

Prognostic Value of Echocardiography in Normotensive Patients With Acute Pulmonary Embolism

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OBJECTIVES The goal of the study was to evaluate the prognostic value of echocardiographic indices of right ventricular dysfunction (RVD) for prediction of pulmonary embolism–related 30-day mortality or need for rescue thrombolysis in initially normotensive patients with acute pulmonary embolism (APE).

BACKGROUND There is no generally accepted echocardiographic definition of RVD used for prognosis in APE.

METHODS We studied the prognostic value of a set of echocardiographic parameters in 411 consecutive patients (234 women, age 64 ± 18 years) with APE hemodynamically stable at admission.

RESULTS Thirty-day APE-related mortality was 3% (14 patients), all-cause mortality was 5% (21 patients). Nine patients received thrombolysis as a result of hemodynamic deterioration, and 7 of them survived. The clinical endpoint (CE), which included APE-related death or thrombolysis, occurred in 21 patients. At univariable Cox analysis, the hazard ratio (HR) for CE of the right ventricular (RV)/left ventricular (LV) ratio was 7.3 (95% confidence interval [CI]: 2.0 to 27.3; $p = 0.003$). However, multivariable analysis showed that tricuspid annulus plane systolic excursion (TAPSE) was the only independent predictor (HR: 0.64, 95% CI: 0.54 to 0.7; $p < 0.0001$). Moreover, the area under the curve (AUC) in receiver-operating characteristic analysis for TAPSE (0.91, 95% CI: 0.856 to 0.935; $p = 0.0001$) in CE prediction was higher ($p < 0.001$) than AUC of RV/LV ratio (0.638, 95% CI: 0.589 to 0.686; $p = 0.001$). TAPSE ≤ 15 mm had a HR of 27.9 (95% CI: 6.2 to 124.6; $p < 0.0001$) and a positive predictive value (PPV) of 20.9% for CE with a 99% negative predictive value (NPV), whereas TAPSE ≤ 20 mm had a PPV of 9.2 with a 100% NPV. RV/LV ratios of >0.9 and >1.0 had a PPV of 13.2% and 14.4% and a NPV of 97% and 94.3%, respectively.

CONCLUSIONS TAPSE is preferable to the RV/LV ratio for risk stratification in initially normotensive patients with APE. TAPSE ≤ 15 mm identifies patients with an increased risk of 30-day APE-related mortality, whereas TAPSE >20 mm can be used for identification of a very low-risk group. (J Am Coll Cardiol Img 2014;7:553–60) © 2014 by the American College of Cardiology Foundation

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Manuscript received October 8, 2013; revised manuscript received November 11, 2013, accepted November 15, 2013.

Although short-term prognosis in acute pulmonary embolism (APE) predominantly depends on the patient's hemodynamic status and comorbidities (1,2), right ventricular dysfunction (RVD) and injury also have a significant prognostic value in hemodynamically stable APE patients (3-5). Right ventricular (RV) enlargement, detected at echocardiography in approximately 30% of normotensive patients with APE (6-8), is regarded as a predictor of poor clinical outcome, even in initially stable patients. American Heart Association guidelines on submassive pulmonary embolism arbitrarily proposed that RVD should be diagnosed when the right ventricular to left ventricular (LV) end-diastolic ratio (RV/LV) measured by echocardiography or tomography exceeds 0.9 (1).

However, a wide range of criteria for RVD on echocardiography were used in different studies (1,2,9,10). Moreover, to our knowledge, no direct comparison of echocardiographic criteria for short-term risk prognosis in APE is available. Therefore, we analyzed the prognostic value of clinically used echocardiographic parameters of RVD for prediction of pulmonary embolism (PE)-related 30-day mortality or need for rescue thrombolysis in initially normotensive patients with APE, and compared their prognostic value with the value of RV/LV ratio, the most frequently used RVD parameter.

ABBREVIATIONS AND ACRONYMS

APE = acute pulmonary embolism

AUC = area under the curve

CE = clinical endpoint

CI = confidence interval

HR = hazard ratio

LV = left ventricle/ventricular

NPV = negative predictive value

PPV = positive predictive value

ROC = receiver-operating characteristic

RV = right ventricle/ventricular

RVD = right ventricular dysfunction

TAPSE = tricuspid annular systolic plane excursion

MATERIALS AND METHODS

Patients and management of APE. The study group comprised 411 consecutive patients with symptomatic APE, hemodynamically stable at admission, who were diagnosed and treated in our department. PE was confirmed by contrast-enhanced multidetector computed tomography when thromboemboli were visualized in an at least segmental pulmonary artery. On admission, all patients had a systemic systolic blood pressure of at least 90 mm Hg and showed no signs of peripheral hypoperfusion. APE was diagnosed when symptoms of PE had been present for no longer than 14 days before the diagnosis. Patients with diagnosed chronic thromboembolic hypertension and participants in therapeutic clinical trials were not included in this study.

Echocardiography. Routine transthoracic echocardiography for the assessment of RVD was performed and interpreted according to a standardized protocol by an experienced physician using a

Philips iE33 or Philips HD11XE system (Philips Medical Systems, Best, the Netherlands), as soon as possible after admission. The examinations were digitally recorded. RV and LV diastolic diameters were measured in the parasternal long-axis view. In the apical 4-chamber view, LV and RV diastolic diameters were measured at the level of the mitral and tricuspid valve tips during late diastole (defined by the electrocardiogram R-wave), and the presence of McConnell's sign was assessed (11,12). Left ventricular ejection fraction was assessed using Simpson's method (13). Tricuspid annular plane systolic excursion (TAPSE) was assessed in the M-mode presentation by placing a cursor in the tricuspid annulus and measuring the amount of longitudinal motion of the annulus at peak systole (12). Tricuspid valve regurgitation was qualitatively assessed by color Doppler, and peak gradient was calculated using a simplified Bernoulli's formula, using tricuspid regurgitant flow peak velocity. In the short parasternal axis, flattening of the interventricular septum was assessed qualitatively, and acceleration time of pulmonary ejection and peak pulmonary valve systolic velocity were measured in the RV outflow tract, proximal to the pulmonary valve. The examination was completed by measurement of the inferior vena cava at late expiration.

Echocardiography was performed immediately on admission in 193 patients, within 24 h in 159 patients, and between 24 and 72 h after admission in 59 patients.

Submassive (intermediate-risk) APE was diagnosed when RVD was diagnosed at echocardiography, whereas the remaining subjects formed the low-risk group. Pre-defined RVD was diagnosed when echocardiography showed: 1) RV free wall hypokinesis and RV/LV >0.9 in the 4-chamber apical view; and/or 2) an elevated tricuspid valve pressure gradient exceeding 30 mm Hg with a shortened acceleration time of pulmonary ejection below 80 ms.

The clinical endpoint (CE) of the study was defined as a combination of 30-day APE-related mortality and/or rescue thrombolysis in patients with hemodynamic deterioration, which was defined by occurrence of at least 1 of the following: 1) the need for cardiopulmonary resuscitation; 2) systolic blood pressure below 90 mm Hg for at least 15 min, with signs of end-organ hypoperfusion; or 3) the need for intravenous catecholamines in vasopressor doses.

This observational study was approved by the local ethics committee.

Statistical analysis. This is a prospective observational cohort study. Data characterized by a normal distribution are expressed as means followed by SD. Parameters without such a distribution are expressed as medians with maximum minimum ranges. Student *t* test or Mann-Whitney *U* test was used for comparisons between 2 groups, whereas comparisons between more than 2 groups were performed by analysis of variance or Kruskal-Wallis tests. The chi-square test was used to compare discrete variables (with Yates' correction when needed). Receiver-operating characteristic (ROC) curves were analyzed to assess the optimal cutoff values of echocardiographic parameters for the CE.

Two different cutoff values of echocardiographic parameters were defined: 1 that identifies patients with a good prognosis (i.e., with a high negative predictive value [NPV] for the CE), and 1 that identifies subjects at risk (i.e., with a high positive predictive value [PPV] for the CE).

Sensitivity, specificity, PPV, and NPV were calculated for the chosen cutoff value. Kaplan-Meier analysis was used to investigate cumulative 30-day survival free of the CE. The impact of echocardiographic parameters on CE was evaluated using univariable Cox proportional-hazards regression. Forward stepwise selection with a 0.1 level for staying in the model was used to identify significant predictors in multivariable analysis. Areas under the ROC curves were compared pairwise according to DeLong et al. (14). All tests were 2-sided. Data were considered significant at *p* < 0.05. The STATISTICA data analysis software system (2011, version 10, StatSoft, Tulsa, Oklahoma) and MedCalc software (version 11.0.0.0, Ostend, Belgium) were used for statistical calculations. The study protocol was approved by the local ethics committee.

RESULTS

Patient characteristics and clinical course. The study included 411 consecutive patients with APE (234 women and 177 men, age 64 ± 18 years). There were 241 patients (58.6%) with submassive APE, and 170 patients (41.4%) with low-risk APE (1) (Table 1). All patients were initially given anticoagulation agents with body mass-adjusted low-molecular-weight heparin or activated partial thromboplastin time-adjusted unfractionated heparin intravenous infusion. Urgent thrombolysis was performed in 9 (3.7%) of 241 patients from the submassive group, 7 of them survived. Clinical deterioration was observed in all these cases, and the time from starting anticoagulation to thrombolysis

Table 1. Clinical Characteristics of Studied Patients With APE

	All Patients (N = 411)	APE-Related Mortality or Thrombolysis (n = 21)	p Value	Remaining Patients (n = 390)
Female/male	234/177	14/7	0.48	220/170
Age, yrs	64 ± 18	70 ± 22	0.13	64 ± 18
HR 1 beat/s	87 ± 19	102 ± 24	0.0002	87 ± 18
Systemic blood pressure, mm Hg	128 ± 20	120 ± 24	0.04	129 ± 20
Comorbidities (COPD, CHF, neoplasm)	142 (35)	9 (43)	0.56	133 (34)
Thrombolysis, %	2	43	—	0
Troponin, ng/ml	0.03 (0.00–5.58)	0.28 (0.00–0.98)	0.014	0.03 (0.00–0.58)
Troponin positive	224 (54)	17 (81)	0.02	207 (53)
NT-proBNP, pg/ml	685 (20–29,071)	4,872 (2,043–25,000)	0.0003	649 (20–29,071)

Values are n, mean ± SD, n (%), or median (maximum–minimum range). Comorbidities were defined as the presence of 1 of chronic obstructive pulmonary disease (COPD), chronic heart failure (CHF), or history of cancer. Troponins were considered positive at levels >0.01 ng/ml.
 APE = acute pulmonary embolism; HR = heart rate; NT-proBNP = N-terminal pro-B-type natriuretic peptide.

ranged from 1 h to 168 h (median 15 h). No patients from the low-risk group received thrombolysis. Vitamin K antagonists were administered to the majority of patients following hemodynamic stabilization, with a target international normalized ratio of 2 to 3.

The 30-day APE-related mortality was 3% (n = 14), whereas all-cause mortality was 5% (n = 21). The 7 non-APE-related deaths were due to cancer (2 cases), advanced congestive systolic heart failure (2 cases), severe aortic stenosis with severe LV dysfunction, gastrointestinal bleeding, and bilateral pneumonia. Nine initially stable patients received thrombolysis due to clinical deterioration, 7 of them survived. Finally, the CE, which included APE-related death or thrombolysis, was observed in 21 patients.

Patients who experienced CE presented with increased heart rate, elevated plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP), and more frequent biochemical signs of myocardial injury than patients with favorable clinical course (Table 1).

Echocardiography. Table 2 includes echocardiographic data of studied patients. Almost all echocardiographic parameters assessing RV morphology and function indicated more significant RV impairment in patients with CE than in subjects with an uncomplicated clinical course. Only RVD, both in the long parasternal axis and apical 4-chamber apical view, and RV/LV ratio measured in the long-axis parasternal view did not differ

Table 2. Echocardiographic Characteristics of Studied Patients With APE

	All Patients (N = 411)	APE-Related Mortality or Thrombolysis (n = 21)	p Value	Remaining Patients (n = 390)
RVlax, mm	27 (17–58)	29 (17–39)	0.97	27 (17–58)
LVlax, mm	43 (13–66)	40 (29–51)	<0.01	43 (13–66)
RV/LVlax	0.63 (0.32–2.00)	0.69 (0.45–1.03)	0.13	0.62 (0.32–2.00)
RV4C, mm	37 (20–60)	39 (20–60)	0.18	36 (21–59)
LV4C, mm	42 (22–67)	39 (22–54)	0.01	42 (25–67)
RV/LV4C	0.88 (0.46–2.00)	1.08 (0.48–2.00)	0.003	0.87 (0.46–1.93)
PVvel, cm/s	0.8 (0.4–1.7)	0.6 (0.4–1.1)	<0.001	0.8 (0.4–1.7)
AcT, ms	88 (30–170)	70 (30–111)	0.002	90 (34–170)
TR, moderate/severe, %	22 (5)	4 (19)	0.02	18 (5)
TRPG, mm Hg	31 (7–100)	45 (15–100)	0.03	30 (7–88)
TAPSE, mm	21 (6–34)	12 (6–20)	<0.0001	21 (6–34)
IVS flattening, %	102 (25)	10 (48)	0.01	92 (24)
McConnell sign, %	77 (18)	9 (43%)	<0.01	68 (17)
LVEF, %	60 (15–70)	55 (15–68)	<0.01	60 (15–70)
IVC, mm	15 (5–35)	18 (10–26)	0.03	15 (5–35)

Values are median (maximum–minimum range) or n (%).
 AcT = pulmonary ejection acceleration time; APE = acute pulmonary embolism; CI = confidence interval; HR = hazard ratio; IVC = inferior vena cava; IVS = interventricular septum; LV4C = left ventricular dimension in apical four chamber view; LVEF = left ventricular ejection fraction; LVlax = left ventricular dimension in the parasternal long-axis; PVvel = pulmonary valve peak systolic velocity; RV4C = right ventricular dimension in apical four chamber view; RVlax = right ventricular dimension in the parasternal long-axis; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid valve regurgitation; TRPG = tricuspid valve peak gradient.

between groups. Interestingly, the CE group presented with significantly lower left ventricular ejection fraction. We observed a correlation between TAPSE and plasma NT-proBNP level ($r = -0.661$, $p < 0.0001$).

Hazard risk of echocardiographic predictors of CE in univariable analysis. Univariable Cox proportional hazards regression analysis showed that most of the measured echocardiographic parameters significantly predicted clinical outcome (Table 3). RV/LV ratio measured in the apical 4-chamber view showed the highest hazard ratio (HR) for APE related mortality or rescue thrombolysis (HR: 7.3, 95% confidence interval [CI]: 2.0 to 27.3; $p = 0.003$). Only RV dimension and RV/LV in the parasternal long-axis view were not significantly different between groups. However, multivariable analysis showed that TAPSE (HR: 0.64, 95% CI: 0.54 to 0.7; $p < 0.0001$) was the only independent predictor of 30-day PE-related mortality or thrombolysis.

ROC curve analysis. ROC analysis (Table 4) showed that the area under the curve for TAPSE in the prediction of clinical course was the highest (area under the curve [AUC]: 0.91, 95% CI: 0.856 to 0.935; $p = 0.0001$). Moreover, the AUC of TAPSE was higher than the AUC of RV/LV ratio, $p < 0.001$ (Fig. 1). We defined 2 cutoff values

of TAPSE. TAPSE ≤ 15 mm (17% of studied patients) showed a PPV of 20.9% for CE with a 99% NPV, whereas TAPSE ≤ 20 mm had a PPV of 9.2 with a 100% NPV. Therefore, all patients with TAPSE > 20 mm (53% of studied patients) formed a low-risk group with good prognosis (Fig. 2), whereas TAPSE ≤ 15 mm identified among initially normotensive patients was associated with a 20.9% risk of APE-related death or rescue thrombolysis (Fig. 3). The previously proposed cutoff values of the RV/LV ratio of > 0.9 and > 1.0 had a PPV of 13.2% and 14.4% and NPV of 97% and 94.3%, respectively, for CE. McConnell's sign had a PPV of 38% and NPV of 94% for CE. **TAPSE and RV/LV ratio for outcome prediction in submassive PE.** Most of the CEs occurred in patients with submassive PE (19 of 241 patients), whereas only 2 of 170 patients without RVD experienced CE. ROC analysis showed significantly higher AUC for TAPSE when compared with RV/LV ratio 0.87 (95% CI: 0.82 to 0.91) versus 0.60 (95% CI: 0.53 to 0.67), $p < 0.001$. Cox proportional-hazards regression analysis showed that both TAPSE and the RV/LV ratio significantly predicted clinical outcome in submassive PE. HR for TAPSE was 0.67 (95% CI: 0.56 to 0.80), $p = 0.00001$, and for RV/LV was 4.40 (95%

Table 3. Univariable Predictors of APE-Related Mortality or Rescue Thrombolysis in 411 Initially Normotensive Patients

	HR	95% CI	p Value
RVlax	0.999	0.928–1.075	0.98
RV/LVlax	3.38	0.74–15.51	0.12
RV4C	1.04	0.98–1.10	0.17
RV/LV4C	7.3	2.0–27.3	0.003
IVC	1.09	1.01–1.18	0.03
PVvel	0.003	0.0001–0.0793	0.0005
AcT	0.97	0.95–0.99	0.002
TRPG	1.030	1.003–1.058	0.03
TAPSE	0.71	0.62–0.81	<0.0001
TAPSE ≤15 mm	27.9	6.2–124.6	<0.0001
IVS flattening	3.1	1.3–7.4	0.01
McConnell sign	3.6	1.5–8.7	0.004
TR moderate/severe	4.7	1.6–14.3	<0.01
LVEF, %	0.96	0.93–0.99	0.01

Abbreviations as in Table 2.

CI: 1.07 to 18.0), $p < 0.04$. However, TAPSE < 16 mm showed high HR in the outcome prediction (HR: 14.48, 95% CI: 3.12 to 67.0; $p < 0.001$). Moreover, TAPSE < 16 mm for the prediction of CE in submassive PE showed a PPV of 22.5% (95% CI: 9.6% to 35.4%), whereas RV/LV > 1 had a PPV of 13.1% (95% CI: 5.9% to 20.3%). NPV of TAPSE > 20 reached 100% (95% CI: 100% to 100%), whereas NPV of RV/LV > 1 ratio had NPV of 95% (95% CI: 91.1% to 98.9%).

DISCUSSION

Normotensive patients with APE include, not only subjects with benign clinical course, but also patients with an increased risk of APE-related mortality. Although the former may be candidates for a short hospital stay or even ambulatory treatment, the latter require close monitoring, and in some cases, even more aggressive therapy, including thrombolysis. However, precise short-term stratification of normotensive patients with APE is still a matter of ongoing discussion (15–17). The mortality rate reported in normotensive APE patients with RVD diagnosed according to different criteria varied markedly from 4.3% up to 16.4% (8,18–20). Recently, an increased RV to LV end-diastolic ratio measured by echocardiography or tomography was proposed as a potential indicator of poor outcome (1,9,21). However, although right ventricular dysfunction has been included in the risk stratification

Table 4. ROC Analysis of Significant Echocardiographic Parameters in the Prediction of a Complicated Clinical Course

	AUC	95% CI	p Value	Cutoff Point	PPV	NPV
AcT	0.699	0.652–0.743	0.0001	< 90 ms	8.3	98.0
IVC	0.666	0.616–0.713	0.01	> 15 mm	8.0	97.1
LVEF	0.688	0.639–0.733	0.0003	$< 60\%$	12.8	97.0
PVvel	0.741	0.691–0.787	0.0001	< 0.70 m/s	13.0	97.7
RV/LV4C	0.638	0.589–0.686	0.04	> 1.0	13.2	97.0
				> 0.9	14.4	94.3
TAPSE	0.901	0.856–0.935	0.0001	≤ 15 mm	20.9	99.0
				≤ 20 mm	9.2	100.0
TRPG	0.636	0.585–0.685	0.07	> 42 mm Hg	9.5	97.5

AUC = area under the curve; ROC = receiver-operating characteristic; other abbreviations as in Table 2.

strategy, there is no generally accepted and validated definition of RVD (2,22).

We tried to define the optimal, easily measured echocardiographic criteria of RVD for risk stratification and compare them with the prognostic value of the previously proposed RV/LV ratio of 0.9 or 1.0. Four hundred eleven consecutive patients with

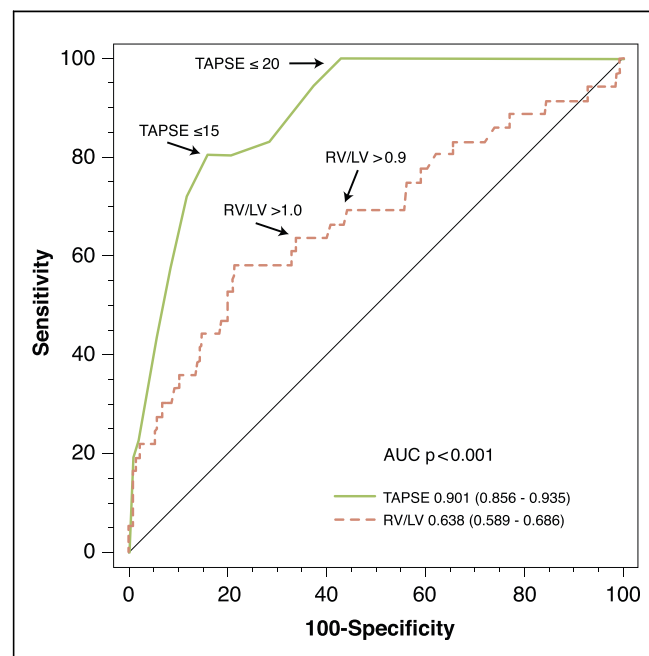


Figure 1. ROC of TAPSE and RV/LV4C for Clinical Endpoint in Normotensive Patients

Receiver-operating characteristic (ROC) analysis of tricuspid annular plane systolic excursion (TAPSE) and right to left ventricular diastolic dimensions ratio measured in 4-chamber view (RV/LV4C) for 30-day pulmonary embolism-related mortality and rescue thrombolysis in normotensive patients. AUC = area under the curve.

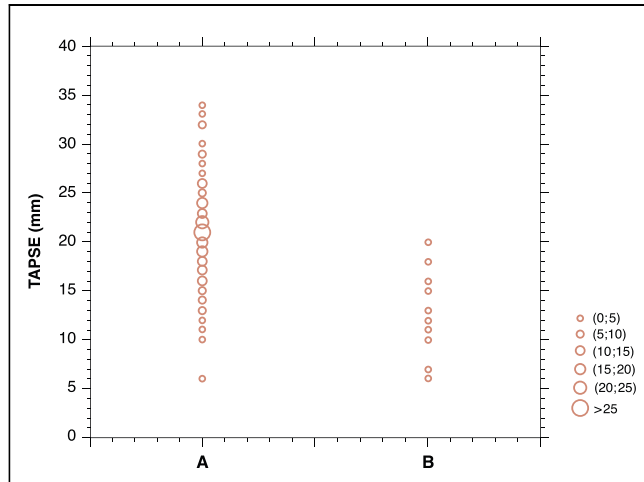


Figure 2. Individual TAPSE Values in Initially Normotensive Patients According to Clinical Course

Distribution of individual tricuspid annular plane systolic excursion (TAPSE) values in initially normotensive patients according to clinical course. (A) Uncomplicated clinical course (n = 390), (B) patients with acute pulmonary embolism (APE)-related mortality or thrombolysis (n = 21).

APE, normotensive at admission, were analyzed. All patients underwent echocardiography as a part of routine assessment. All patients initially were given anticoagulation agents, and thrombolysis was used only in case of deterioration. Thirty-day APE-related mortality or need for rescue thrombolysis due to hemodynamic deterioration were the endpoints of the current study. Fourteen patients died

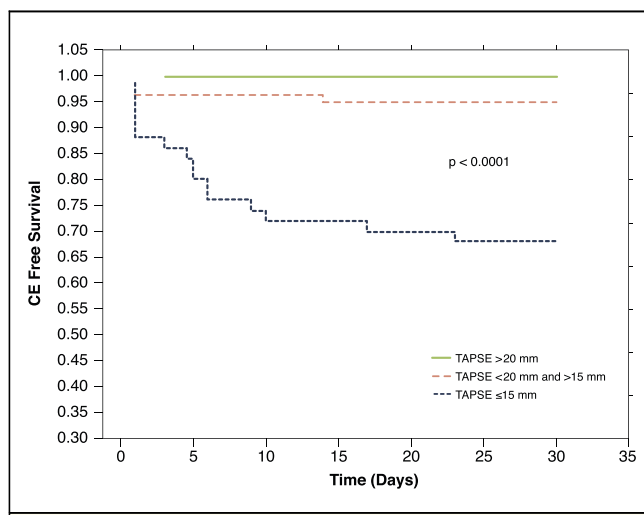


Figure 3. Kaplan-Meier Survival Analysis According to TAPSE in 411 Initially Normotensive Patients With APE

Kaplan-Meier survival analysis according to TAPSE in 411 initially normotensive patients with APE. CE = clinical endpoint; other abbreviations as in Figure 2.

as a result of PE, including 2 who received rescue thrombolysis (APE-related mortality 3.4%). The 12 remaining nonsurvivors did not receive thrombolytic treatment because of high bleeding risk, as assessed by the managing physician. Importantly, 7 of 9 patients who received urgent thrombolysis survived. Therefore, the CE of our study, comprising APE-related mortality and rescue thrombolysis, was present in 21 cases.

Various echocardiographic parameters were found to be significant predictors of CE in univariable analysis. However, in multivariable analysis, only TAPSE was found to be a significant predictor. ROC analysis for CE prediction showed a high AUC for TAPSE (AUC: 0.91, 95% CI: 0.856 to 0.935; $p = 0.0001$). Importantly, the AUC for TAPSE was significantly higher than the AUC of the RV/LV ratio or other echocardiographic parameters. Therefore, we found TAPSE to be the most valuable predictor of clinical course among a wide set of echocardiographic indices. Systolic excursion of the lateral tricuspid annulus is an indicator of longitudinal function of the RV. It is well known that longitudinal myocardial shortening is a significant contributor to RV function, rather than reduction in cavity diameter, as is the case for the LV (12,23). TAPSE reflects global systolic RV function, whereas the RV/LV ratio provides data on RV morphology, and McConnell's sign represents only regional function abnormalities.

It should be underlined that TAPSE is a well-known, easy to measure, and reproducible parameter that does not require sophisticated equipment or prolonged image analysis (24), with a proven prognostic value in congestive heart failure (25). Decreased RV systolic function estimated by TAPSE was found to be associated with increased mortality in patients admitted for heart failure, and is independent of other mortality risk factors in this group of patients (26). Interestingly, in 50 patients with APE, TAPSE reflected the severity of RVD defined by plasma BNP level—a significant correlation with BNP plasma and TAPSE was found ($r = -0.634$, $p < 0.001$) (27), and we observed a similar correlation between TAPSE and plasma NT-proBNP. Moreover, in a group of 37 consecutive patients with pulmonary hypertension, among various echocardiographic parameters, TAPSE exhibited the strongest correlation with cardiac magnetic resonance-derived RV ejection fraction ($r = 0.86$, $p < 0.001$), and only TAPSE significantly predicted cardiac magnetic resonance-derived RV ejection fraction in multiple regression analysis (28). Using ROC analysis, we defined 2 cutoff

values of TAPSE, including ≤ 15 mm, which identified 17% of initially normotensive patients at risk of a complicated clinical course. The PPV for APE-related death or thrombolysis in this group was 20.9%. Interestingly, a TAPSE of 16 mm was recently defined as a lower reference value of RV function (12). Moreover, guidelines on pulmonary arterial hypertension also proposed TAPSE as a prognostic tool, and TAPSE ≤ 15 mm has been regarded as an indicator of poor outcome (29).

The second TAPSE threshold (>20 mm) identified normotensive patients with favorable outcome (53%). None of these patients experienced a complicated clinical course. Interestingly, TAPSE >20 mm has been reported to identify patients with pulmonary arterial hypertension with a favorable prognosis (29). Our results indicate that TAPSE is superior to RV/LV ratio for 30 days prognosis also in patients with submassive PE.

Clinical implications. Measurement of TAPSE may help in the management of normotensive APE patients. Patients with TAPSE >20 mm form a group of approximately 50% of normotensive patients with benign clinical course, free of APE-related complications. If other factors are considered, such as a lack of coexisting diseases, influencing outcome and low bleeding risk, the duration of their hospitalization may be very short. On the other hand, patients with TAPSE ≤ 15 mm should be at least closely monitored. Probably, TAPSE ≤ 15 mm identifies a group in whom

thrombolysis may be considered, especially when additional parameters such as elevated troponin levels indicate increased risk.

Study limitations. This is a single-center observational study. Causes of death were not adjudicated. Because of the limited number of CEs observed in our study, the ability of stepwise multivariable methods to select models from among 11 significant predictors in univariable analysis should be regarded with caution. Therefore, our results should be validated in an external population with APE. Although we tried to perform echocardiography as soon as possible after admission, in some patients, it was performed with some delay.

CONCLUSIONS

Our data indicate that TAPSE is preferable to RV/LV ratio for risk stratification in initially normotensive patients with APE. TAPSE ≤ 15 mm identifies patients with an increased risk of 30-day APE-related mortality or rescue thrombolysis, whereas TAPSE >20 mm can be used for identification of a very low-risk group, who may be candidates for a short hospital stay or even outpatient treatment.

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Key Words: echocardiography ■ prognosis ■ pulmonary embolism.