ORIGINAL ARTICLE

The relationship between right ventricular outflow tract fractional shortening and Pulmonary Embolism Severity Index in acute pulmonary embolism

Akut pulmoner embolide sağ ventrikül çıkış yolu fraksiyonel kısalması ile pulmoner emboli ciddiyet indeksi arasındaki ilişki

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ABSTRACT

Objective: Right ventricular (RV) functions are clinically important in acute pulmonary embolism (APE). Measurement of systolic function of the right ventricular outflow tract (RVOT) with echocardiography is a simple method to evaluate RV function. The aim of this study was to determine the relationship between RVOT systolic function and the Pulmonary Embolism Severity Index (PESI).

Methods: A total of 151 patients diagnosed with APE by pulmonary computed tomography angiography or ventilation/perfusion scintigraphy were included. Patients were assigned to 2 groups based on the simplified PESI (sPESI): sPESI <1 (n=85) and sPESI ≥1 (n=66). RV conventional parameters, RVOT dimensions, and fractional shortening (RVOT-FS) were also measured.

Results: Mean age was similar between sPESI <1 and >1 patients (58.7±12.9 years vs. 61.1±12.7 years, respectively). Frequency of male gender was significantly higher in PESI <1 group (61.2% vs. 40.2%, p=0.013). No significant differences were found between the groups in fasting glucose, serum creatinine, hemoglobin, C-reactive protein, erythrocyte sedimentation rate, troponin, and D-dimer levels, and left ventricular ejection fraction. RVOT-FS was higher in patients with sPESI <1 than in patients with sPESI ≥1 (34.41±3.56 vs. 22.98±4.22), and this difference was significant (p<0.001). Tricuspid annular plane systolic excursion values were lower and pulmonary artery systolic pressure values were higher in the sPESI ≥1 group, which was also statistically significant (p<0.05). Mortality occurred in 7 patients with sPESI <1 and in 16 patients with sPESI ≥1. The mortality rate was higher in patients with lower RVOT-FS, and a RVOT-FS <0.22 predicted mortality with a sensitivity of 54.5% (AUC: 0.674, 95% CI 0.552-0.796; p=0.009).

Conclusion: The RVOT-FS is a noninvasive measurement of RV systolic function, is well-correlated with the sPESI score, and associated with mortality in patients with APE. This easily applied measurement may be used to predict short-term mortality in patients with APE.

ÖZET

Amaç: Sağ ventrikül (SaV) fonksiyonları, akut pulmoner embolide (APE) klinik önem taşır. SaV çıkış yolu (SaVÇY) sistolik fonksiyonu ölçümleri, SaV fonksiyonlarını değerlendiren ekokardiyografik yöntemlerdir. Bu çalışmanın amacı, SaVÇY sistolik fonksiyonları ile pulmoner emboli ciddiyet indeksi (PESI) skoru arasındaki ilişkiyi saptamaktır.

Yöntemler: Pulmoner bilgisayarlı tomografi (BT) ya da ventilasyon perfüzyon (V/Q) sintigrafisi ile tanı konmuş, SaV değerlendirmesi ve ölçümleri, SaVÇY fraksiyonel kısalma (SaVÇY-FS) ölçümleri yapılmış 151 APE'li hasta çalışmaya dahil edildi. Hastalar PESI skorlarına göre sPESI <1 (n=85) ve sPESI ≥1(n=66) olarak iki gruba ayrıldı.

Bulgular: sPESI <1 grubunda ortalama yaş 59.71±12.98 yıl, sPESI ≥1 grubunda ortalama yaş 61.14±12.67 yıldı (p>0.05). sPESI <1 grubunda 52 erkek (%61.2), sPESI ≥1 grubunda 27 erkek (%40.2) hasta mevcuttu (p=0.013). Her iki grup arasında glukoz, serum kreatinin, hemoglobin, C-reaktif protein, eritrosit sedimantasyon hızı, troponin ve D-dimer seviyelerinde anlamlı fark yoktu. SaVÇY-FS oranı sPESI ≥1 grubunda (n=66) (34.41±3.56 vs. 22.98±4.22) istatistiksel olarak anlamlı şekilde yüksekti (p<0.001). Her iki grup arasında sol ventrikül ejeksiyon fraksiyonu (LVEF) değerinde fark yoktu (p>0.05). sPESI ≥1 grubunda istatistiksel olarak anlamlı şekilde TAPSE değerleri düşük, SPAB değerleri yüksekti (p<0.05). sPESI <1 grubunda 7, sPESI ≥1 grubunda 16 ölüm görüldü. Düşük RVOT-FS'li hastalarda mortalite oranı daha yüksekti ve RVOT-FS'nin <0.22 olması mortaliteyi %54.5 duyarlılıkla öngördürmekteydi (AUC: 0.674,%95 GA 0.552-0.796; p=0.009).

Sonuç: SaVÇY-FS oranı, SaV sistolik fonksiyonlarının noninvaziv ölçüm yöntemlerinden biridir ve akut pulmoner embolili hastalarda sPESI skoru ve mortalite ile ilişkili bulunmuştur. Bu kolay elde edilebilen ölçüm, APE'li hastalarda kısa dönem mortalitesini öngördürücü olarak değerlendirilebilir.

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Acute pulmonary embolism (APE) is one of the most serious clinical presentations at the emergency department, and is associated with significant short- and long-term complications and a mortality rate of 15% to 20%.[1] The Pulmonary Embolism Severity Index (PESI) is the most widely accepted prognostic score for patients with APE.[2] Jimenez et al.[3] used the PESI to develop the new, simplified PESI (sPESI). In their study results, APE patients with a high sPESI score (sPESI ≥1) had a higher mortality rate compared with patients with a low sPESI score (sPESI <1) (mortality rates: 8.9% and 1.1%, respectively).

Right ventricle (RV) systolic and diastolic functions have an important prognostic role in patients with cardiopulmonary disease. However, evaluation of RV function is difficult as a result of the complicated anatomy and physiology. Also, RV performance is sensitive to preload and to alterations in pulmonary pressure.[4,5] Due to its easy availability, echocardiography may be the first-line imaging modality chosen for assessment of left ventricle (LV) and RV dimensions and function, but a simple, extensively validated and generally applicable measurement of RV function has not yet been described.[4,6] RV assessment is performed in the 3 areas of the inflow portion, the trabeculated apical portion, and the outflow tract (infundibulum or conus) portion. The accepted opinion is that the inlet part of the RV contributes more to overall RV function compared with the infundibulum, but in some studies, researchers found that the movement and/or contraction of the RV outflow tract (RVOT) can be used as a marker of RV systolic function.[7–10] The aim of this study was to examine the relationship between RVOT function, SPESI score, and mortality in patients with APE.

METHODS

The data of 742 patients diagnosed with APE were obtained for this retrospective study. Patients were diagnosed with ventilation/perfusion scintigraphy and/or pulmonary computed tomography angiography. All patients with atrial fibrillation, infectious disorders, malignant tumor, unstable angina, LV dysfunction, mitral valve disorder, or any other cardiac disorder that causes pulmonary hypertension were excluded. In all, 151 patients were included in the study.

Abbreviations:

APE	*Acute pulmonary embolism*
ESC	*European Society of Cardiology*
LV	*Left ventricle*
PASP	*Pulmonary artery systolic pressure*
PESI	*Pulmonary Embolism Severity Index*
RV	*Right ventricle*
RVOT	*Right ventricular outflow tract*
RVOT-FS	*RVOT fractional shortening*
sPESI	*Simplified PESI*
TAPSE	*Tricuspid annular plane systolic excursion*

The baseline characteristics of the study patients were collected from patients files. Heart rate, oxygen saturation and body temperature values, biochemical blood test results, troponin-I and D-dimer values, and hemogram parameters were obtained from the records of the first medical contact examination conducted in the emergency department.

PESI scores and sPESI scores of all of the patients were calculated according to the clinical data and the European Society of Cardiology (ESC) guidelines.[2,3] Patients were assigned to 2 groups according to sPESI score: sPESI <1 (n=85) and sPESI ≥1 (n=66).

Transthoracic echocardiography analysis was performed using a Philips HD 11 XE ultrasound machine with a S5-1 transducer (Koninklijke Philips N.V., Amsterdam, Netherlands). Echocardiographic examination was performed in the left lateral decubitus position. The assessment of pulmonary artery systolic pressure (PASP) was done by calculating the systolic transtricuspid gradient (via the Bernoulli equation, using the maximal tricuspid regurgitation velocity measured with continuous wave Doppler) and then adding an assumed right atrial pressure.[11,12] Tricuspid annular plane systolic excursion (TAPSE) was assessed with M-mode from the RV free wall (between the RV apex and the tricuspid annulus), measuring the distance (in millimeters) of tricuspid annular movement from end-diastole to end-systole of the same cardiac cycle.[13] The parasternal short-axis view at the level of the aortic root was used to measure RVOT dimensions and RVOT fractional shortening (RVOT-FS). M-mode recordings of the RVOT were acquired using the endocardial leading-edge methodology. RVOT dimension measurements were obtained at end-diastole (onset of the Q wave) and end-systole (end of the T wave) of the same cardiac cycle. FS was calculated as reported by Lindqvist et al. to determine the percentage of the size reduction of the RVOT.[8]

$$FS(\%) = \frac{(RVOT\ end\ diastole - RVOT\ end\ systole)}{(RVOT\ end\ diastole)}$$

Table 1. The baseline characteristics of study patients

Variables	sPESI ≥1 (n=66)			sPESI <1 (n=85)			*p*
	n	%	Mean±SD	n	%	Mean±SD	
Age (years)			61.14±12.67			59.71±12.99	0.499
Gender							
Male	27	40.9		52	61.2		**0.013**
Female	39	59.1		33	38.8		
Smoking	44	66.7		47	55.3		0.157
Hypertension	26	39.4		29	34.1		0.504
Diabetes mellitus	29	43.9		30	35.3		0.280
Coronary artery disease	8	16.0		13	17.8		0.793
Systolic blood pressure (mmHg)			108.79±15.09			113.88±13.37	0.030
Disatolic blood pressure (mmHg)			71.36±9.14			72.12±7.73	0.584
Heart rate (bpm)			115.83±20.09			86.12±15.61	**<0.001**
Pulmonary Embolism Severity Index score			91.14±17.79			71.82±18.64	**<0.001**

SD: Standart deviation; sPESI: Simplified Pulmonary Embolism Severity Index.

The statistical analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, USA). sPESI score <1 was the criterion used to form the 2 study groups. Continuous variables were presented as mean±SD or median, and data were presented as percentage for categorical variables. The Kolmogorov-Smirnov test was used to test the distribution pattern. Categorical variables were tested with Pearson's chi-squared test. Normally distributed continuous variables were analyzed with an independent T-test, and those with non-normal distribution were analyzed using the Mann-Whitney U test. Pearson's correlation analysis was used to investigate correlations between variables. In all analyses, statistical significance was defined as $p<0.05$.

RESULTS

A total of 151 patients who were diagnosed with APE using pulmonary computed tomography angiography or ventilation/perfusion scintigraphy were included in the research. The baseline characteristics of the study patients are shown in Table 1. The first group included 66 patients with sPESI ≥1 and the second group comprised 85 patients with sPESI <1. There were no significant differences between the groups in age and gender distribution, or presence of diabetes mellitus, hypertension, smoking, history of coronary artery disease, or diastolic blood pressure and heart rate (Table 1). Systolic blood pressure, however, was significantly different between the groups (p=0.030). There were no significant differences in biochemical blood test results (included glucose, creatinine, liver enzymes, electrolyte, and C-reactive protein levels, erythrocyte sedimentation rate, D-dimer and troponin-I levels) or hemogram parameters (included hematocrit percentages, hemoglobin level, white blood cell count, platelet count, red cell distribution width, and mean

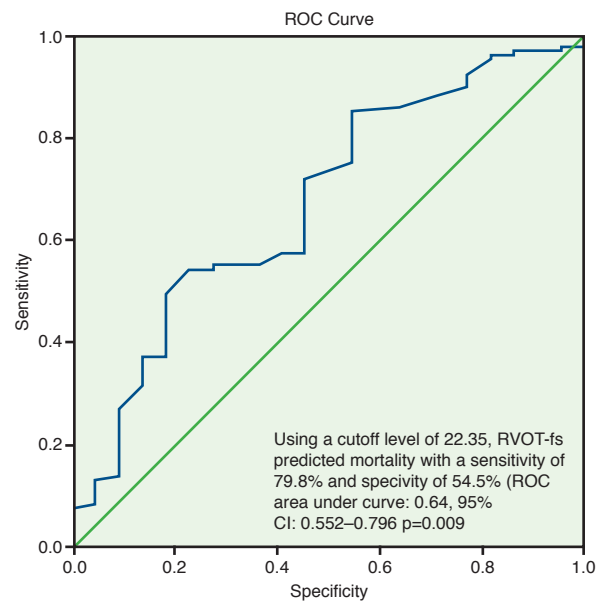

Figure 1. Receiver operating characteristic curve analysis.

Table 2. Biochemical blood tests results and hemogram parameters of the study patients

Variables	sPESI ≥1 (n=66)	sPESI <1 (n=85)	*p*
Glucose (mg/dL)	115.89±24.92	118.59±36.54	0.609
Creatinin (mg/dL)	0.889±0.237	0.908±0.369	0.752
Uric acid (mg/dL)	5.06±1.70	5.42±2.11	0.255
Albumin (g/dL)	3.95±0.44	3.94±0.51	0.902
Total bilirubin (mg/dL)	0.766±0.354	0.695±0.599	0.393
Aspartate aminotransferase (U/L)	21.89±9.25	30.51±6.52	0.254
Alanine aminotransferase (U/L)	22.44±13.62	28.54±20.09	0.238
Gamma-glutamyl transpeptidase (U/L)	43.89±38.48	44.18±40.19	0.965
Lactate dehydrogenase (U/L)	223.10±52.24	244.60±127.66	0.198
Sodium (mmol/L)	138.71±3.35	138.58±3.62	0.830
Potassium (mmol/L)	4.34±0.46	4.29±0.47	0.523
Calcium (mmol/L)	9.18±0.39	9.21±0.48	0.707
C-reactive protein (mg/dL)	5.56±8.64	4.16±6.26	0.249
Erythrocyte sedimentation rate (mm/h)	35.97±22.37	34.51±22.83	0.694
D-Dimer (ng/mL) (median, min-max)	1330 (400–30030)	2040 (450–26610)	0.130
Troponin (pg/mL) (median, min-max)	15.0 (1.0–623.0)	19.1 (1.0–510.0)	0.563
White blood cells ($10^3/\mu L$)	8782±326	9226±369	0.442
Neutrophil ($10^3/\mu L$)	6220±306	6610±331	0.465
Monocyte ($10^3/\mu L$)	530±31	580±28	0.279
Lymphocyte ($10^3/\mu L$)	1860±760	1940±1010	0.621
Platelet ($10^3/\mu L$)	239±82	239±86	0.776
Hemoglobin (g/dL)	13.60±1.81	13.68±1.31	0.757
Red cell distribution width (%)	16.24±3.18	16.01±2.28	0.598
Mean platelet volume (fL)	7.61±1.16	7.53±1.14	0.627

sPESI: Simplified Pulmonary Embolism Severity Index.

platelet volume), which are summarized in Table 2. Among study population, in-hospital mortality was observed in 23 patients. The longest length of time between diagnosis and death was 22 days. Mortality occurred in 7 patients with sPESI <1 (8.2%) and in 16 patients with sPESI ≥1 (24.2%) (p=0.007). The mortality rate was higher in patients with lower RVOT-FS patients compared to others (p=0.009). In receiver operating characteristic (ROC) curve analysis using a cut-off level of 22.35, RVOT-FS predicted mortality with a sensitivity of 79.8% and specificity of 54.5% (ROC area under curve: 0.674; 95% CI, 0.552-0.796; p=0.009) (Fig. 1).

The echocardiographic findings of all of the patients are summarized in Table 3. The RVOT-FS was lower in the sPESI ≥1 group (n=66) than in the patients with sPESI <1 (22.98±4.22 vs 34.41±3.56; p<0.001) (Table 3) (Fig. 2). A negative correlation was found between RVOT-FS and sPESI score (-0.828; p<0.001). sPESI scores were inversely correlated with TAPSE (-0.325; p<0.001) and positively correlated with PASP (+0.237; p=0.003). There were no significant differences in LV end-diastolic diameter or systolic function.

DISCUSSION

In this study, we found that RVOT systolic function determined by RVOT-FS was lower in patients with sPESI ≥1 (n=66) than in the patients with sPESI <1, and that sPESI scores were correlated inversely with TAPSE and positively with PASP. Furthermore, PESI

Table 3. Echocardiographic findings of the patients

Variables	sPESI ≥1 (n=66)	sPESI <1 (n=85)	*p*
Left ventricle ejection fraction (%)	58.20±8.34	57.67±6.99	0.674
Left ventricle end-diastolic diameter (mm)	50.06±2.85	49.31±3.04	0.122
Pulmonary artery systolic pressure (mmHg)	37.67± 9.31	33.14±9.01	**0.003**
Tricuspid annular plane systolic excursion (mm)	21.11±2.39	22.75±2.38	**<0.001**
Diastolic diameter of the right ventricular outflow tract (mm)	28.59±3.02	26.14±2.79	**0.003**
Systolic diameter of the right ventricular outflow tract (mm)	20.42±2.63	16.51±2.11	**<0.001**
Right ventricular outflow tract fractional shortening (%)	22.98±4.22	34.41±3.56	**<0.001**

sPESI: Simplified Pulmonary Embolism Severity Index.

score was negatively correlated with the RVOT-FS rate. Mortality was more common in the sPESI ≥1 group and was related to a lower RVOT-FS value. According to the relationship between sPESI score and RVOT-FS observed in this study, RV systolic function measurements (evaluated with RVOT-FS) may be used to predict short-term mortality in APE.

Pulmonary embolism, myocardial infarction, and stroke can be accepted as "the big three" in cardiovascular disorders. The in-hospital mortality rate for patients with pulmonary embolism is nearly 7%, and for patients with hemodynamic instability, it is approximately 30%. The PESI is the most widely accepted prognostic score for patients with APE2. Jimenez et al. developed the sPESI. In their study results, APE patients with a high sPESI score (sPESI ≥1) had a higher mortality rate than patients with a low sPESI score (sPESI <1) (mortality rate: 8.9% and 1.1%, respectively). Prior studies have demonstrated a relationship between an increased mortality rate and a higher PESI score and/or RV diastolic diameters in patients with APE.

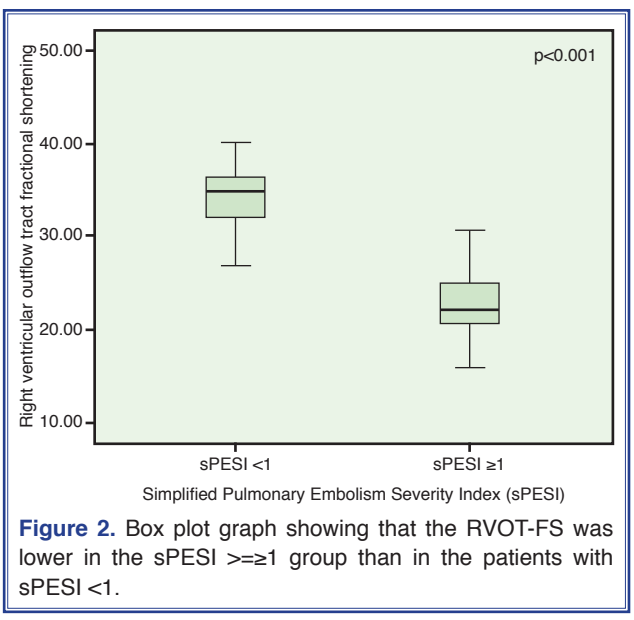

Figure 2. Box plot graph showing that the RVOT-FS was lower in the sPESI >=≥1 group than in the patients with sPESI <1.

Mortality in hospitalized APE patients most often results from right heart failure. RV failure is a main determinant of prognosis in these patients. Assessing RV function is recommended as a part of the clinical approach according to the ESC guidelines. However, evaluation of RV function is difficult due to the complex anatomy and physiology. No single echocardiographic view provides enough information to fully evaluate RV function. The volumetric approximation of the RV is the primary means of echocardiographic evaluation of RV function; however, this approach has some limitations, as the geometry of the RV and the ejection fraction of RV are affected by loading conditions. Geometry-independent parameters, such as TAPSE and the Tei index, can provide information about RV function and can be used to overcome these limitations.[4,5] Lindqvist[8] and Asmer[9] have reported the value of RVOT function and defined the possibility of using the movement or contraction of RVOT to evaluate RVOT systolic function. Lindqvist et al.[8] demonstrated a positive correlation between RVOT-FS and TAPSE. A moderate, inverse correlation was reported between the RVOT-FS and the transtricuspid Doppler gradient, and the RVOT-FS has been shown to be correlated with pulmonary hypertension more than with TAPSE8. Similar to the RVOT-FS, RVOT systolic excursion, a component of RVOT-FS, was defined by Asmer at al.[9] as a novel, simple, and en-

couraging parameter for the evaluation of RV function. Three-dimensional echocardiography, magnetic resonance imaging, tissue Doppler imaging, and strain are better in assessing RV function; however, sometimes simple evaluation of RVOT-FS with 2-dimensional echocardiography may be better.

Our study has some limitations. First, the parasternal short-axis view used to measure RVOT dimensions was not standardized; intra- and interobserver variability may have resulted due to underestimating the RVOT-FS value or overestimating RVOT dimensions. Secondly, the lack of a comparative gold standard technique (such as magnetic resonance imaging and/or cardiac catheterization) for the evaluation of RV function may be a limitation of our research.

Conclusion

The RVOT-FS is a noninvasive measurement of RV systolic function, is well-correlated with sPESI score and is associated with mortality in patients with APE. This easily performed measurement may be used to predict near-term mortality in APE patients.

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REFERENCES

1. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). Lancet 1999;353:1386–9. [CrossRef]
2. Aujesky D, Obrosky DS, Stone RA, Auble TE, Perrier A, Cornuz J, et al. Derivation and validation of a prognostic model for pulmonary embolism. Am J Respir Crit Care Med 2005;172:1041–6. [CrossRef]
3. Jiménez D, Aujesky D, Moores L, Gómez V, Lobo JL, Uresandi F, et al; RIETE Investigators. Simplification of the pulmonary embolism severity index for prognostication in patients with acute symptomatic pulmonary embolism. Arch Intern Med 2010;170:1383–9. [CrossRef]
4. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 2010;23:685–713. [CrossRef]
5. Vitarelli A, Terzano C. Do we have two hearts? New insights in right ventricular function supported by myocardial imaging echocardiography. Heart Fail Rev 2010;15:39–61. [CrossRef]
6. Higham MA, Dawson D, Joshi J, Nihoyannopoulos P, Morrell NW. Utility of echocardiography in assessment of pulmonary hypertension secondary to COPD. Eur Respir J 2001;17:350–5. [CrossRef]
7. Kutty S, Zhou J, Gauvreau K, Trincado C, Powell AJ, Geva T. Regional dysfunction of the right ventricular outflow tract reduces the accuracy of Doppler tissue imaging assessment of global right ventricular systolic function in patients with repaired tetralogy of Fallot. J Am Soc Echocardiogr 2011;24:637–43. [CrossRef]
8. Lindqvist P, Henein M, Kazzam E. Right ventricular outflow-tract fractional shortening: an applicable measure of right ventricular systolic function. Eur J Echocardiogr 2003;4:29–35. [CrossRef]
9. Asmer I, Adawi S, Ganaeem M, Shehadeh J, Shiran A. Right ventricular outflow tract systolic excursion: a novel echocardiographic parameter of right ventricular function. Eur Heart J Cardiovasc Imaging 2012;13:871–7. [CrossRef]
10. Geyik B, Tarakci N, Ozeke O, Ertan C, Gul M, Topaloglu S, et al. Right ventricular outflow tract function in chronic obstructive pulmonary disease. Herz 2015;40:624–8. [CrossRef]
11. Yock PG, Popp RL. Noninvasive estimation of right ventricular systolic pressure by Doppler ultrasound in patients with tricuspid regurgitation. Circulation 1984;70:657–62. [CrossRef]
12. Bossone E, Duong-Wagner TH, Paciocco G, Oral H, Ricciardi M, Bach DS, et al. Echocardiographic features of primary pulmonary hypertension. J Am Soc Echocardiogr 1999;12:655–62. [CrossRef]
13. Kaul S, Tei C, Hopkins JM, Shah PM. Assessment of right ventricular function using two-dimensional echocardiography. Am Heart J 1984;107:526–31. [CrossRef]

Keywords: Echocardiography; fractional shortening; pulmonary embolism; Pulmonary Embolism Severity Index; right ventricular function.

Anahtar sözcükler: Ekokardiyografi; fraksiyonel kısalma; pulmoner emboli; Pulmoner Emboli Ciddiyet İndeksi; sağ ventrikül fonskiyonları.