Relationship between the Degree of Pulmonary Artery Obstruction and Echocardiographic Parameters in Patients with Pulmonary Thromboembolism

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ABSTRACT

BACKGROUND

Venous thromboembolism clinically presents as a pulmonary embolism or deep vein thrombosis. Pulmonary embolism presents as acute pulmonary obstruction caused by an embolus, and in 95 % of cases the embolus originates from the deep veins of the lower extremity, most often the popliteal vein and veins above it, or from the venous plexuses of the pelvis, while the rest present emboli from the right heart cavities, some other veins and in situ pulmonary artery thrombosis.

METHODS

This is a prospective study conducted among 52 consecutive patients who were hospitalised at the Department of Cardiology, Clinic for Heart, Blood Vessel and Rheumatic Diseases, Clinical Centre University of Sarajevo, Sarajevo, Bosnia and Herzegovina, from January 2017 - April 2019, diagnosed with pulmonary thromboembolism. Pulmonary artery obstruction index was calculated based on computed tomography (CT), and pulmonary angiography. Transthoracic echocardiography was performed for each patient to assess the degree of tricuspid regurgitation, right ventricle systolic pressure, right heart cavities dimension – right ventricle and right atrium, ejection fraction, D-dimer and left ventricular internal diameter end diastole.

RESULTS

There was statistically significant difference between pulmonary artery obstruction scores and echocardiographic parameters including severity of the degree of tricuspid regurgitation, dimensions of the right atrium, right ventricle dimensions and right ventricular pressure values. In this study 19 % of patients had normal values of pulmonary hypertension (mean rank = 11.95) compared to 28 % of patients with severe (mean rank = 32.15) and very severe pulmonary hypertension. There was statistically significant correlation between pulmonary artery obstruction scores and D-dimer, tricuspid regurgitation, and between pulmonary artery obstruction index (PAOI) scores and right ventricular pressure. Tricuspid regurgitation has the highest correlation with PAOI score.

CONCLUSIONS

Level of pulmonary obstruction via pulmonary artery obstruction score in patients with pulmonary embolism can be a useful parameter which is easy to calculate and can be used as a leverage in the assessment of severity of condition in patients with pulmonary embolism as well as a method for evaluation of prognostic outcome.

KEY WORDS

Pulmonary Embolism, Computed Tomography Angiography, Heart

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BACKGROUND

Venous thromboembolism is clinically present as a pulmonary embolism (PE) or deep vein thrombosis (DVT).[1,2] PE presents acute pulmonary obstruction caused by an embolus, and in 95 % of cases the embolus originates from the deep veins of the lower extremity, most often the popliteal vein and veins above it, or from the venous plexuses of the pelvis, while the rest, present emboli from the right heart cavities, some other veins and in situ pulmonary artery thrombosis.[1,3] Dyspnoea, chest pain, and cough are the most common symptoms of PE, while clinical picture is characterised by fever, tachycardia, abnormal pulmonary signs and peripheral vascular collapse.[4] Diagnosis of pulmonary embolism is made on the basis of auscultatory examination of the lungs, auscultation of the heart, laboratory findings, monitoring of oxygen saturation, prediction scores (with consideration of possible aetiological factors), findings of thoracic x-ray, electrocardiogram and transthoracic echocardiogram (TTE) parameters and the final diagnosis of PE is made by computed tomography pulmonary angiogram (CTPA) with evaluation of PAOI or ventilatory perfusion scintigraphy of the lungs.[5,6] TTE is characterised by enlarged pulmonary arterial system and right ventricle, leading to right ventricular dysfunction.[6] A defect in the contrast filling of the corresponding segment of the lung indicates obstruction of its blood flow. A negative CT finding in a large number of cases excludes the existence of severe pulmonary thromboembolism.[1] The discrepancy between the ventilatory and perfusion scintigrams of the lungs speaks in favour of pulmonary thromboembolism. Ventilation perfusion scintigraphy of the lungs is today the gold standard in the diagnosis of PTE.

Increase in afterload in patients with massive and sub-massive pulmonary embolism leads to remodelling of right ventricle, as well as haemodynamic collapse and subsequently death.[7,8] Taking this into account, it is essential to quantify the level of pulmonary obstruction caused by thrombus itself in patients with pulmonary embolism. An objective and reproducible method which can be used in interdisciplinary communication can be achieved with adequate definition of PAOI score in patients with PE.

Wells score has been described by Bankier et al.[9] in order to objectify the level of pulmonary obstruction in patients with PE. However, calculation of this score tends to be complicated and can often mislead in assessment of the condition of pulmonary circulation. For example, incomplete obstruction of main branch of pulmonary artery could theoretically lead to a score of 100 %.

However, a certain level of blood flow towards distal parts of pulmonary artery can still be observed in these patients. That is the main reason this score has not been frequently used in medical practice. Due to these limitations, Qanadli et al. have developed PAOI score in order to discriminate complete and incomplete pulmonary obstruction.[10] This method is a simple and reproducible method in assessment of the level of obstruction of pulmonary arteries. The calculation of PAOI score is based on the number of obstructed segmental arteries as well as the number of segmental arteries with its origin in obstructed vessel.[10] It is important to emphasise that this method can be used in risk calculation even in patients with certain anatomic variations in number or course of pulmonary arteries.

We wanted to study the echocardiographic changes in patients with pulmonary thromboembolism, and to determine correlation between the degree of pulmonary artery obstruction and echocardiographic changes in patients with pulmonary thromboembolism.

METHODS

The study was observational and included 52 consecutive patients who were hospitalised at the Department of Cardiology, Clinic for Heart, Blood Vessel and Rheumatic Diseases, Clinical Centre University of Sarajevo, Sarajevo, Bosnia and Herzegovina, from January 2017 - April 2019.

Patients were hospitalised under a diagnosis of pulmonary thromboembolism, which was confirmed on the basis of the following criteria: clinical picture, changes in the electrocardiogram (ECG), serum D-dimer values and CT angiography with contrast.

Criteria for inclusion in the study were: patients who were hospitalised and discharged from the hospital with a diagnosis of pulmonary thromboembolism, patients with CTPA, patients with a diagnosis of PE who underwent TTE, and patients who consented

The degree of pulmonary artery obstruction index[9] was calculated at the Radiology Clinic, Clinical Centre University of Sarajevo. Criteria for exclusion from the study were: patients with systemic inflammatory and septic conditions, previously diagnosed malignancy, patients with primary pulmonary hypertension, patients with pulmonary fibrotic disease, patients with previously verified heart failure and patients with renal failure.

Measures

According to the previously mentioned criteria, data for: sex, age, D-dimer values, echocardiographic parameters and haemodynamic parameters were taken from the anamnestic data.

Of the total number of patients, 17 (32.7 %) were men while 32 were women (67.1 %). According to Mann-Whitney U test there was no statistically significant difference between patients' gender and PAOI scores. The mean age was 69.1 ± 12.44 years. In the female patient population, the mean age was 72.3 ± 10.14 years. In the male patient population, the mean age was 62.6 ± 14.45 years.

The presence of a thrombus in the segmental artery was counted as 1 point if the obstruction was incomplete and as 2 points if it was complete. If the thrombus was more proximal than a given segmental artery, the score was calculated for the number of segmental arteries that are from that vessel. Subsegmental embolism was calculated as incomplete segmental embolism and was marked as number 1. There are 20 segments, so maximum score can be 40. PAOI score, therefore, can have a value of 0 - 40. Index can be converted to percentages by following formula

$$\text{PAOI Index (\%)} = \frac{\text{PAOI } (0-40)}{40} * 100^{9,10}$$

Echocardiographic examination was performed during diagnostic processing of a patient on a Philips iE33 device (Amsterdam, Netherlands) according to Simpson at the Clinic for Heart, Blood Vessel and Rheumatic Diseases, Clinical Centre University of Sarajevo. The parameters of the qualitative assessment of the existence of enlargement of the right atrium and right ventricle were taken from the echocardiographic findings. The severity of the degree of tricuspid regurgitation (TR) was defined by the following values: 0 (none), mild regurgitation (1 +), moderate (2 +), moderate (3 +), and severe regurgitation (4 +). Right ventricle systolic pressure (RVSP) was calculated based on the rate of return flow of blood through the tricuspid valve due to tricuspid insufficiency. Values up to 25 mmHg were considered normal. Values of 40 - 50 mmHg defined as mild, 50 - 60 moderate, 60 - 70 severe and above 70 mmHg very severe pulmonary hypertension.[11] The value of the ejection fraction of left ventricle (EFLV) was also determined by ultrasound examination. Regular values of the EFLV are considered to be from 53 % to 66 %. From biochemical analyses, the serum value of the D-dimer was analysed. The analysis was performed in the Institute for Biochemistry, Clinical Centre University of Sarajevo by enzyme-linked immunoassay (ELISA) method. D-dimer reference values were 0 - 0.55 µg / mL. If D-dimer values were determined repeatedly during the hospitalisation period, the highest values were used in analysis.

Statistical Analysis

For statistical analysis of the obtained data, the software package SPSS Windows (version 21.0, SPSS Inc, Chicago, Illinois, USA) was used. The normality of distribution was tested. Due to the significant deviation of distribution from normality, the collected data was analysed by nonparametric procedures. For data processing Kruskal-Wallis test and Spearman's correlation coefficient were used. All analysis results with $P < 0.05$ or at a 95 % confidence level were considered statistically significant.

RESULTS

Table 1 presents difference between echocardiographic parameters and PAOI score. Difference between severity of the degree of tricuspid regurgitation and PAOI score were statically significant ($x^2 = 22.013$, $P < 0.001$). In this study we had 40 % (mean rank = 18.71) of patients with normal degree of TR compared to 37 % of patients with moderate severe (mean rank = 28.90) and very severe degree of TR (mean rank = 41.29). In the total population of 52 (100 %) patients, echocardiographic examination revealed that 19 (36.5 %) patients had normal dimensions of the right atrium while 33 (63.5 %) patients had enlarged dimensions of the right atrium. Normal dimensions of the right ventricle were present in 24 (46 %) patients compared to 28 (54 %) patients who had enlarged dimension of the right ventricle.

According to results there was statistically significant difference in PAOI scores between patients who had increased RV ($x^2 = 9.848$, $p < 0.01$) than patients who had normal RV, or who had increased RA ($x^2 = 12.231$, $P < 0.001$) than patient who had normal RA. Difference between right RVSP and PAOI score were statistically significant ($x^2 = 22.576$, $P < 0.001$). In this study 19 % of patients had normal values of pulmonary hypertension (mean rank = 11.95) compared to 28 % of patients with severe (mean rank = 32.15) and very severe pulmonary hypertension (mean rank = 41.50).

	Variables	N	Mean Rank	x^2	P
Tricuspid regurgitation (mmHg)	None	21	18.71	22.013	.000
	Mild regurgitation	6	16.25		
	Moderate	6	27.50		
	Moderate severe	5	28.90		
	Very severe	14	41.29		
Right heart cavities dimension – right Ventricle (mm)	Normal RV	24	19.42	9.848	.002
	Increased RV	28	32.57		
Right heart cavities dimension – right Atrium (mm)	Normal RA	19	16.87	12.231	.000
	Increased RA	33	32.05		
RVSP	Up to 25 mmHg	10	11.95	22.576	.000
	Mild PH (25 - 40)	17	21.82		
	Moderate PH (41 - 55)	5	30.20		
	Severe PH (56 - 70)	10	32.15		
	Very severe PH (> 70)	10	41.50		

Table 1. Kruskal Wallis Test Results (RVSP - Right Ventricle Systolic Pressure, RV - Right Ventricle, PH - Pulmonary Hypertension)

	PAOI Score	D-Dimer	TR	LVID	EFLV	RVSP
PAOI score	1	.564†	.662†	.197	- .074	.653†
D-dimer		1	.475†	- .316*	- .308*	.426†
TR			1	.248	- .148	.844†
LVID				1	- .404†	.180
EFLV					1	- .096
RVSP						1

Table 2. Correlation between PAOI Score and Echocardiographic Parameters (LVID - Left Ventricular Internal Diameter End Diastole, EFLV - Ejection Fraction of Left Ventricle, RVSP - Right Ventricle Systolic Pressure)

*statistically significant at level of 0.05; † statistically significant at level of 0.01

Table 2 presents correlations between PAOI scores and echocardiographic parameters. Correlation analysis indicated a significant relationship between D-dimer ($r = 0.564$, $P < 0.01$), TR ($r = 0.662$, $P < 0.01$), RVSP ($r = 0.653$, $P < 0.01$) and PAOI score. According to the results tricuspid regurgitation had the highest correlation with PAOI score, and also there was a very high correlation between PAOI score and RVSP, so they are one of the most important echocardiographic parameters monitored in the study.

DISCUSSION

There was statistically significant difference between PAOI scores and echocardiographic parameters including severity of the degree of tricuspid regurgitation, dimensions of the right atrium, right ventricle dimensions and right ventricular pressure values.

In this study there were statistically significant correlation between PAOI scores and D-dimer, tricuspid regurgitation and between PAOI scores and right ventricular pressure.

According to the results women have been more often diagnosed with PE, probably due to their older age, which was statistically confirmed. Old age, higher risk of falling and injuries, and subsequent risk of bone fractures have been

confirmed as independent risk factors for PE. Both can lead to immobilisation, higher hospitalisation rate and more operative procedures. All of these are considered to be independent risk factors for PE.[12]

According to previous research calculation of PAOI score can be used as an objective parameter in evaluation of pulmonary obstruction and subsequently in evaluation and follow-up of patients diagnosed with PE.[6,10]

Our research has proven statistically significant connection between values of D-dimer and PAOI score in patients with PE. Based on these results, it can be concluded that patients with higher level of pulmonary obstruction are diagnosed with increased values of D-dimer due to greater volume of the thrombus itself. Our results were conclusive with results of Ghanima et al.[13] who evaluated 100 patients with the diagnosis of PE. Their research evaluated correlation between D-dimer and values of PAOI score. The mean value of D-dimer in their research was 5 µg / ml and it was concluded that there was statistically significant positive correlation between values of D-dimer and PAOI score. It has been concluded that values of D-dimer positively correlate with severity of PE based on radiological, biochemical and clinical results.

Ji Y et al. evaluated a group of 69 patients with PE.[14] Their results were conclusive with results from our study. Ji Y et al[14] have proven that values of PAOI score positively correlate with right ventricle enlargement. Moreover, patients with values of PAOI score above 23, 1 % are diagnosed with increased level of D-dimer compared to patients with PAOI score under 23, 1 %.

Although, in this research there were no correlation between PAOI score and EFLV, it is important to emphasize that heart ultrasound is routinely used to assess EFLV. One might assume that EFLV should be within normal range in patients with PE. However, due to the fact that heart acts as one united entity, right ventricle dysfunction consequently leads to left ventricle dysfunction. In patients diagnosed with massive PE, blood influx in left ventricle is reduced which leads to decreased EFLV. Moreover, in those patients, right ventricle is enlarged due to the development of pulmonary hypertension, which leads to the protrusion of interventricular septum towards left ventricle, whose volume is also reduced.

As we expected there was statistically significant correlation between PAOI score and level of tricuspidal regurgitation. Furthermore, level of tricuspidal regurgitation and PAOI score have been strongly positively correlated. In this study we also calculate difference in degree of severity of tricuspidal regurgitation and PAOI scores, which also were statistically significant, i.e., patients with higher degree of severity have also higher PAOI score than those patient with normal or mild regurgitation. According to Antunes & Barlow[15] increased pulmonary vascular resistance causes the formation of tricuspidal regurgitation, due to an increase in pressure in the right cavity.

Kumar et al[16] have analysed correlation between PAOI score and right ventricle dysfunction. One of the evaluated parameters in their research was severity of regurgitation of tricuspidal valve as a predictor of right ventricle dysfunction. They have determined that values of PAOI score can be used as a good predictor of right ventricle dysfunction and that these two variables are reciprocally correlated. Additionally, PAOI score can be used as a good predictor of negative outcome in patients with PE.[14] Wu As et el[17] have proven that 83 % of patients diagnosed with PE and PAOI score above 60 % have died during the treatment, whereas 98 % of patients with score under 60 % survived. In our research, there were statistically significant difference between PAOI score and dimensions of right ventricle pressure. Based on this, we can assume that level of pulmonary obstruction necessarily leads to increased pressure in main branch of pulmonary artery and consequently in right ventricle.

Analysis of 130 patients in research by Krca et al[18] has shown similar results. They evaluated PAOI score and its' correlation with different echocardiographic findings and patterns in patients with PE. Our results were conclusive with those from Qanadli et al. They have proven that patients with PAOI score above 40 % are in 90 % of cases diagnosed with right ventricle dilatation.[10] Cildag et al[6] have shown that there is a significant difference in diameter of right ventricle in patients with and without right ventricle dysfunction. Moreover, it was confirmed that statistically significant correlation existed between diameter of right ventricle and PAOI score during follow-up period.

Increased right ventricular pressure leads to loading of both RA and RV. The PAOI score was significantly correlated with pressure in the right cavities. It is imperative to treat pulmonary thromboembolism in adequate time due to the function of the right ventricle.[19]

The first limitation of this study was the small sample size. This study may be a good basis for new research, with a larger number of subjects, and a comprehensive approach to the patient, in terms of risk factor analysis for pulmonary thromboembolism, coagulation system, initial pharmacological treatment, and possibly invasive measures of pulmonary vascular resistance. Second limitation of this study was that we had only one measure point. It was important to monitor the patient 6 months after the incident, and to indicate echocardiographic parameters after the monitored time and to correlate the parameters with the initial finding.

CONCLUSIONS

Level of pulmonary obstruction via PAOI score in patients with PE can be a useful parameter which is easy to calculate and can be used as a leverage in the assessment of severity of condition in patients with PE as well as a method for evaluation of prognostic outcome.

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A.Dz, E.B. and M.B. gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. Each author had role in drafting the work and revising it critically for important intellectual content and gave final approval.

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