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Clinical Symptoms and Echocardiographic Markers Regarding the Severity of Embolism in Patients with Acute Pulmonary Embolism

Shahabaddin Sorouri [1], Maryam Naseri [2], Sepideh Hejazi [3]

[1] Lung Diseases Research Center, Mashhad University of Medical Sciences, Mashhad, Iran, [2] Department of Pediatrics, Mashhad University of Medical Sciences, Mashhad, Iran, [3] Lung Diseases Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

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Correspondence to: Hejazi S
Address: Lung Diseases Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
Email address: Hejazis@mums.ac.ir

Background: Echocardiography can be used for risk stratification in patients with acute pulmonary embolism (PE). While the severity of PE has been assessed through laboratory criteria in most studies, the Pulmonary Embolism Severity Index (PESI) scoring system was used in this study to evaluate the severity of echocardiographic criteria in acute PE patients.

Materials and Methods: All PE patients admitted to Ghaem Hospital in Mashhad between 2021-2022 were included in the study. Clinical symptoms and echocardiographic markers were checked and recorded when the patients entered the study. Data were analyzed in SPSS version 24 at a significance level of 0.05 using the Chi-square test and t-test.

Results: Of 40 patients, 80% were at a high risk of PESI. The most common clinical symptoms were dyspnea (97.5%) and pleuritic chest pain (75%). Right ventricle (RV) size enlargement and its dysfunction were recorded in 57.5% of patients. The average age of patients in the high-risk group was significantly (p-value: 0.001) higher than the low-risk group. There was a significant correlation between MID-right ventricle and pulmonary artery pressure with the severity of embolism, so that mid-right ventricle and pulmonary artery pressure in the high-risk group were significantly higher (p-value: 0.000) than in the low-risk group. Also, the severity of PE was significantly related to RV size (P = 0.026) and function (P = 0.038).

Conclusion: RV size, function, and dilatation, and pulmonary artery pressure variated significantly in different severities of PE.

Keywords: Acute pulmonary embolism; Echocardiography; Clinical symptoms

INTRODUCTION

Acute pulmonary embolism (PE) is the third most common cause of cardiovascular death among hospitalized patients in the Western world after acute myocardial infarction and stroke. Early diagnosis and intervention are critical because most deaths from acute PE occur within the first few hours to days. The most common risk factor for PE is a history of previous deep vein thrombosis (DVT) (1). PE is often caused by thrombosis in a systemic blood vessel, usually a deep vein of the lower extremity. In Western countries, the incidence of PE in the general population is approximately 60 to 120 cases per 100,000 persons per year (2). Worldwide, the overall 3-month mortality rate of all PE patients is approximately 15%, and 50% have shock (3). Because symptoms are nonspecific, PE remains a diagnostic challenge, and less than 10%

of patients evaluated for PE are ultimately diagnosed with PE (2).

Venous thromboembolism (VTE) is caused by the interaction of environmental and structural risk factors that can be hereditary or acquired and may be due to non-modifiable factors such as older age or potential temporary factors such as immobility (2,4). Clinical manifestations of PE range from asymptomatic to hemodynamic collapse and death. Although PE alters pulmonary gas exchange and can cause hypoxemia, hemodynamic impairment is the most important factor for a worse prognosis. The increase of pulmonary vascular resistance increases RV afterload and leads to reduced left ventricular preload and cardiac output. The hemodynamic response to PE depends on the size of the obstruction and the presence of chronic right heart failure and left heart failure (5). Because the symptoms associated with PE are nonspecific, identifying PE can be challenging. The primary symptoms are chest pain and dyspnea (6). A study of 881 patients in France reported that approximately 30% of patients with chest pain were evaluated for PE (7). PE may also present as unexplained syncope. In 2 cohort studies of patients with syncope, the overall incidence of PE at 30 days was 0.6% and 2.2% (8,9). The first step to assess the clinical possibility of acute pulmonary thromboembolism is a physical examination. With low clinical probability, a D-dimer test should be requested. A normal D-dimer usually rules out pulmonary thromboembolism. If D-dimer is elevated, CT angiography must be done (10). In suspicion of PE, bedside echocardiography is suggested (2).

Wide variation in the prognosis of PE indicates the importance of early diagnosis and risk classification (11). There are common signs and symptoms between patients with and without PE, which shows the importance of diagnostic tests (12) such as echocardiography (13). While most studies investigating the severity of PE have used laboratory markers such as TPI or PROBNP, in the present study, clinical symptoms and echocardiographic criteria were investigated based on the severity of the PE, using a scoring system.

MATERIALS AND METHODS

Study design

This prospective descriptive-analytical study was conducted in Qaem Hospital, Mashhad, Iran, in the lung, internal, and heart departments between 2021 and 2022. All hospitalized patients diagnosed with PE were included in the study. Patients whose clinical symptoms and echocardiographic findings were not determined at the time of admission and patients who died at the time of diagnosis were excluded from the study. Due to the lack of a similar study to determine the sample size, the sample size was estimated based on the clinical judgment of the researcher, and finally, 40 patients were included in the study by the census method.

Outcome measures

The main outcome was the pulmonary embolism severity index (PESI). Secondary outcomes included dyspnea, pleuritic chest pain, non-massive hemoptysis, hypotension, RV status, including size and dysfunction, PAP, MID RV, and S(tv). Patient characteristics and clinical symptoms as well as echocardiographic markers, were checked and recorded when the patients entered the study. PESI was used to check the severity of embolism. In the simplified PESI scoring system, score 1 is assigned in the presence of factors including age>80, history of cancer, chronic cardiopulmonary disease, PR≥110, SBP<100, and O_2 sat < 90. A score of zero is considered low risk and a score of one or more is considered high risk (14). PESI is a widely validated and used risk score for predicting mortality in acute PE. Likewise, its simplified version (sPESI) has also been successfully validated and has provided similar prognostic accuracy. Both scores are based only on clinical parameters assessed at the first time of the patient's presentation, which leads to a better orientation of the treatment of PE patients according to the estimated mortality (11).

Ethical considerations and statistical analysis

Throughout the research process, all members of the team maintained the confidentiality of patient information. The data was entered into SPSS software version 24. Central and dispersion indices and frequency tables were used to describe the data. A T-test was used to compare quantitative variables in two independent groups. The chi-square test was used to check the relationship between two qualitative variables. P values less than 0.05 were considered statistically significant.

RESULTS

Baseline characteristics of the study population

Table 1 shows demographic information about the study participants. Out of 40 patients, 22 (55%) were male and 18 (45%) were female. The mean and standard deviation of the age of the patients were 58.10 and 15.57 years, respectively. The oldest patient was 90 years old, and the youngest was 27 years old. The results of the evaluation of sPESI are shown in Figure 1. As can be seen, 8 patients (20%) were included in the low-risk group (score 0) and 32 patients (80%) were included in the high-risk group (score 1 or more). According to the t-test, the average age of the patients in the high-risk group was significantly higher (p-value: 0.001) than the low-risk group.

The results related to the clinical symptoms of the patients at the beginning of the study are presented in Figure 2. Out of 40 patients, 39 (97.5%) had dyspnea, 30 patients (75%) suffered from pleuritic chest pain, 17 patients (42.5%) experienced massive hemoptysis, and 1 patient (2.5%) faced a pressure drop.

Table 1. Demographic information of acute PE patients

Age			Sex		
Mean		58.10		**Frequency**	**Valid Percent**
Std. Deviation		15.57			
Minimum		27.00	**Male**	22	55
Maximum		90.00			
	25	48.00			
Percentiles:	50	59.00	**Female**	18	45
	75	70.00			

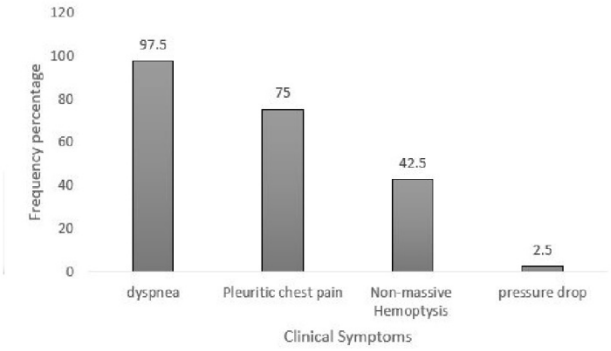

Figure 1. The frequency percentage of scores indicating the embolism severity index

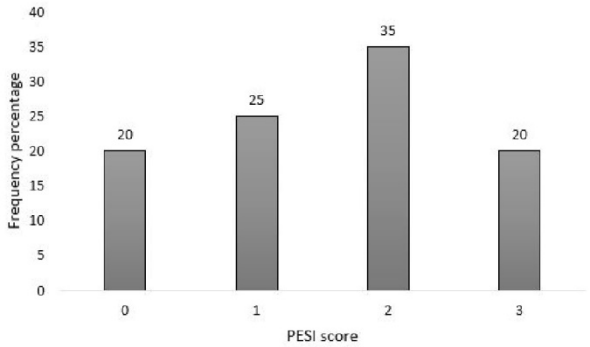

Figure 2. Frequency percentage of clinical symptoms in patients with acute pulmonary embolism

Association between embolism severity and variables

The chi-square test was used to investigate the relationship between embolism severity index and clinical symptoms. In this study, all patients had dyspnea, except for one patient who was in the low-risk group in terms of the severity of the embolism. According to the chi-square test, which obtained a p-value of 0.2, there was no statistically significant relationship between dyspnea and embolism severity.

In determining the relationship between the severity of embolism and pleuritic chest pain, half of the patients in the low-risk group experienced chest pain, while 81.3% of those in the high-risk group reported this pain (p-value: 0.089). Although a higher percentage of people in the high-risk group had chest pain than in the low-risk group, this difference was not found to be significant based on the chi-square test. In exploring the relationship between the severity of embolism and non-massive hemoptysis, these

clinical signs were not observed in 75% of the low-risk group and 53.1% of the high-risk group. Additionally, 88.2% of the cases were related to the high-risk group. According to the chi-square test, with a p-value equal to 0.428, there was no significant relationship between non-massive hemoptysis and the severity of pulmonary embolism in the studied patients.

In terms of blood pressure drop and its relationship with the severity of embolism, no pressure drop was recorded among the low-risk group in terms of the severity of embolism. In 96.9% of the high-risk group, there was no pressure drop. The chi-square test with a p-value equal to 1 also showed that there is no relationship between the patient's embolism severity and blood pressure drop.

According to the echocardiography results, the value of MID RV in 50% of patients was more than 3.55 cm (a diameter greater than 3.5 cm indicates RV dilatation). The amount of S(tv) in 25% of patients was less than 9 cm/s (the normal reference limit is more than 9.5 cm/s). PAP was more than 25 mmHg in 75% of patients.

To investigate the relationship between embolism severity index and echocardiography criteria, including MID RV, S(tv), and PAP, a t-test was used. The values of these variables according to the embolism severity index are shown in Table 2. The average MID RV in the high-risk group was significantly (p-value<0.001) higher than in the low-risk group. The difference between the low-risk and high-risk groups was not significant in terms of S(tv) (p-value: 0.062). The average pulmonary artery pressure in the high-risk group was about twice that of the low-risk group, which was statistically significant (<0.001 p-value).

Table 2. The relationship between embolism severity index and echocardiography criteria in PE patients

	Mean & Std. Deviation	sPESI	Mean	Std. Deviation	P-value
MID RV	3.49±0.609	high risk	3.6562	0.55471	<0.001
		low risk	2.8250	0.27646	
S(tv)	10.59±2.3	high risk	10.3688	2.49185	0.062
		low risk	11.5000	1.06904	
PAP	45.7±22.63	high risk	50.5938	22.72253	<0.001
		low risk	26.1250	4.54933	

Table 3 presents the results related to the size and function of the right ventricle. RV size was normal in 42.5% of patients, and 57.5% had increased RV size in different degrees of mild, moderate, and severe. RV function was normal in 42.5% of patients, and various degrees of RV dysfunction were reported in 57.5% of patients.

Table 3. Findings related to RV size and function in PE patients

		Frequency	Valid Percent
RV size	Normal	17	42.5
	Mild enlargement	5	12.5
	Moderate enlargement	11	27.5
	Severe enlargement	7	17.5
RV function	Normal	17	42.5
	Mild dysfunction	2	5.0
	Moderate dysfunction	16	40.0
	Severe dysfunction	5	12.5

To investigate the relationship between RV size and function with embolism severity index, the chi-square test was used (Table 4).

Table 4. Investigating the relationship between embolism severity index and RV size and function

Variables	Degree of changes		sPESI score		Total
			Low risk	High risk	
RV size	Normal	Count	7	10	17
		% within PESI	87.5%	31.3%	42.5%
	Mild enlargement	count	1	4	5
		% within PESI	12.5%	12.5%	12.5%
	Moderate enlargement	Count	0	11	11
		% within PESI	0.0%	34.4%	27.5%
	Severe enlargement	Count	0	7	7
		% within PESI	0.0%	21.9%	17.5%
RV function	Normal	Count	7	10	17
		% within PESI	87.5%	31.3%	42.5%
	Mild dysfunction	Count	0	2	2
		% within PESI	0.0%	6.3%	5.0%
	Moderate dysfunction	Count	1	15	16
		% within PESI	12.5%	46.9%	40.0%
	Severe dysfunction	Count	0	5	5
		% within PESI	0.0%	15.6%	12.5%

All cases of severe and moderate RV size increase were related to the high-risk group. Also, 80% of the cases of mild increase in RV size were reported in the high-risk group. Also, 87.5% of patients in the low-risk group were

in normal condition in terms of RV size. While only 31.3% of people in the high-risk group were in normal condition. The p-value was 0.026, which confirms a significant relationship between RV size and the severity of pulmonary embolism. Examining the severity of embolism concerning RV function showed that out of 23 cases of dysfunction, 22 cases belonged to the high-risk group. Thus, RV function was normal in only 31.3% of patients in the high-risk group. While 46.9% of people in this group had moderate dysfunction, 15.6% had severe dysfunction, and 6.3% had mild dysfunction. The p-value was 0.038, which showed a significant relationship between RV function and the severity of pulmonary embolism.

DISCUSSION

In the present study, the average age of patients in the high-risk group was about 20 years older than the low-risk group. Also, among the echocardiographic markers, RV size and function, MID RV, and pulmonary artery pressure showed a significant relationship with embolism severity.

In a retrospective study with a 4-year data analysis by Bajaj et al. regarding the clinical characteristics of PE, all hospitalizations and emergency department admissions over 18 years of age with a diagnosis of PE were included in the study. PE was confirmed in 334 patients during the study period. The average age of the subjects was 65.8 years (±16.4, range 98-22). 54% of the studied subjects were women. Dyspnea, chest pain, and cough were present in 72, 38, and 19% of patients, respectively. Dyspnea was the only presenting symptom in 29%. Tachypnea, hypoxia, and tachycardia were present in 39, 35, and 33%, respectively (15). Similarly, in our study, shortness of breath and chest pain were the two clinical symptoms with the highest frequency among the patients. In this study, the rate of pulmonary embolism increased with age, which is consistent with the results of other studies. In fact, age is not an independent factor in the aggravation of the disease, but underlying diseases and immobility, and accompanying conditions are predisposing factors for this disease at older ages (16).

In a prospective observational study by Dresden et al. regarding patients with suspected or confirmed pulmonary embolism, bedside echocardiography was performed for the participants to evaluate right ventricular dilatation and right ventricular dysfunction. 30 out of 146 patients had pulmonary embolism. Right ventricular dilatation in echocardiography had a sensitivity of 50% and a specificity of 98%. In this study, it was found that right ventricular dilatation and right ventricular dysfunction detected in echocardiography performed by an emergency physician are highly specific for pulmonary embolism but have poor sensitivity (17).

In the study of Kurnicka et al., echocardiographic findings of pulmonary embolism were investigated. In this study, which included 511 consecutive patients with confirmed PE (281 women and 230 men; mean age 64 ± 18.6 years), there were 16 cases (3.1%) of high-risk PE, while the remaining 495 patients (96.9%) were hemodynamically stable on admission (non-high-risk PE). RV dysfunction was observed in 20% of patients. RV enlargement was reported in 27.4% of patients (18). In our study, 42.5% of patients were in a normal condition regarding RV size and function. It is worth mentioning that about half of all patients with acute pulmonary thromboembolism have normal echocardiographic findings. On the other hand, symptoms of right ventricular overload or dysfunction may also be observed in the absence of acute pulmonary embolism, and this may be due to concurrent cardiac or respiratory disease (19).

In a research by Eid et al., 40 patients with pulmonary embolism were examined to study risk factors and echocardiographic markers. According to the results of this study, all patients experienced shortness of breath, 18 patients (45%) experienced chest pain, 8 patients (20%) experienced hypotension, and only four patients (10%) experienced hemoptysis. Echocardiography in this study showed that 27.5% of patients had no significant findings of pulmonary thromboembolism. In this study, RV dilatation and its dysfunction had a significant relationship with the severity of embolism in high-risk pulmonary

embolism patients (3). Several studies have shown that RV dilatation and RV dysfunction are independently associated with hemodynamic instability and higher mortality in patients presenting with acute PE (20,21). In our study, similar to the Eid study, a significant percentage of patients experienced shortness of breath and chest pain. Also, the present study showed a significant relationship between RV dilatation and its dysfunction with the severity of embolism, which is in line with the results of other studies. An individual patient-level meta-analysis of 6 prospective cohort studies that included 2874 normotensive patients with PE reported that right ventricular dysfunction was associated with an increased risk of death, shock, or recurrent PE (22).

In the present study, the average pulmonary artery pressure in the high-risk embolism group was about twice that of the low-risk embolism group. It is clear that acute embolism affects both blood circulation and lung gas exchange. If more than 30 to 50% of the total cross-section area of pulmonary arterial vessels is blocked by thromboembolism, pulmonary arterial blood pressure increases. Vasoconstriction caused by pulmonary thromboembolism, through the release of thromboxane A2 and serotonin, causes an increase in pulmonary vascular resistance (10).

CONCLUSION

According to PESI criteria, in acute PE patients who have risk factors such as underlying disease, low oxygen saturation, drop in blood pressure, and high heart rate, more detailed follow-up must be conducted through echocardiography.

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