

Comparison of conventional and developed echocardiographic criteria of pulmonary embolism

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The aim of the study was to compare the conventional and developed echocardiographic (EchoCG) criteria of severity of the course and prognosis of pulmonary embolism (PE) outcomes and to establish the most significant of them.

Methods. The study included 428 patients with PE, of whom 42 died and 51 had hemodynamically significant course of the disease. The remaining patients were hemodynamically stable. Of these, 193 had evidence of right heart overload on echocardiography and 142 did not. The prevalence of commonly accepted and developed EchoCG criteria was assessed in the study groups with subsequent comparative analysis and determination of the significance of each parameter.

Results. The significance of such common EchoCG criteria of right heart overload as the presence of interventricular septal flattening (74.1% and 82.6%, respectively) and right ventricular free wall dyskinesia (67.3% and 88.2%, respectively), which have the highest diagnostic

sensitivity and specificity for determining the severity of the disease course and fatal outcome, was confirmed. It has been proved that it is more informative to estimate not the level of pressure in the pulmonary artery, but to calculate the pressure gradient on its valve. Decrease of this parameter less than 16 mmHg is highly ($r=0.99$) associated with hemodynamically significant course of the disease, and less than 12 mmHg — with death. The calculated volume of tricuspid regurgitation, especially in correlation with the right atrial volume, more clearly and informatively reflects the overload of the right heart chambers than the degree of tricuspid regurgitation, and allows to assess its dynamics during therapy.

Conclusion. The determined generally accepted and developed EchoCG criteria allow to optimize the stratification of patients according to the severity of PE course and prediction of its outcomes.

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Introduction

Pulmonary embolism (PE) is the sudden complete or partial occlusion of a branch of the pulmonary artery by a thrombotic mass that obstructs normal blood flow, resulting in increased pressure and enlargement of the right ventricle (RV) [1, 2]. In patients with significant RV overload due to functional insufficiency of the tricuspid valve, there may be increased severity of blood regurgitation into the right atrium with dilation of the inferior vena cava more than 20 mm and reduction of its collapse during breathing, as well as development of dyskinesia zones, usually of the RV free wall with preserved mobility of the apex [3, 4]. All these signs can be diagnosed by echocardiography (EchoCG), which is the most widespread and accessible method to evaluate morphological and functional changes of the heart and its valvular apparatus. The convenience of cardiac ultrasound in PE lies, first of all, in the possibility to evaluate all changes in real time at the patient's bedside, and in case of severe condition helps to diagnose the disease quickly [5, 6].

According to modern concepts, EchoCG plays a significant role in determining the severity of disease progression and the probability of death in patients with PE. In a hemodynamically unstable patient with suspected PE, incontrovertible signs of pressure overload or RV dysfunction become the basis for urgent initiation of reperfusion therapy in the absence of CT-angiography [1, 6, 7].

However, taking into account the features of RV geometry, there is no single EchoCG parameter to rapidly and reliably detect RV dysfunction, and the course of the disease is not always accompanied by typical signs [8, 9]. Therefore, EchoCG diagnosis of PE is difficult, and the significance of EchoCG criteria varies in different studies [10, 11]. All this determines the importance of searching for new, more accurate criteria reflecting the degree of RV dysfunction [12, 13].

The aim of the study was to compare the conventional and developed echocardiographic (EchoCG) criteria of severity of the course and prognosis of PE outcomes and to establish the most significant of them.

Methods

The course of PE was analyzed in 428 patients hospitalized between 2010 and 2022. Of these, 42 died despite treatment (fatal PE). They formed the first comparison group. There were 18 men and 24 women. The age of the patients ranged from 34 to 92 years, with a mean age of 66.5 ± 12.0 years. According to the Pesi scale of early PE-associated death, 38.1 % of patients had class 4 and 61.9 % class 5.

Hemodynamically significant PE was present in 51 patients who constituted the second group. There were 23 men and 28 women. The age of the patients ranged from 27 to 84 years with a mean age of 62.6 ± 11.8 years. According to the Pesi scale of early PE-associated death, 17.7 % of the patients had class 3, 72.5 % class 4, and 9.8 % class 5.

The third group, PE patients with hemodynamically stable course and presence of EchoCG criteria for RV overload, consisted of 193 patients. There were 108 men and 85 women. The age of the patients ranged from 23 to 95 years, with a mean age of 64.7 ± 13.6 years. According to the Pesi scale, 48.2 % of the patients had class 3, 40.9 % class 4 and 10.9 % class 5 early PE-associated death.

The fourth, additional control group consisted of 142 patients aged 28 to 80 years with a mean age of 55.5 ± 16.2 years. This group was used to determine the thresholds of the developed EchoCG parameters in patients without evidence of right heart overload. There were 70 males and 72 females. The first class of early PE-associated death according to the Pesi

scale was found in 37.3 % of patients in this group, the second class — in 62.7 % of patients.

The groups were comparable by PE duration and comorbidities. Patients were treated according to the European Society of Cardiology risk stratification for early death from PE.

Inclusion criteria: age 18 years and older; presence of PE reliably confirmed by CT-angiopulmonography; general clinical and biochemical blood tests with determination of plasma concentration of troponin and D-dimer, electrocardiography, EchoCG, ultrasound angioscan of the lower limb veins on the first day of hospitalization.

The severity of the disease course was assessed using the Pesi index, which includes a large number of clinical characteristics. The probability of early PE-associated death was evaluated according to the European Society of Cardiology criteria.

Exclusion criteria of patients from the study were: death or discharge from the hospital before completion of all necessary investigations.

Statistical analysis

The volume of tricuspid regurgitation (V_{tr}) and the pressure gradient on the pulmonary artery valve (ΔP_{pa}) were calculated on the basis of the formula of elementary physics for the volume of fluid flowing through an orifice of a certain diameter under a pressure gradient on its different sides (1) [14, 15].

$$V = \eta x S \sqrt{\frac{2x\Delta P}{\rho}} \quad (1),$$

where:

V — the volume of blood flowing through the orifice during one systole;

μ — jet compression coefficient, equal to 0.62 for small orifices;

ΔP — pressure gradient on different sides of the orifices;

ρ — blood density of 1060 kg/m³;

S — cross-sectional area of fluid flow through the orifices.

The formula (2) was used to calculate the pulmonary artery pressure (P_{pa}):

$$P_{pa} = P_{RV} - \Delta P_{pa} \quad (2),$$

where:

P_{pa} — calculated pulmonary artery pressure;

P_{RV} — Right ventricular pressure, which is currently calculated as “systolic pulmonary artery pressure” during EchoCG;

ΔP_{pa} — the difference of pressure in the right ventricle and pulmonary artery, which was calculated according to the formula established earlier.

Based on these formulas, we determined the volume of tricuspid regurgitation and its ratio to the right atrial volume (V_{tr}/V_{RA}), as well as the pressure gradient across the pulmonary artery valve and the pressure in the pulmonary trunk. Thresholds were established for each of these parameters.

The methods of descriptive statistics were used to evaluate the prevalence of conventional and developed EchoCG criteria in the studied groups, to establish the correlation dependence of each conventional and advanced parameter with the severity of the disease course and mortality, to determine their diagnostic characteristics with subsequent comparative analysis.

Statistica 10.0 (Stat Soft Inc., USA) was used for statistical processing and analysis of the results. Data are presented as: absolute number of cases (n), prevalence of the trait (%), mean (M), and standard deviation (SD). Quantitative data were assessed for conformity to a normal distribution using the Shapiro-Wilk test (when n was less than 50) or the Kolmogorov-Smirnov test (when n was greater than 50). All distributions were normal. Statistical significance of differences was evaluated using Student's t-test. The significance of each parameter and its diagnostic characteristics were determined using Pearson's correlation (r) and the odds ratio method. Differences were considered statistically significant at $p < 0.05$.

Results

In PE patients of the first, second and third comparison groups, the prevalence of conventional EchoCG criteria such as: increase in the ratio of basal sizes of the right and left ventricles more than 0.9, which was 61.8 %, 58.8 % and 58 % of patients, respectively; presence of RV free wall dyskinesia, which was registered in 4.8 %, 9.8 % and 6.2 % of patients, respectively; flattening of the interventricular septum — in 31 %, 15.7 % and 25.4 % of patients, respectively. No statistically significant difference ($p > 0.05$) was found when the data were compared. However, a high correlation was found with the severity of the disease ($r = 0.76$) according to the Pesi scale, with the moder-

ate-high ($r=0.71$) and high ($r=0.70$) risk of early PE-related death according to the European Society of Cardiology criteria, and with the fatal outcome ($r=0.79$) for the presence of interventricular septal flattening on EchoCG. A moderate correlation was found between the same data and visualization of RV free wall dyskinesia, with correlation coefficients of 0.67, 0.53, 0.59, and 0.54, respectively. The diagnostic values of interventricular septal flattening and RV free wall dyskinesia were among the highest among the compared conventional parameters and were as following: sensitivity — 74.1% and 67.3%, respectively, specificity — 82.6% and 88.2%, respectively.

The next widely used criterion for diagnosis and severity assessment in patients with PE is the increase in pulmonary artery systolic pressure. We confirmed a significant correlation ($r=0.58$) between the increase in pulmonary artery systolic pressure of more than 55 mm Hg and class 5 severity of the disease course according to the Pesi scale, as well as high ($r=0.69$) and moderately high ($r=0.68$) risk of early PE-associated death according to the criteria of the European Society of Cardiology. However, considering the diagnostic sensitivity (66.1% and 71.2%, respectively) and specificity (57.5% and 68.3%, respectively), which are not very high for predicting mortality and patient severity, we attempted to develop a new method for calculating pulmonary artery pressure. Nearly identical physiological data were obtained. In the absence of right heart overload, the calculated pressure in the pulmonary trunk ranged from 2 to 12 mmHg, and the higher this index was, the more severe was the disease. At Ppa values higher than 35 mmHg, PE was hemodynamically significant in 68.6% of patients, and at the level of more than 45 mmHg — resulted in death in 83.3% of patients. This was confirmed by correlation analysis, which showed a high correlation with the severity of the disease ($r=0.79$) according to the Pesi scale and a high risk of early death associated with PE according to the ESC criteria ($r=0.93$). When comparing the results obtained, it was found that the increase in pulmonary artery pressure according to the developed method correlates better with the severity of the disease and the outcome than the calculation of systolic pulmonary artery pressure. Moreover, the latter is not a real method, but the determination of the pressure in the RV cavity, while the proposed method is a variant of the calculation of the pressure in the pulmonary ar-

tery trunk. However, when comparing the diagnostic characteristics of the proposed method of calculating the pressure in the pulmonary trunk and the generally accepted measurement of systolic pressure in the pulmonary artery, no significant increase was found. Diagnostic sensitivity and specificity were also not high, at 66.7% and 78.3%, respectively. This is most likely due to the fact that the pressure in the right ventricular cavity (pulmonary artery systolic pressure with its measurement errors) was used to calculate the pressure in the pulmonary artery trunk, according to generally accepted principles. Calculated determination of pressure gradient across the pulmonary artery valve, free from calculation of pulmonary artery systolic pressure, had more reliable diagnostic characteristics.

The mean calculated pressure gradient across the pulmonary artery valve in patients without evidence of RV overload was 24.1 ± 2.8 mmHg. This parameter was lower in patients with more severe course of the disease and hemodynamic instability. In all patients with fatal outcome it did not exceed 12 mmHg, in 94.1% of patients with hemodynamic instability it was in the range of 12 to 16 mmHg, and in 96.9% of patients with hemodynamic stability it was higher than 16 mmHg. These data were confirmed by correlation analysis, which showed a strong correlation with the severity of disease progression. The calculated pressure gradient across the pulmonary artery valve at its values from 4 to 12 mmHg highly correlated with class 4 ($r=0.72$) and very highly — with class 5 ($r=0.99$) of disease severity according to the Pesi scale, high probability of early PE-associated death according to ESC criteria ($r=0.96$), and fatal outcome ($r=1$). The disease tended to be hemodynamically significant ($r=0.78$) with ΔP_{pa} values between 12 and 16 mmHg, and at values greater than 16 mmHg the course of PE was stable ($r=0.77$).

The sensitivity and specificity of this parameter are quite high. They are 92.7% and 97.8%, respectively, for the severity of the disease course and 100% and 98.7%, respectively, for mortality. This indicates the greater importance of pressure gradient calculation in determining the severity of pulmonary embolism and prognosis compared with the determination of systolic blood pressure or pressure in the pulmonary artery trunk according to the proposed formula.

Determining the calculated volume of tricuspid regurgitation per one systole, it was found that it fully

corresponded to the degree of tricuspid regurgitation according to literature sources, namely, in patients with the 1st degree of regurgitation it did not exceed 30 ml, in the 2nd degree it ranged from 30 to 60 ml, and in the 3rd degree it was more than 60 ml. At the same time, of course, it was found out that the greater the volume of regurgitation, the more often it is associated with dilatation of the inferior vena cava more than 2 cm and absence of its collapse during inspiration by 50 % and more. Thus, at values of tricuspid regurgitation volume less than 30 ml, dilatation of inferior vena cava more than 2 cm and absence of its collapse during inspiration by 50 % and more occurred in 12.6 % and 2.6 % of patients, respectively, at values from 30 to 60 ml — in 29.4 % and 19.6 %, respectively, and at regurgitation volume more than 60 ml — in 86.4 % and 68.3 % of patients, respectively.

When comparing the values of the estimated volume of tricuspid regurgitation per systole, no differences were found in the severity of the patients' condition in the compared groups, as well as in the prevalence of the degree of tricuspid regurgitation, dilatation of the inferior vena cava by more than 2 cm and absence of its collapse during inspiration by 50 % or more.

To assess the severity of tricuspid regurgitation, it is important to evaluate not only the volume of tricuspid regurgitation, but also its ratio to the volume of the right atrial cavity, which is similar to the method used to determine the degree of tricuspid regurgitation. Equivalent values were obtained between the area and volume ratios. Thus, in the absence of pathological changes, V_{tr}/V_{RA} was not higher than 0.36, which is comparable to the first degree of regurgitation, and clinically manifested PE was at values higher than 0.6, which is comparable to the second degree and higher. However, the determination of V_{tr}/V_{RA} is clearer and more informative and allows us to assume that the blood volume exits the right atrium, resulting in dilatation of the inferior vena cava by more than 2 cm and the absence of its collapse during inspiration by 50 % or more due to volume and pressure overload. This is confirmed by the correlation analysis, which showed a high correlation between V_{tr}/V_{RA} and inferior vena cava dilation of more than 2 cm ($r=0.79$) and the absence of its collapse on inspiration by 50 % and more ($r=0.76$). The above indicates the possibility of estimating the volume of tricuspid regurgitation and its relation to the volume of the right atrium with greater informative value than dilatation of the inferior vena

cava more than 2 cm and absence of its collapse on inspiration by 50 %.

When comparing the mean values of V_{tr}/V_{RA} , it was found that in patients with fatal outcome and hemodynamically unstable patients they were statistically significantly higher ($p<0.01$) than in patients with stable hemodynamics: 0.57 ± 0.2 and 0.66 ± 0.31 versus 0.48 ± 0.18 , respectively, and when comparing the prevalence of the degree of tricuspid regurgitation in all groups, no statistically significant differences were obtained ($p>0.05$). This confirms the usefulness of using the calculated numerical parameters of regurgitation and V_{tr}/V_{RA} compared to the degree of tricuspid regurgitation both at the initial contact and, to a greater extent, to assess the dynamics of changes on the background of treatment.

When estimating the correlation dependence of the currently used method of determining the degree of tricuspid regurgitation, it was found that its increase more than the second degree weakly reflects the severity of the disease course and moderately ($r=0.31$) correlates with the onset of fatal outcome, and V_{tr}/V_{RA} significantly correlates with 4 ($r=0.52$) and 5 ($r=0.69$) classes of the severity of the disease course according to the Pesi scale and with mortality ($r=0.68$). The diagnostic sensitivity and specificity of the degree of tricuspid regurgitation and V_{tr}/V_{RA} were practically equal and amounted to 71.5 % and 76.4 % for the mortality (sensitivity — 71.5 % and 76.4 %, specificity — 59.4 % and 54.1 %, respectively) and for the severity of the disease course (70.7 % and 64.3 %, sensitivity — 57 % and 53.6 %, respectively).

Discussion

We demonstrated that among the currently widely used EchoCG criteria of RV dysfunction in patients with PE, the most significant in determining the severity of the disease course are flattening of the interventricular septum and dyskinesia of the RV free wall, which is consistent with literature sources [1, 10, 11].

Such EchoCG criteria as the increase in systolic pressure in the pulmonary artery and the degree of tricuspid regurgitation, regardless of its severity, are less informative in determining the severity of the course of PE and predicting its outcome than the proposed calculation of the pressure gradient across the pulmonary artery valve and determination of the ratio of the volumes of tricuspid regurgitation and the right atrium [3, 5, 6].

The calculated volume of tricuspid regurgitation per systole does not have a strong diagnostic and prognostic significance, but in contrast to the determination of the degree of tricuspid regurgitation, which is currently used for indirect assessment of right atrial overload, it allows for a clear and informative assessment of the dynamics of blood flow through the tricuspid valve during systole [8, 9].

Conclusion

To determine the severity of the PE course, it is most effective to use such conventional EchoCG criteria

of right ventricular overload as flattening of the interventricular septum and right ventricular free wall dyskinesia, while the determination of the level of systolic pressure in the pulmonary artery and the degree of tricuspid regurgitation should be replaced by the calculation of the pressure gradient across the pulmonary valve and the ratio of tricuspid regurgitation to right atrial volume.

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