

Right Ventricular Assessment by Tissue-Doppler Echocardiography in Acute Pulmonary Embolism

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Abstract

Background: Assessment of the right ventricular (RV) function by echocardiography in patients with pulmonary thromboembolism (PE) is complex and frequently qualitative. Tissue Doppler has been used for the semiquantitative assessment of this chamber, although with some limitations.

Objective: To evaluate RV function in PE using tissue-Doppler echocardiography, in addition to atrial natriuretic peptide (BNP).

Methods: Patients with PE were studied using tissue-Doppler echocardiography and BNP up to 24 hours after diagnosis; myocardial velocities (s'), strain, strain rate and RV myocardial performance index were obtained. RV dysfunction was diagnosed by chamber hypokinesia, abnormal septal motion and a RV/LV ratio ≥ 1 . According to their BNP levels, the patients were divided into Group I, BNP < 50 pg/mL and Group II, BNP ≥ 50 pg/mL.

Results: Of 118 patients, 100 (60 men, age = 55 ± 17 years) were analyzed; RV dysfunction was observed in 28%, more frequently in group II (19 vs. 9 patients, $p < 0.001$). Patients in group II were older (64 ± 19 vs. 50 ± 15 years), and had lower s' velocity (10.5 ± 3.5 vs. 13.2 ± 3.1 cm/s), and higher pulmonary pressure (48 ± 11 vs. 35 ± 11 mmHg), $p < 0.001$. The cut-off point of s' for RV dysfunction was 10.8 cm/s (specificity = 85%, sensitivity = 54%), with moderate correlation between BNP and s' wave ($r = -0.39$).

Conclusion: In PE, RV dysfunction on echocardiography is accompanied by BNP elevation; although tissue-Doppler imaging adequately confirms the presence of RV dysfunction, it has a limited sensitivity for this diagnosis. (Arq Bras Cardiol. 2013;100(6):524-530)

Keywords: Ventricular Function, Right; Echocardiography, Doppler / diagnosis; Pulmonary Embolism.

Introduction

Pulmonary thromboembolism (PE) is an important cause of morbidity and mortality, with poor prognosis if associated with hemodynamic instability, a situation in which mortality can reach approximately 20%¹. The adequate assessment of the right ventricular (RV) function is crucial in PE¹. However, its analysis using noninvasive methods such as two-dimensional echocardiography is limited because of the anatomical complexity of this chamber. In this sense, other echocardiographic techniques such as tissue Doppler imaging have been added to complement the diagnosis², with studies showing an adequate correlation between systolic velocities on tissue Doppler imaging and RV ejection fraction on magnetic resonance imaging³, as well as the identification of RV impairment in patients with PE⁴. The assessment of the RV function can also be complemented by the

determination of atrial natriuretic peptide (BNP) levels⁵, which are elevated in the presence of increased intracardiac pressures⁶. However, the relationship between tissue Doppler measurements for the RV assessment in PE is not fully understood, with different values found for myocardial velocities in this situation^{7,8}, and it is even more limited for measurements such as strain and strain rate. More over, comparing the relationship between RV systolic dysfunction on tissue Doppler echocardiography and the functional reflex of RV overload, as estimated from BNP, would be of potential clinical interest.

The objective of this study was to evaluate the RV systolic function using two-dimensional tissue Doppler echocardiography in patients with acute PE and to analyze its correlation with BNP.

Methods

Patients

From August 2007 to January 2010, all patients admitted to the Emergency Unit or hospitalized with clinically suspected PE (pain/sudden-onset dyspnea in the past week) were recruited to participate in the study. PE was confirmed by thoracic multislice computed tomography showing complete or partial

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filling defect in pulmonary branches or by ventilation/perfusion pulmonary scintigraphy showing a high probability of PE. Patients with left ventricular (LV) dysfunction, as characterized by an ejection fraction < 55% on echocardiography, were excluded from the study to minimize the influence of this condition on BNP levels⁹. Other exclusion criteria were the presence of chronic obstructive pulmonary disease, arrhythmias (atrial fibrillation or frequent extrasystoles) and an inadequate echocardiographic window. All patients received anticoagulation therapy (unfractionated or low-molecular-weight heparin, at the discretion of the assisting clinician). Patients with hemodynamic instability (systemic blood pressure < 90/60 mmHg, signs of poor peripheral perfusion) were given thromboembolytic treatment (tissue plasminogen activator, 100 mg intravenously in two hours). The study was approved by the Institutional Research Ethics Committee, according to the Declaration of Helsinki, and all patients gave written informed consent to participate.

Echocardiography

The patients underwent echocardiography (Vivid 7, GE Medical Systems, Horten, Norway) with measurements of the LV and ejection fraction according to the recommendations of the American Society of Echocardiography¹⁰ up to 24 hours after diagnosis of acute PE. The LV and RV diameters were measured in the 4-chamber apical view to obtain the RV/LV ratio. The parasternal, apical and subcostal views were used for the subjective assessment of the RV systolic function. RV systolic dysfunction was considered when hypokinetic chamber was present. Abnormal septal motion (flattening) and/or RV dilatation (RV/LV ≥ 1) were added to the subjective analysis of function analysis in order to improve it. RV function was evaluated by two observers; in case of discordance, the opinion of a third observer was requested. The pulmonary artery systolic pressure was derived from the tricuspid regurgitation added to right atrial pressure as estimated from the inferior vena cava diameter and collapsibility. E and A wave velocities were measured from the transmitral flow for the analysis of the LV diastolic function.

Tissue Doppler imaging

Tissue Doppler tracings were obtained from the lateral and septal annulus and from the lateral tricuspid annulus using the 4-chamber apical view to obtain measurements of the myocardial velocities (s' and e' waves), with the sample volume as parallel to the wall as possible, so as to minimize the influence of the angle on Doppler velocities. LV filling pressure was estimated from the ratio between the early transmitral filling wave (E) and the mean of septal and lateral e' waves. Diastolic dysfunction was considered in the presence of increased LV filling pressures ($E/e' > 13$)¹¹. Images were obtained with the patient in breath-hold or breathing slowly, as much as possible. Color mapping was used to obtain tissue Doppler in the 4-chamber apical view with sector adjustment and depth to keep a minimum of 100 frames/min. The right ventricular myocardial performance index (MPI) was calculated as the ratio between the sum of the isovolumic contraction time (ICT) and isovolumic relaxation time (IRT) divided by the ejection time (ET): $MPI = (ICT + IRT)/ET$ ¹²,

with measurements obtained from tissue Doppler imaging of the tricuspid annulus. Images were digitalized and the mean of 3 measurements was used, with further analysis.

BNP determinations

Plasma BNP levels were determined up to 24 hours after PE had been confirmed. After blood draw, the sample was put in an EDTA-containing tube and separated by centrifugation. BNP level was determined using a radioimmunoassay kit (Advia Centaur assay, Siemens Healthcare Diagnostics, Bayswater, Australia). The patients were divided into two groups according to their BNP levels¹³: group I, with BNP < 50 pg/mL, and group II with BNP ≥ 50 pg/mL. For pulmonary thromboembolism, BNP values < 50 pg/mL were described as adequate to identify patients with lower intracardiac pressures and consequently a more favorable prognosis¹³.

Statistical Analysis

Continuous variables are expressed as mean \pm SD, and categorical variables, as percentages or frequencies observed. The groups were tested using the Student t test for continuous variables and the chi square test or Fischer test for categorical variables. The ROC (Receive Operating Characteristic) curve was used to identify the best cut-off point of tissue Doppler measurements more adequate to identify RV dysfunction. Correlation between BNP and the variables related to RV were tested using the Pearson's correlation. The analysis was carried out using the SPSS statistical software program (version 17.0; SPSS, Inc, Chicago, IL), and the level of significance was set at 0.05. Measurements of s' velocities, strain, strain rate obtained from tissue Doppler imaging were repeated after three months by the same observer and by a distinct observer in 10 patients for measurements of intra and interobserver variability, and compared using the intraclass correlation coefficient.

Results

A total of 118 patients had the diagnosis of PE confirmed by tomography (n = 114) or pulmonary scintigraphy (n = 4). Of these, 5 refused to participate; 2 did not have their BNP collected; 7 did not show an adequate echocardiographic window; 2 showed left ventricular dysfunction; and 2 had significant arrhythmia. Thus, the final study group was comprised of 100 patients. Predisposing factors for PE included venous thromboembolism (29%), neoplasia (24%), surgery (22%) and long-distance flight (6%). Predisposing factors for PE were not identified in 19% of patients. Only 4 patients were hemodynamically unstable and, therefore, underwent thrombolysis; the other patients were treated medically. Most of the patients were males (60%), with a mean age of 55 ± 17 years. Tricuspid regurgitation was observed in 66 patients, and the pulmonary artery systolic pressure from the tricuspid regurgitation was 41 ± 13 mmHg.

RV assessment

Proper pulsed tissue Doppler tracings could be obtained for s' wave measurement in all patients. For strain

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measurements, 17% of patients did not show satisfactory tracings for the analysis and in 26% of patients satisfactory tracings were not obtained for strain rate measurements, and this measurement was not used for the analysis. The tissue Doppler analysis showed a mean s' wave velocity of 12.4 ± 3.4 cm/s, with mean values of $21.4 \pm 9.5\%$ for strain, and increased MPI (0.53 ± 0.25). Of the 100 patients, 28 had RV systolic dysfunction on two-dimensional echocardiography. The ability of tissue Doppler s' wave to predict RV systolic dysfunction was analyzed by the ROC

curve, which showed a cut-off value of 10.8 cm/s, with 85% specificity, 54% sensitivity, and area under the curve of 0.78 (Figure 1). The strain measurements did not permit the identification of a proper cut-off point for the identification of RV dysfunction. The correlation between BNP levels and tissue Doppler myocardial velocities was tested, showing a significant, but modest, inverse correlation ($p = 0.01$) ($r = -0.39$) (Figure 2). However, no significant correlation was observed between BNP levels and MPI, or for strain measurements.

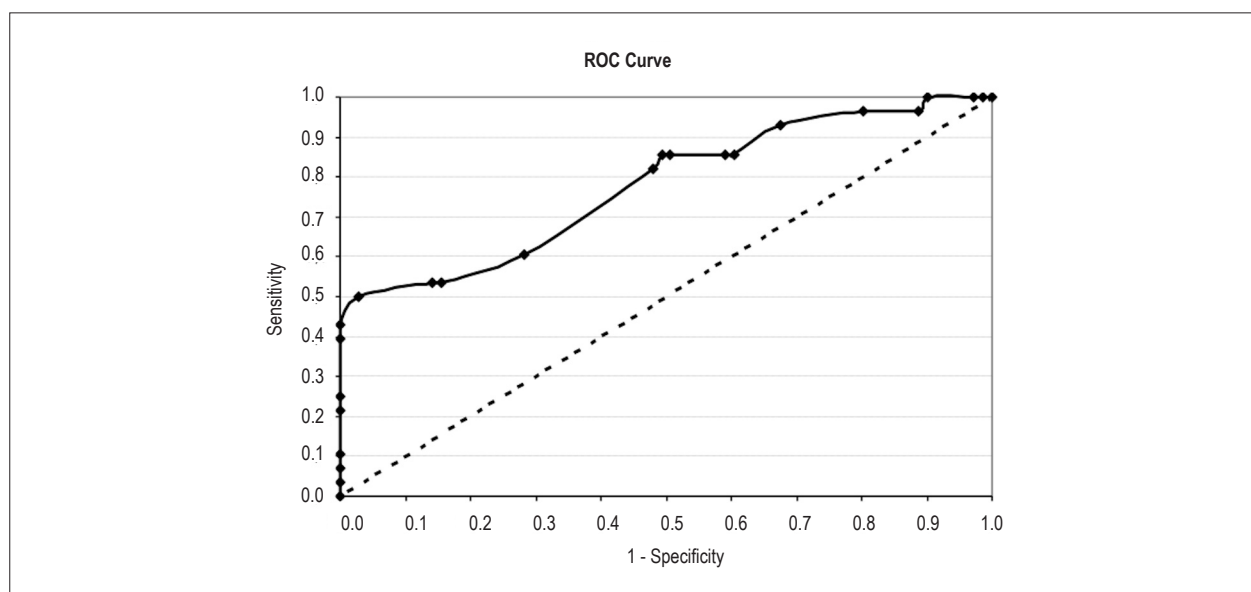


Figure 1 – ROC (Receiver Operating Characteristic) curve for the definition of the best cut-off point of systolic wave velocity (s') by tissue Doppler imaging for right ventricular dysfunction.

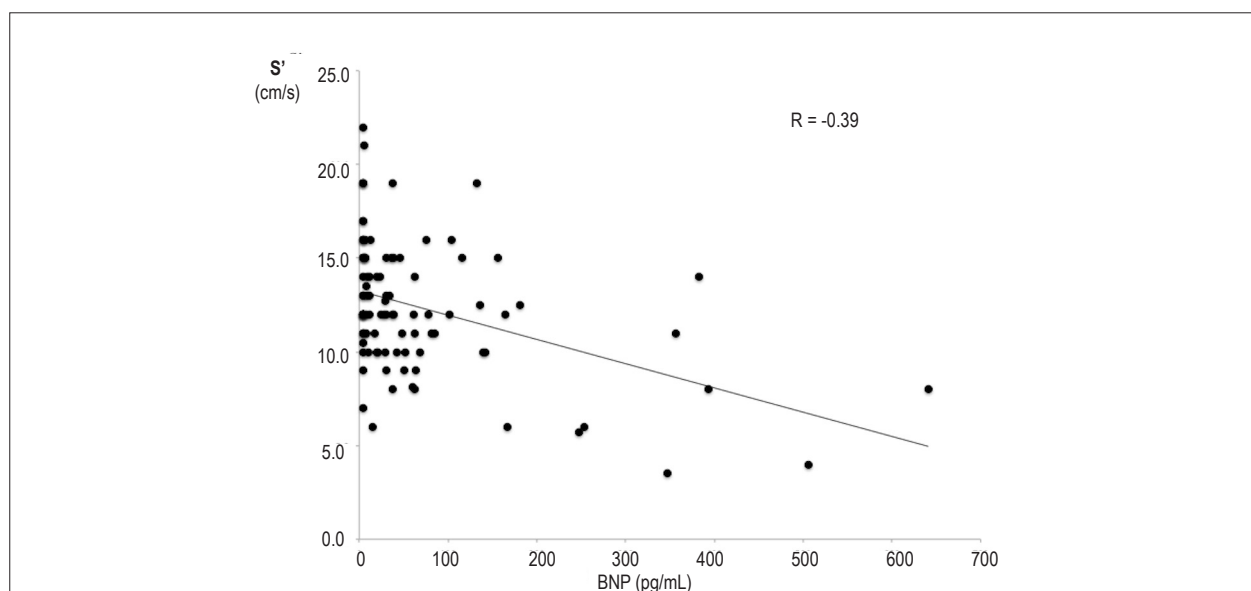


Figure 2 – Correlation between atrial natriuretic peptide (BNP) levels and right ventricular systolic velocity (s') by tissue Doppler imaging.

Groups assessment

Sixty eight patients showed BNP < 50 pg/mL, and were included in group I. Group II (n = 32) consisted of older patients (Table 1), with a higher prevalence of tricuspid regurgitation (88% vs. 56%, $p < 0.01$) and higher pulmonary artery pressures (48 ± 11 vs. 35 ± 11 mmHg, $p < 0.001$) when compared to group I patients. Group II also showed a higher prevalence of RV systolic dysfunction (59% vs. 13%, $p < 0.001$) and lower s' velocities and RV strain. However, there was no difference between MPI, which was increased in both groups (Table 2). The estimated LV filling pressures (E/e' ratio) was similar in both groups.

Intra and interobserver variability

The intraclass correlation coefficient was 0.98 (intraobserver) and 0.96 (interobserver) for s' wave velocity, and 0.91 (intraobserver) and 0.90 (interobserver) for strain measurements. The strain rate values were not used for the analysis due to their great variability and difficulty to be obtained.

Discussion

Pulmonary thromboembolism is an important cause of morbidity and mortality, and its prognosis is associated

with the hemodynamic instability resulting from RV systolic dysfunction¹. In the literature, the prevalence of RV dysfunction on echocardiography varies from 30% to 50%^{1,2}. In our case series, the prevalence of RV dysfunction was slightly lower (28%), possibly because patients with LV systolic dysfunction were excluded, thus eliminating an occasional RV impairment associated with the cardiomyopathy. Increased BNP levels (≥ 50 pg/mL) were associated with a higher prevalence of RV systolic dysfunction, both qualitatively (on two-dimensional echocardiography) and semiquantitatively, as measured by tissue Doppler variables (s' wave velocities and RV strain). Tissue Doppler imaging is a simple, fast and noninvasive method for the assessment of ventricular performance. However, cut-off values for the identification of RV systolic dysfunction are not fully consistent^{7,8}. In our case series, s' wave values < 10.8 cm/s were able to identify RV systolic dysfunction with a good specificity, but low sensitivity. We believe that this was basically due to two reasons: first, myocardial velocity values are particularly influenced by age¹⁴; thus, the decrease in s' wave in RV dysfunction could be not so significant in younger patients who usually show higher myocardial velocities, a situation that is particularly evident in mild RV dysfunction. Unlike

Table 1 – Clinical characteristics of group I (BNP < 50 pg/mL) and group II (BNP \geq 50 pg/mL)

	Group I (n = 68)	Group II (n = 32)	p
Age (years)	50 \pm 14	64 \pm 19	0,001
Male gender (n, %)	18 (56)	42 (62)	NS
Neoplasia (n, %)	13 (19)	11(34)	0,09
Surgery (n, %)	12 (18)	10 (31)	NS
DVT (n, %)	17 (25)	12 (37)	NS
Hypotension/shock (n)	0	4	0.009

BNP: atrial natriuretic peptide; DVT: deep venous thrombosis.

Table 2 – Echocardiographic characteristics of Group I (BNP < 50 pg/mL) and Group II (BNP \geq 50 pg/mL)

	Group I	Group II	p
LVEF (%)	67 \pm 5	68 \pm 7	NS
RV MPI	0.50 \pm 0.2	0.59 \pm 0.3	NS
RV s' (cm/s)	13.1 \pm 3.1	10.5 \pm 3.4	< 0.001
Septal e' (cm/s)	8.7 \pm 2.9	7.4 \pm 2.8	0.05
E/e' (LV)	8.3 \pm 3.0	8.2 \pm 2.7	NS
RV strain (%)	24 \pm 9	19 \pm 9	0.03
RV/LV ratio	0.9	1.1	< 0.001
RV dysfunction (n,%)	9 (13)	19 (59)	< 0.001
PASP (mmHg)	35 \pm 11	48 \pm 11	0.002

BNP: atrial natriuretic peptide; LV: left ventricle; EF: ejection fraction; MPI: myocardial performance index; RV: right ventricle; s' : systolic velocity on tissue Doppler imaging; e' : early diastolic velocity on tissue Doppler imaging; E: early transmitral diastolic velocity; PASP: pulmonary artery systolic pressure.

in the literature, the mean age of patients in our case series was lower (55 years), with a significant proportion of young individuals in the postoperative period. Furthermore, cut-off values for s' velocities proposed in the literature for the identification of RV dysfunction were obtained from studies including completely different populations, i.e., from the comparison between a group of healthy individuals and patients with RV dysfunction, which resulted in a more precise separation between the groups. Hsiao et al¹⁵ studied patients with PE using tissue Doppler imaging and showed that these patients had lower s' wave values (10.6 cm/s) when compared to a group of normal individuals (13.1 cm/s). Meluzin et al⁷, in turn, studied patients with heart failure and right ventricular dysfunction, and obtained a slightly lower cut-off point (10.5 cm/s) for concomitant RV systolic dysfunction, also in comparison to normal individuals. Since our population consisted exclusively of patients with the disease (PE), we observed different RV performances, ranging from completely normal ventricles to global chamber failure; in this situation, there is a higher probability of estimate overlapping, and consequently a lower sensitivity of the method. In some cases, we also observed that the assessment of the basal RV region by tissue Doppler imaging did not reflect the change seen in the other walls, which occasionally could be hypokinetic and/or with local dilatation.

Intracardiac pressure assessment by BNP

In relation to BNP, increased levels of this biomarker have been found primarily in the presence of RV systolic dysfunction (predominantly marked RV dysfunction), thus suggesting that a significant impairment of this chamber is crucial for the elevation of the levels of this peptide. Because of the pulmonary vasoconstriction resulting from PE, there is an increase in the RV workload in an attempt to keep the pulmonary pressure high; depending on the degree of pressure elevation, RV dilatation and failure may occur. Since BNP is secreted in response to increased ventricular or atrial stress, it reflects volume or pressure overload¹⁶, which results in its elevation in patients with RV systolic dysfunction. However, the correlation between RV dysfunction and BNP is not linear, with countless factors influencing this relationship, including the biomarker secretion and clearance. Left ventricular systolic dysfunction, for instance, is strongly associated with increased intracardiac pressures (and consequently increased BNP levels); because of this association, patients with decreased LV ejection fraction were excluded. Since the diastolic dysfunction is also correlated with increased BNP levels¹⁷, its influence was analyzed from the estimated intraventricular pressure by tissue and conventional Doppler imaging (obtained from the E/e' ratio); in our case series, although patients with higher BNP levels were older, and presumably with a higher prevalence of diastolic dysfunction, both groups had similar LV filling pressure measurements. Diastolic dysfunction shows only a modest correlation with BNP levels^{18,19}, particularly in patients without associated systolic dysfunction. Thus, we believe that the influence of diastolic dysfunction on BNP levels may be minimized in this group.

In relation to MPI, we observed that this index was increased in patients with PE, regardless of the presence of RV dysfunction or BNP levels. Increased pulmonary resistance (as seen in PE) causes a prolonged isovolumic contraction interval and, thus, even in the absence of RV dysfunction, we can anticipate an increased MPI. Hsiao et al¹⁵ observed that patients with PE could be specifically identified by means of MPI in relation to patients with pulmonary hypertension from other causes. In our case series, however, this index was not able to differentiate between patients with BNP levels higher and those with lower than 50 pg/mL.

Limitations

Some comments should be made in relation to the study limitation: the methodology for RV assessment was essentially subjective, even when semiquantitative parameters were added. Other techniques, such as the measurement of the RV fractional area change (FAC) and ejection fraction by Simpson's method could add more consistency to the results. However, the characteristic of the study population (tests performed frequently at bedside, with dyspneic patients) limited this assessment in a significant number of patients. Also, only the basal segment of the RV wall was analyzed by tissue Doppler imaging, and possible changes in other segments could thus have been missed. However, in PE, involvement of the RV occurs more commonly in the entire extension of its wall, occasionally preserving the apex (McConnell sign)²⁰, thus permitting the use of tissue Doppler imaging as representative of the global RV performance. Also, the color mapping used by tissue Doppler imaging is extremely dependent on the quality of image; thus, a high number of frames is necessary for adequate tracings to be obtained. The influence of breathing, which in many cases is faster, added to the difficulty to acquire the images, with variables such as strain and strain rate being more affected. Finally, as for any technique related to Doppler, the insonation angle may influence the measurements; thus, careful attention was given so that images could be properly obtained.

Conclusion

Increased BNP levels are a marker of RV dysfunction on echocardiography in patients with acute PE. Myocardial velocities measurements by tissue Doppler imaging are adequate to confirm RV dysfunction; however, its limited sensitivity suggests that its use should be left mainly as a complement for other techniques.

Author contributions

Conception and design of the research: Rodrigues ACT, Cordovil A, Monaco C, Guimarães L, Cury A, Lira-Filho E, Vieira MLC, Morhy S; Acquisition of data: Rodrigues ACT, Cordovil A, Monaco C, Guimarães L, Cury A, Naccarato GAF, Fischer CH, Lira-Filho E, Vieira MLC; Analysis and interpretation of the data: Rodrigues ACT, Guimarães L; Statistical analysis: Rodrigues ACT; Obtaining funding: Rodrigues ACT, Morhy S; Writing of the manuscript: Rodrigues ACT; Critical revision of the manuscript for intellectual content: Rodrigues ACT, Monaco C, Fischer CH, Vieira MLC.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any post-graduation program.

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