ORIGINAL ARTICLE

The value of isovolumic acceleration for the assessment of right ventricular function in acute pulmonary embolism

Murat Selcuk¹, Nurten Sayar², Serafettin Demir³,*, Aydin Rodi Tosua⁴, Vedat Aslan²

¹ Department of Cardiology, Van Education and Research Hospital, Van, Turkey
² Department of Cardiology, Siyami Ersek Education and Research Hospital, Istanbul, Turkey
³ Department of Cardiology, Adana Public Hospital, Adana, Turkey

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KEYWORDS
Pulmonary embolism; Isovolumic acceleration; Right ventricular function

Abstract
Aim: The aim of this study was to assess the value of tricuspid annulus myocardial isovolumic acceleration (IVA) in the assessment of right ventricular function in patients with acute pulmonary embolism (PE).

Methods: Fifteen patients (mean age 60.6±11.3 years) with acute PE were enrolled and a control group was formed of 15 patients with a similar mean age (60.3±11.5). Patients who were diagnosed with acute PE by thoracic computed tomography angiography underwent transthoracic echocardiography at the time of diagnosis and at one month after diagnosis.

Results: In the control group IVA was 2.8±0.2 m/s², while in the acute PE group, it was 2.0±0.1 m/s² at the time of diagnosis and 2.9±0.1 m/s² at the end of the first month. When IVA values of acute PE patients at the end of the first month were compared with their initial values and those of the control group, they had normalized (control and acute PE p<0.0001; control and PE at one-month follow-up p=0.983).

Conclusion: In our study, IVA was shown to be a reliable marker of right ventricular systolic function in patients with acute PE.

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* Corresponding author.
E-mail address: demirkardiyoloji@hotmail.com (S. Demir).

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Introdução

A embolia pulmonar (EP) é uma condição relativamente comum de emergência cardíaca. É difícil de diagnosticar e pode ser desconsiderada, mesmo que não apresente um quadro clínico distintivo. No entanto, o tratamento precoce pode ser altamente eficaz, tornando a pesquisa de diagnóstico uma questão essencial.

Inicia-se a avaliação clinicamente orientada, no entanto, o exame de imagem é crucial. A angiotomografia torácica e a ecocardiografia transesofágica oferecem um perfil mais detalhado, incluindo a detecção e a mensuração dos trombos. A ecocardiografia transesofágica também permite o diagnóstico de disfunção ventricular direita.

Os pacientes com EP podem apresentar disfunção sistólica ventricular direita, e a sua presença é um marcador de pior prognóstico. A EF (Ejection Fraction) é uma medida comumente usada para avaliar a função ventricular direita.

Recentemente, a isovolumétrica do anel tricúspide (IV A) foi associada à disfunção ventricular direita, sugerindo um papel importante nos processos de embolia pulmonar.

Metodologia

Os pacientes foram divididos em dois grupos. O grupo controle foi composto por 15 doentes com idade média semelhante à do grupo intervenção (60,3 ± 11,5 anos). Após o diagnóstico de EP aguda por angiotomografia torácica computorizada, os doentes foram avaliados com ecocardiografia transtorácica, na altura do diagnóstico e no final do primeiro mês após o diagnóstico.

Resultados: O efeito do IV A foi de 2,8 ± 0,2 no grupo controle, no grupo EP aguda foi 2,0 ± 0,1 na altura do diagnóstico e 2,9 ± 0,1 no final do primeiro mês. Quando comparados com os valores de IV A do EP aguda no final do primeiro mês, os valores iniciais e os valores do grupo controle, verificou-se que os valores do grupo controle foram significativamente menores (controle EP aguda p < 0,001; controle EP p < 0,001).

Conclusão: O estudo revelou um marcador adequado da função sistólica ventricular direita em casos de EP aguda.

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etiological risk factors, diagnosis, and RV echocardiographic parameters at the end of the first month were recorded for each patient.

**Transthoracic echocardiography and Doppler imaging**

Before thrombolytic treatment was started, patients diagnosed with acute PE underwent standard transthoracic echocardiography in left lateral decubitus position using a Vivid 3 ultrasound system and a 2.5 mHz phased array transducer. Doppler recordings were made at 100 mm/s by synchronous single-lead electrocardiography. All measurements were obtained in three consecutive cycles, which were later averaged. All Doppler measurements were conducted at end-expiration so that the flow parameters were unaffected by respiration and were more consistent. The gain setting was set for optimum visualization of spectral view and the endocardial borders. Ejection fraction (EF) (to assess systolic function) and E-wave, A wave, E/A ratio, isovolumic relaxation time and deceleration time (to assess left ventricular diastolic function) were determined using tissue Doppler. Right ventricular ejection fraction (RVEF), as an indicator of RV systolic and diastolic function, was determined via two-dimensional RV fractional area change, two-dimensional RVEF, isovolumic relaxation time and tissue Doppler-derived tricuspid lateral annular systolic velocity (S). RV E wave, A wave, E/A ratio, RV shortening time, tricuspid annular plane systolic excursion (TAPSE), myocardial performance index (MPI), and IVA were also measured.6

**Tricuspid annular plane systolic excursion**

To determine tricuspid valve annular plane systolic excursion, an M-mode trace was recorded in apical 4-chamber view from the point where the tricuspid annulus joins the lateral free wall.6

**Myocardial performance index**

RV MPI was calculated based on the measurements from the tricuspid and RV outflow tract Doppler flow traces. The tricuspid flow Doppler trace was obtained with the sample volume of the pulsed wave Doppler at the tips of the tricuspid valve. In parasternal short-axis view, the sample volume was located immediately below the pulmonary valve so that the Doppler flow trace was obtained from the RV outflow tract. In pulsed Doppler recordings in apical 4-chamber view, the time elapsed from the end of the A wave until the end of the E wave was defined as the ejection time (MPI-a), while in the RV outflow tract pulsed Doppler recordings in parasternal short-axis view, the time elapsed from the beginning to the end of the systolic flow was defined as the ejection time (MPI-b).1,4 The following formula was used to calculate MPI: MPI=−((MPI−a)−(MPI−b))/(MPI−b).

**Isovolumic acceleration time**

The measurement was made by placing the pulsed tissue Doppler probe at the point where the tricuspid annulus joins the lateral free wall in apical 4-chamber view. IVA was calculated by dividing the peak isovolumic velocity, just before the peak of the R wave on the ECG and in front of the systolic wave on the tissue Doppler trace, by the time to peak velocity.1,6

**Statistical analysis**

The statistical analysis was carried out using SPSS version 16.1 (SPSS Inc., Chicago, IL, USA). Due to the small number of patients, non-parametric tests were employed. The Mann-Whitney U test was used for two independent variables, while the Kruskal-Wallis test was used for dependent variables. The results are expressed as means ± standard deviation and categorical variables as percentages. Statistical significance is based on a value of p<0.06.

**Results**

Demographic and laboratory characteristics of the PE and control groups are presented in Table 1. No statistically significant differences in these parameters were observed between the two groups.

The etiologies of acute PE are summarized in Table 2, which shows that six patients (40%) had DVT, three (20%) had a history of orthopedic surgery, one (6.6%) had a history of cancer, and five (33.3%) had no risk factors.

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**Table 1** Patient characteristics.

<table>
<thead>
<tr>
<th></th>
<th>PE group (n=15)</th>
<th>Control group (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.6±11.3</td>
<td>60.3±11.5</td>
</tr>
<tr>
<td>Gender (female/male)</td>
<td>7/15</td>
<td>8/15</td>
</tr>
<tr>
<td>Hypertension (n; %)</td>
<td>7 (46.7)</td>
<td>8 (53.3)</td>
</tr>
<tr>
<td>Diabetes (n; %)</td>
<td>4 (26.7)</td>
<td>5 (33.3)</td>
</tr>
<tr>
<td>Smoking (n; %)</td>
<td>6 (40)</td>
<td>5 (33.3)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.4±3.8</td>
<td>26.2±4.1</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>128.2±19.6</td>
<td>131.3±26.1</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>78.7±8.9</td>
<td>79.4±16.1</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>12.7±2.2</td>
<td>12.6±2.4</td>
</tr>
<tr>
<td>Blood glucose (mg/dl)</td>
<td>115±63</td>
<td>103±55</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>28.3±10.4</td>
<td>23.6±12.4</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.9±0.3</td>
<td>0.9±0.4</td>
</tr>
<tr>
<td>Sodium (mmol/l)</td>
<td>139.4±4.5</td>
<td>140.8±4</td>
</tr>
<tr>
<td>Potassium (mmol/l)</td>
<td>4.6±0.8</td>
<td>4.5±0.5</td>
</tr>
</tbody>
</table>

BMI: body mass index; BUN: blood urea nitrogen; DBP: diastolic blood pressure; PE: pulmonary embolism; SBP: systolic blood pressure.

**Table 2** Underlying etiological factors in patients with acute pulmonary embolism.

<table>
<thead>
<tr>
<th>Etiology of acute PE (n=15)</th>
<th>6 (40%)</th>
<th>3 (20%)</th>
<th>1 (6.6%)</th>
<th>5 (33.3%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep vein thrombosis</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Orthopedic surgery</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Cancer</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic</td>
<td></td>
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</tbody>
</table>

PE: pulmonary embolism.
The RV echocardiographic parameters of the control and PE groups are summarized in Table 3. RV end-diastolic and end-systolic volumes were significantly greater and RVEF was significantly lower in the PE group than in the control group. MPI, RV end-diastolic diameter, and pulmonary artery pressure (PAP) were significantly higher in the PE group than in controls, while TAPSE and IVA were significantly lower in the PE group.

Comparison of the echocardiographic parameters of the PE and control groups at the end of the first month is presented in Table 4. IVA, MPI, RVEF, and PAP had normalized, while TAPSE was greatly improved and was close to physiological values.

While mean IVA was 2.8±0.2 m/s² in the control group, the value measured in the patients with acute PE was 2.0±0.1 m/s². In the follow-up examination of these patients performed one month later, it was found to be 2.9±0.2 m/s². The IVA values of the patients with acute PE had normalized at the end of the first month compared with the control group and their own values one month earlier (Figure 1).

**Discussion**

PE is one of the leading vascular emergencies; it is common, difficult to diagnose and can cause life-threatening acute RV failure due to obstruction of the pulmonary arteries. Since PE occurs frequently, has various clinical manifestations, and – most importantly – leads to high mortality, an early diagnosis is of the utmost importance. However, diagnosis is difficult and the condition may be overlooked since it does not present with a distinctive clinical manifestation. The main effects of a pulmonary thromboembolic episode
are hemodynamic. Large and/or multiple embolisms may abruptly increase pulmonary vascular resistance to a level of afterload which cannot be matched by the right ventricle.7

RV function parameters are closely dependent on EF and tricuspid velocity, age, Doppler sample volume location and heart rate, as well as load and contractility.7,8 The complicated structure and asymmetrical shape of the right ventricle makes assessment of right heart function difficult.9 This has prompted the development of methods such as the non-geometric MPI, also known as the Tei index, and TAPSE.10-13 MPI is a non-invasive parameter that enables assessment of global systolic and diastolic ventricular function by Doppler.4,14 and is used in various clinical conditions including pulmonary hypertension, cardiomyopathy, complex congenital heart disease and obstructive sleep apnea. Its reliability and value have been demonstrated in numerous studies.14-18 TAPSE is related to RVEF and has also been shown to have prognostic value in patients with symptomatic heart failure and low EF.11,19 To the best of our knowledge, this study is the first to assess MPI and TAPSE in patients with acute PE. It indicates a decrease in TAPSE and an increase in MPI, both statistically significant, at the time of diagnosis, when patients with acute PE were compared to the control group. Although the one-month follow-up after the diagnosis showed no significant difference between the PE and control groups. We observed the same changes in RVEF, used to assess RV function, and other echocardiographic parameters, except for PAP.

In right-sided disease such as chronic obstructive pulmonary disease, RV infarction and pulmonary hypertension, pulsed tissue Doppler imaging indicates RV systolic and diastolic function are affected.6,19 Although tissue Doppler is a new method, its applications are limited since myocardial velocities depend on volume load.20,21 Studies in recent years have demonstrated that IVA measured by tissue Doppler is a reliable parameter for assessment of RV systolic function independently of variations in pre- and afterload. Voegle et al. reported that RV IVA measured by tissue Doppler is a reliable parameter unaffected by volume load in assessment of RV contraction.5 In a study assessing RV systolic function in patients with mitral stenosis, Teyyareci et al. observed that IVA is negatively correlated with the Tei index and other classical parameters, and is significantly lower in patients with severe mitral stenosis. They also emphasized that it is a non-invasive and reliable alternative to determine the severity of mitral stenosis in patients without systemic findings of venous congestion.22 Tugcu et al. demonstrated that in patients with obstructive sleep apnea syndrome, although pulmonary and systemic arterial pressures are normal, of the echocardiographic parameters used to assess RV function only IVA shows a significant change. They associated this with subclinical RV dysfunction.23 Bayram et al. assessed RV function in 28 patients with obstructive sleep apnea syndrome undergoing continuous positive airway pressure therapy and observed a statistically significant improvement in IVA before and after treatment (before treatment: 4.1±0.5 m/s²; after treatment: 5.0±0.4 m/s²).24 In a study by Pauliks et al., a significant improvement in IVA was found in 39 patients with atrial septal defect before and after defect closure (before closure: 1.8±0.6 m/s²; after closure: 2.1±0.6 m/s²).25

Our study is the first to use IVA to assess RV function in patients with acute PE. We observed significantly lower IVA at the time of diagnosis of PE in comparison to the control group. During the follow-up examination one month later, we observed that IVA had normalized compared to the values from one month earlier. Also, when the patients with PE were compared to the control group one month after diagnosis, no statistically significant difference was seen between IVA values.

Conclusion

Measurement of RV function in acute PE is important to differentiate high- and low-risk groups in terms of prognosis. In our study, we assessed IVA and parameters widely used for assessment of RV function (RV end-diastolic and end-systolic volume, RVEF, PA, RV end-diastolic diameter, TAPSE, and MPI), and reached the conclusion that RV tissue Doppler IVA is a reliable parameter for the assessment of RV systolic function in acute PE.

Study limitations

The most important limitation of our study was the angle-dependent nature of pulsed tissue Doppler and the probable presence of artefacts. This means that inter-observer and intra-observer variability may be high. When obtaining measurements with routinely used transthoracic echocardiography devices, it is necessary to ensure that the device is optimally calibrated, and the procedure should be carried out carefully by experienced staff. Technological advancements in the equipment used for tissue Doppler imaging may reduce these limitations in the future. Finally, the number of patients in our study was only 15, and therefore further studies with a larger number of patients are needed to confirm our findings.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Conflicts of interest

The authors have no conflicts of interest to declare.

References