Right ventricular function assessment by 3D echocardiography and 2D speckle-tracking imaging in acute pulmonary embolism

Nguyen Thi Thu Hoai*,***, *Bach Mai Hospital,
Pham Nguyen Son,***** **108 Military Central Hospital,
***University of Medicine and Pharmacy, Hanoi National University.

Summary

Objective: To assess changes in right ventricular (RV) function parameters determined by three-dimensional (3D) echocardiography and two-dimensional (2D) speckle-tracking echocardiography in patients with acute pulmonary embolism without systemic hypotension, as compare to a control population. *Subject and method:* Fifty-seven intermediate-high risk pulmonary embolism patients were prospectively studied at the onset of the acute episode and after median follow-up periods of 30 days. A control group of age-and sex-matched subjects were selected. All patients and the controls underwent 2D and 3D transthoracic echocardiography within 24 hours of pulmonary embolism diagnosis and one month after hospital discharge. Tricuspid annular peak systolic velocity (s'), tricuspid annular plane systolic excursion (TAPSE), RV diameter, RV fractional area change (FAC), 3D RV ejection fraction (EF), 2D RV global strain and RV free wall strain were measured. *Result:* From Dec. 2019 to March 2022, fifty-seven patients with acute intermediate-high risk of early mortality PE were included. Mean age was 56 ± 14 years. Men accounted for 47.4% (27/57). Control group consisted of 34 subjects. Pulmonary embolism patients initially had RV dysfunction as assessed by 2D and 3D parameters: RV diameter: 29.3 ± 4.6mm; TAPSE: 14.6 (9.1-15.7) mm; FAC: 31.5 (30.5-39.9)%; 3DRVEFL 31.9 ± 7.7%; RVGS: -9.8 ± 3%, RVFWS: -8.9 ± 3.3%. At 30-day follow-up: s', TAPSE, RV diameter, RV FAC were restored compared to the control group, systolic pulmonary artery pressures decreased significantly, right atrial pressure, also decreased significantly at follow-up, contrary to 3DRVEF and RV 2D global strain and free wall strain. *Conclusion:* After 1 month of anticoagulant therapy in patients with intermediate-high risk pulmonary embolism, RV function has not fully recovered as assessed by 3D RVEF and 2D strain imaging, while the traditional echocardiographic assessment could not detect this incomplete recovery. Further studies are needed to assess the prognostic role and implications of this residual 3DRVEF and 2D RV strain impairment after PE.

Keywords: 3D echocardiography, speckle-tracking echocardiography, right ventricular function, pulmonary embolism, pulmonary hypertension.

1. Background

Pulmonary embolism (PE) is a fatal disease and is defined as the migration into the pulmonary artery tree of an embolus responsible for the obliteration of the trunk, or one or more branches of the pulmonary artery [1]. The obstruction of the pulmonary tree may lead to right ventricular (RV) dysfunction which can be evaluated with echocardiography. The in-hospital mortality of patients with pulmonary embolism (PE) varies from 5% to 50% [2]. Echocardiographic quantification of RV function is gaining increasing interest, especially in cardiac diseases that affect the right heart

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***Correspondence to**: Nguyen Thi Thu Hoai, Vietnam National Heart Institute, Bach Mai Hospital*
***Email:** hoainguyen1973@gmail.com*

chambers [3]. Two-dimensional (2D) speckle-tracking echocardiography (STE) is an emerging modality to assess myocardial wall movements and deformation, and the indexes derived from STE can be used as an adjunctive tool in the comprehensive evaluation of RV function [4]. Real-time three-dimensional (3D) echocardiography allows the measurement of RV end-diastolic volume (RVEDV) and RV ejection fraction (RVEF) irrespective of its shape and more reliably compared with 2D echocardiography [5]. The application of STE in RV dysfunction in patients with acute PE has been previously described [6], however, data on 3D RVEF in this clinical setting are in paucity. The aim of the study was *to investigate the RV adaptation to acute intermediate-high risk PE at time of diagnosis and its recovery at 30-day follow-up after discharge.*

2. Subject and method

2.1. Study design and patients

We conducted a prospective case control and longitudinal study on adult patients admitted for acute PE in Vietnam National Heart Institute (VNHI), Bach Mai Hospital from Dec 2019 to March 2022.

Inclusion criteria of the PE patients: Intermediate-high risk PE adult patients according to the ESC guidelines (2014) [7]: (positive cardiac biomarkers: NT-proBNP and/or hs-troponin T; evidence of RV dysfunction, no shock or hypotension). PE diagnosis was confirmed by the presence of thrombi in the pulmonary arteries on thoracic computed tomography.

Inclusion criteria of controls: Healthy volunteers from the outpatient clinic who were matched for age and sex to the patients' group and had normal electrocardiographic and echocardiographic results.

Exclusion criteria: Moderate or greater valvular disease, coronary artery disease, chronic congestive heart failure, chronic obstructive pulmonary disease, a prior documented episode of PE, comorbidity with life expectancy < 6 months, and insufficient ultrasound image quality (defined as more than two myocardial segments that were not well-visualized on 2D echocardiography.

Sampling method: We collected all PE patients who met the inclusion during the study period. Patients were recruited consecutively.

Data collection: Transthoracic echocardiography was performed at the onset of the acute episode (within 24 hours after admission) and after a median follow-up period of 30 days. All patients were treated with anticoagulant. Information about symptoms and functional criteria New York Heart Association (NYHA) class was collected. Written informed consent was obtained.

2.2. Standard echocardiography

Echocardiographic examination was performed using a GE Vivid E95 ultrasound system (USA 2019) at the echocardiography laboratory of VNHI, Bach Mai hospital, Hanoi. Echocardiography was performed according to the recommendations of the American Society of Echocardiography (2015) [4]. The following parameters were measured and averaged over three consecutive cycles: Left ventricular (LV) ejection fraction, right atrial pressure according to the inferior vena cava dimension and collapsibility, systolic pulmonary artery pressure, tricuspid annular peak systolic velocity (s'), tricuspid annular plane systolic excursion (TAPSE), RV diameter, RV fractional area change (FAC), presence of paradoxical septum motion. The presence of the McConnell's sign, defined by regional RV wall motion abnormality of the basal and mid free wall with apical RV hyper-contractility, was also assessed [8].

2.3. Three-dimensional echocardiography

Three-dimensional echocardiography was performed using a dedicated broadband, matrix-array transducer to enable full coverage of the entire right ventricle by the high volume rate and wide-angle mode (full-volume mode). Before each acquisition, the images were optimized for endocardial border visualization by increasing the overall gain and modifying the time gain and compression. Echocardiographic images were stored digitally in DICOM format for offline analysis using ECHOPAC software. RV end-diastolic volume (RVEDV) and RV end-systolic volume (RVESV) were measured from each 3D echocardiographic data set. RVEF was calculated as follows: RVEF = [(RVEDV - RVESV)/RVEDV] x 100% (Figure 1). The process of volume determination was done two times for each patient.

2.4. Two-dimensional speckle tracking echocardiography

Apical RV focused four-chamber view was used, we ensured to take an adequate field of view to image the entire right ventricle. 2D peak systolic RV longitudinal strain was measured using a six-segment RV model (basal free wall, mid free wall, apical free wall, apical septum, mid septum, and basal septum). Peak systolic strain was recorded for the three RV myocardial free wall (RVFWS) and septal segments and the entire RV wall (RVGS) using the ECHOPAC software.

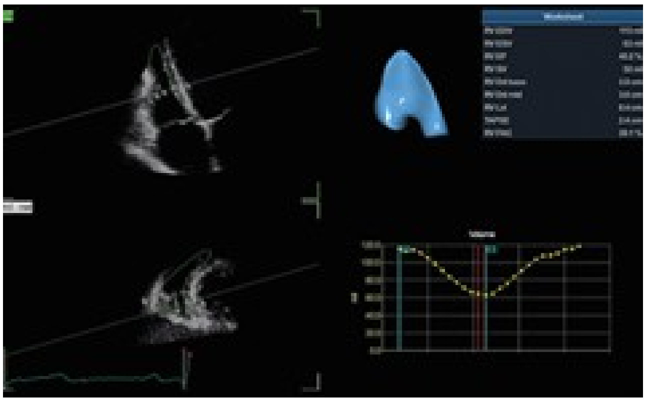

Figure 1. Measurements of three-dimensional RV volumes and RVEF

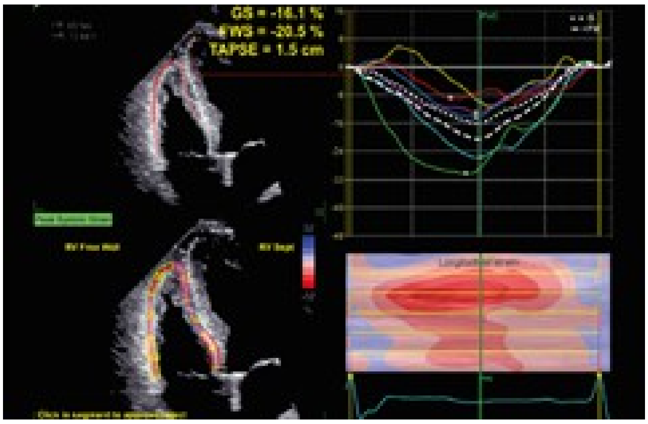

Figure 2. Measurements of RV global strain (RVGS) and free wall strain (RVFWS) using two-dimensional speckle-tracking echocardiography

2.5. Statistical analysis

Data were summarized as mean ± standard deviation for continuous variables with normal distribution; median [95% confidence interval] for other continuous variables and number of subjects (%) for categorical variables. Comparisons between PE patients on admission and after 1 month were tested by the paired Student t-test for normally distributed variables or by the Wilcoxon test otherwise. Comparisons between PE patients and controls were performed using the Student t-test for normally distributed variables or by the Mann-Whitney U-test otherwise. Categorical variables were compared using Fisher's exact test. In all analyses, statistical significance was defined as a p-value <0.05.

3. Result

Fifty-seven patients with acute intermediate-high risk of early mortality PE were included. Mean age was 56 ± 14 years. Men accounted for 47.4% (27/57). Control group consisted of 34 healthy subjects.

Table 1. Baseline clinical characteristics of the PE patients

Parameters (n = 57)	$\overline{X}$ ± SD or n (%)
Age (y)	56 ± 14
BSA (m^2)	1.73 ± 0.12
SBP (mmHg)	121 ± 13
DBP (mmHg)	78 ± 9
Hear rate (bpm)	89 ± 11
Tarchycardia (>100 bpm)	13 (22.8%)
NYHA ≥ II	35 (61.4%)
SpO2 (%) < 90%	15 (26.3%)
DVT	25 (43.9%)
Thrombolysis	8 (14.0%)
Embolectomy	5 (7.0%)

BSA: Body surface area, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, NYHA: New York Heart Association, DVT: Deep vein thrombosis.

The baseline characteristics of all patients with PE are described in Table 1. Sixty-one percent (n = 35) of the patients had limitations of functional capacity (New York Heart Association functional class ≥ II). Thirteen patients (22.8%) had tachycardia (heart rate > 100bpm).

Table 2. Echocardiographic characteristics of studied population

Parameters	Echo 1 Baseline (n = 57)	Echo 2 1 month (n = 50)	Controls (n = 34)	p (Echo1vs Echo2)	p (Echo1 vs controls)	p (Echo2 vs controls)
RV diameter (mm)	29.3 ± 4.6	24.3 ± 4.6	23.3 ± 4.6	**<0.05**	**<0.05**	>0.05
TAPSE (mm)	14.6 (9.1-15.7)	20.1 (19.3-23.9)	21.3 (19.9-24.7)	**<0.05**	**<0.05**	>0.05
TVs' (cm/s)	10.5 ± 1.6	12.1 ± 3.5	13.5 ± 1.4	**<0.05**	**<0.05**	>0.05
RVFAC (%)	31.5 (30.5-39.9)	35.7 (31.9-42.8)	41.1 (36.5- 45.8)	**<0.05**	**<0.05**	>0.05
sPAP (mmHg)	51.5 ± 17.2	42.4 ± 19.6	27.4 ± 7.3	**<0.05**		
3DRVEDV (ml)	98.3 ± 32.7	72.3 ± 19.9	61.3 ± 17.5	**<0.05**	**<0.05**	>0.05
3DRVEF (%)	31.9 ± 7.7	33.6 ± 7.6	52.3 ± 9.6	**>0.05**	**<0.05**	**<0.05**
RVGS (%)	-9.8 ± 3	-11.6 ± 6.3	-13.7 ± 4.0	**>0.05**	**<0.05**	>0.05
RVFWS (%)	-8.9 ± 3.3	-10.7 ± 4.8	-13.5 ± 2.9	**>0.05**	**<0.05**	>0.05
LVEF-Simpson (%)	61.2 ± 8.1	69.2 ± 9.0	62.2 ± 6.7	**<0.05**	**<0.05**	>0.05
E/e'	7.4 ± 1.9	7.5 ± 2.8	8.2 ± 2.9	>0.05	>0.05	>0.05
IVC diameter (mm)	20.7 ± 4.9	15.4 ± 2.5	14.4 ± 2.8	**<0.05**	**<0.05**	>0.05

(FAC: Fractional area change; LV: Left ventricular; LVEF: Left ventricular ejection fraction; RV: Right ventricular; sPAP: Systolic pulmonary artery pressure; TV: Tricuspid valve, IVC: Inferior vena cava, 3DRVEF: 3D right ventricular ejection fraction, RVGS: Right ventricular global longitudinal strain, RVFWS: Right ventricular free wall strain. Bold values indicate significant p-value).

After 30 days, six patients died, one patient was lost to follow-up. The echocardiographic parameters of baseline and follow-up characteristics of our cohort are summarized in Table 2. Systolic pulmonary artery pressures decreased significantly in patients after 1 month of therapy, from 51.5 ± 17.2mmHg to 42.4 ± 19.6mmHg ($p<0.05$). Right atrial pressure, estimated using the diameter of the inferior vena cava, also decreased significantly at follow-up ($p<0.05$).

At the acute phase, patients had RV dilatation that improved significantly at 1 month after discharge ($p<0.05$). The McConnell's sign was present in 44 patients (77.2%) and in none of the controls. There was no significant difference in mean RV diameter between controls and the follow-up patients ($p<0.05$), indicating a complete recovery of RV size. RV function improved significantly as evaluated by the median TAPSE, mean tricuspid peak s wave and RV fractional area change ($p<0.05$). There was no difference between controls and the follow-up patients for these three parameters. Because of the lack of measurable PA pressures in controls, the comparison with controls was not possible. LV ejection fraction was normal in patients at the initial phase of PE but significantly improved at follow-up ($p<0.05$). In contrast, no difference in E/e' ratio (at the lateral mitral annulus) was found. 3D RV end-diastolic volumes decreased significantly ($p<0.05$), while 3D RV ejection fraction did not improve ($p>0.05$). Three-dimensional RV end-diastolic volumes were significantly higher in baseline patients than in controls ($p<0.05$). 3D RVEF was also significantly lower in baseline patients compared to controls ($p<0.05$). Follow-up patients' volumes were not significantly different from controls' ones ($p>0.05$). However, 3DRVEF remained lower in follow-up patients compared controls ($p<0.05$).

There was no significant change in 2D RV longitudinal strain from baseline to follow-up ($p>0.05$). RVGS and RVFWS were impaired at baseline and remains low at follow-up as compared to controls ($p<0.05$).

4. Discussion

Our study sought to assess the clinical utility of 3D echocardiography and 2D speckle tracking imaging in acute PE patients. The European guidelines and American guidelines emphasize that on the diagnosis and management of acute PE, the functional consequences determined by RV dysfunction and elevations of cardiac biomarkers are more relevant for risk stratification than the assessment of the anatomic burden and distribution of the pulmonary artery thrombus [3], [4], [7]. RV dysfunction has been shown as a predictor of event in acute PE, but some questions arise, and no uniform criteria have been used to assess the presence of RV dysfunction.

The analysis of traditional echocardiographic parameters of RV function is limited. Most of RV deformation as assessed in controls comes from the body of the lateral wall and not from the excursion of the tricuspid annulus. FAC can only describe the function of inlet right ventricle [4], [5], [6].

In our study, RV systolic function as measured by conventional echocardiographic parameters appeared to be restored at 1 month. There was no difference between follow-up patients and controls regarding the TAPSE, the tricuspid valve s', the RV dimensions. However, 3D RVEF assessment leads to different conclusions: RV ejection fraction was still impaired in follow-up patients compared to controls ($p<0.05$) and was not significantly different from the baseline data. Two-dimensional echocardiographic methods of quantitating RV volumes use geometric models that do not represent the irregular RV shape accurately. Three-dimensional echocardiography can overcome 2D limitations by neglecting geometric assumptions and using multiple images to reconstruct the RV chamber. This measurement allows much more confidence compared with two-dimensional methods with less underestimation of RVEDV and RVESV and improved test-retest variability [9-12].

Right ventricular strains (RVGS and RVFWS) were also very low at the baseline and unchanged after 30-day follow-up. This suggests a slow and an incomplete recovery of 2D strain at 1 month, indicates a lower degree of recovery (or insufficiently long delay) of patients after PE. The observations of RVEF and RV strain are consistent at follow-up. 2D strain has been suggested as a significant RV dysfunction parameter in acute PE, RV free-wall longitudinal strain being reduced in high-risk patients [6].

3D echocardiography and speckle-tracking imaging are therefore of interest to evaluate RV dysfunction in the acute phase of PE and to investigate persistent symptoms after PE in the absence of pulmonary hypertension. Impaired strain and RVEF after PE could indicate high risk patients for the development of persistent dyspnea and functional limitation after acute PE, the "post-PE syndrome", described in up to 50% of patients after PE [13].

The results of the present study showed that the combined assessment of 3D RVEF and speckle-tracking echocardiographic values had a better performance in the evaluation of the changes of RV function after acute PE.

5. Conclusion

After 1 month of anticoagulant therapy in patients with intermediate-high risk pulmonary embolism, right ventricular function has not fully recovered as assessed by 3D RV EF and 2D strain imaging, while the traditional echocardiographic assessment could not detect this incomplete recovery. This may show either an after effect of PE that would persist over time and eventually be associated with chronic post-embolic dyspnea / chronic post-embolic pulmonary hypertension or a slower recovery of RV myocardial mechanical dysfunction than predicted.

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