPG, tricuspid valve peak systolic gradient; other — see Table 1

Table 3. Efficiency of different clinical scores and their modifications in predicting fatal outcome in non-high-risk patients with acute pulmonary embolism within 30-day follow-up. The dichotomous approach to scores was used (sPESI: 0 vs. ≥1 points; all Bova scores: ≤4 vs. >4 points)

	AUC, value, (95% CI)	**Sensitivity, value, (95% CI)**	**Specificity, %, value, (95% CI)**	**Positive predictive value, %, value, (95% CI)**	**Negative predictive value, %, value, (95% CI)**	**Correctly classified, n (%)**	***P*-value**
sPESI score	0.815 (0.706, 0.925)	75 (42.81–94.51)	71.72 (61.78–80.31)	71.72 (61.78–80.31)	95.95 (88.61–99.16)	80 (72.07)	<0.001
Bova score AD 2014	0.679 (0.523, 0.835)	44.44 (34.45–54.78)	75 (42.81–94.51)	14.06 (6.64–25.02)	93.62 (82.46–98.66)	53 (47.75)	0.03
Bova score modification AD 2016	0.597 (0.419, 0.775)	41.67 (15.17–72.33)	60.61 (50.28–70.28)	11.36 (3.79–24.56)	89.55 (79.65–95.7)	65 (58.56)	0.26
Bova score modification AD 2018	0.675 (0.518, 0.833)	43.43 (33.5–53.77)	75 (42.81–94.51)	13.85 (6.53–24.66)	93.48 (82.1–98.63)	52 (46.85)	0.03
Bova score with RVTD/LVTD >1 and TAPSE <16 mm	0.652 (0.486, 0.818)	25 (5.49–57.19)	91.92 (84.7–96.45)	27.27 (6.02–60.97)	91 (83.6–95.8)	94 (84.68)	0.03
Bova score with 60/60 sign	0.731 (0.586, 0.877)	41.67 (15.17–72.33)	84.85 (76.24–91.26)	25 (8.66–49.1)	92.31 (84.79–96.85)	89 (80.18)	0.01
Bova score with RVFWLS >–19%	0.701 (0.529, 0.874)	41.67 (15.17–72.33)	81.82 (72.8–88.85)	21.74 (7.46–43.7)	92.05 (84.3–96.74)	86 (77.48)	0.02
Bova score with RVGLS >–17%	0.663 (0.496, 0.83)	16.67 (2.09–48.41)	93.94 (87.27–97.74)	25 (3.19–65.09)	90.29 (82.87–95.25)	95 (85.59)	0.053

Abbreviations: AUC, area under the curve; CI, confidence interval; other — see Tables 1 and 2

Table 4. Hazard risk analysis of different scores in predicting 30-day all-cause mortality in patients with acute pulmonary embolism. The dichotomous approach to scores was used (sPESI: 0 vs ≥1 points; all Bova scores: ≤4 vs >4 points)

	Hazard risk	**95% confidence interval**	***P*-value**
sPESI	2.02	1.38–2.95	<0.001
Bova score AD 2014	1.59	1.05–2.38	0.03
Bova score modification AD 2016	1.22	0.89–1.67	0.21
Bova score modification AD 2018	1.58	1.05–2.38	0.03
Bova score with RVTD/LVTD >1 and TAPSE <16 mm	1.46	1.04–2.05	0.03
Bova score with 60/60 sign	1.43	1.10–1.85	0.01
Bova score with RVFWLS >–19%	1.45	1.04–2.02	0.03
Bova score with RVGLS >–17%	1.49	1.02–2.18	0.04

Abbreviations: see Tables 1 and 2

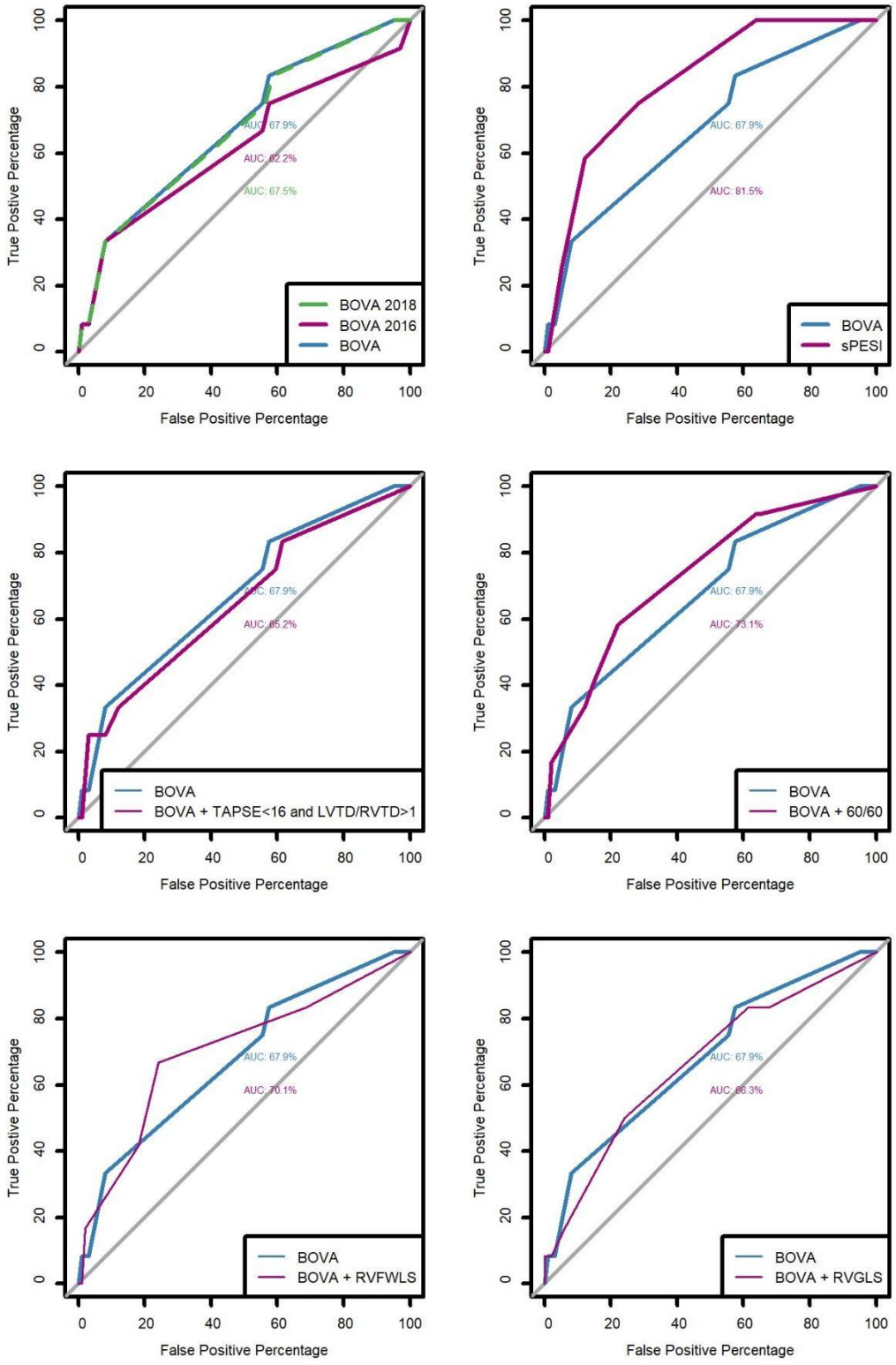

Figure 1. Comparison of receiver operating characteristic curves for simplified Pulmonary Embolism Severity Index (PESI) and different models of Bova score with various echocardiographic parameters of right ventricular dysfunction

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