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30-day mortality risk in all-comers with acute pulmonary embolism**

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Peak systolic velocity of right ventricular free wall myocardium by tissue Doppler imaging does not help to identify patients with acute pulmonary embolism and stratify 30-day mortality risk in all-comers with acute pulmonary embolism

Short title: Systolic velocity of right ventricular free wall and acute pulmonary embolism

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INTRODUCTION

Transthoracic echocardiography (TTE) is not a first-line tool in pulmonary embolism (PE) diagnostics and is underrated in PE prognosis stratification [1, 2]. Right ventricular (RV) dysfunction is associated with increased risk of short-term mortality even in initially normotensive patients with PE, thus its detection helps to identify individuals at high risk for

hemodynamic deterioration and early death. Nevertheless, RV dysfunction assessed with TTE has no commonly accepted definition [3]. Different TTE techniques have been used and the search for easily obtainable, reproducible and efficient parameters in this area is still ongoing. The estimation of myocardial celerity by tissue Doppler imaging (TDI) is a potential one [4]. The motion of RV walls' myocardium appraisal with TDI in patients with acute PE could replace RV longitudinal strain echocardiography due to its comprised accessibility and other limitations [5].

The aim of the study was to assess the usefulness of peak systolic velocity (S') of RV free wall myocardium by TDI for making a diagnosis of acute PE and for 30-day mortality prediction in all-comers with PE.

METHODS

Study group

This was a cross-sectional observational single-center study including consecutive patients of the Internal Medicine Department of the Blessed Marta Wiecka District Hospital with high clinical probability of PE with PE confirmation upon computed tomography pulmonary angiography (CTPA), from August 1, 2018 to November 30, 2020. The diagnostic algorithm and treatment regimens were based on the guidelines of the European Society of Cardiology [1]. TTE was performed within 24 hours of admission to the ward. Exclusion criteria and TTE assessment methodology are described in the Supplementary material.

The study endpoint was 30-day all-cause mortality. Data collection during this follow-up was described in detail in the previous publication [7].

Ethical issues

The study protocol complied with the Declaration of Helsinki and was approved by the Bioethics Committee of the Regional Medical Chamber in Tarnow, Poland (No. 3/0177/2019).

Statistical analysis

Quantitative variables are expressed as median with interquartile range (IQR) and qualitative variables are expressed as numbers (percentage). Mann–Whitney U-test and Fisher test or χ^2 test were used for their comparisons when adequate, respectively. Typical statistical tools of receiver-operating characteristic, Cox-proportional hazard and Spearman's rank correlation coefficient were employed. Two-sided *P*-values <0.05 were considered statistically significant. Detailed statistical analysis is described in the Supplementary material.

RESULTS AND DISCUSSION

The study included 212 consecutive patients with suspicion of PE, 5 of whom had contraindications to CTPA and were transferred to another unit for further diagnostics. Another 23 patients had echocardiograms of poor quality (23 strain analysis and 15 of them also TDI analysis of RV wall velocity) that were disqualified. Five patients had nondiagnostic CTPA. In effect, 189 individuals were eligible to be enrolled into the analysis. Baseline characteristics of these patients are presented in Supplementary material, *Table S1*.

As many as 99 patients had PE confirmed in CTPA while 90 patients had no radiological signs of PE. During 30-day follow-up 11 patients died. The clinical course of the study participants is described in the Supplementary material.

Average S' of RV free wall correlated with RV free wall longitudinal strain ($r = -0.46$; 95% CI, -0.32 to -0.55 ; $P < 0.001$) and with tricuspid annular plane systolic excursion (TAPSE) ($r = 0.49$; 95% CI, 0.37 – 0.59 ; $P < 0.001$).

Acute PE diagnosis

Considering clinical and biochemical data, the individuals with PE as compared to patients without PE had less often diagnosed chronic heart failure and higher serum concentration of D-dimer (Supplementary material, *Table S1*). Among TTE parameters, PE study participants had increased values of RV to left ventricle (LV) ratio and presented more often with this ratio values of more than 0.9. Significantly more frequently they could be diagnosed with the 60/60 sign, and McConnell sign or RV segmental or generalized hypokinesia (Supplementary material, *Table S2*). There were no differences regarding RV free wall TDI parameters.

30-day mortality prediction

The deceased patients in comparison to survivors were older, had higher concentrations of N-terminal pro-B-type natriuretic peptide and troponin T and higher score of Pulmonary Embolism Severity Index, and in TTE had more often the 60/60 sign (Supplementary material, *Table S1* and *S2*). Among TTE markers the 60/60 sign was an efficient predictor of early mortality — hazard ratio 4.69 (95% CI, 1.43–15.38, $P = 0.01$) and RV to LV ratio was a poor predictor (area under the curve of 0.593, $P = 0.03$), whereas neither TAPSE nor any of the TDI derived parameters were significantly associated with mortality (Supplementary material, *Table S3*).

Clinical significance

TDI parameters of LV segments were shown to be independent predictors of outcome in acute coronary syndrome and response to cardiac resynchronization therapy in chronic heart failure patients [10, 11]. Considering RV, as the interventricular septum does not exclusively reflect RV function, it should not be used alone to assess RV and the assessment of the mid and apical ventricular free wall velocities is not encouraged in a routine echocardiographic examination, because of lower rates of obtaining adequate signals and greater variability. Nevertheless, their S' values showed good correlations and good discriminative ability between normal and abnormal RV ejection fraction evaluated with radionuclide angiography and with TTE parameters of RV free wall longitudinal strain and TAPSE in our study [8, 9]. As for PE, the values of S' of the basal and mid third of the RV free wall did not differ among the groups of patients with acute PE of various sizes of perfusion defect upon ventilation/perfusion scintigraphy and healthy age-matched controls [12]. The studies on clinical significance of TDI assessment of RV wall motion in different diseases are lacking.

Among the most reliably and reproducibly imaged regions of RV are the tricuspid annulus and the basal free wall segment. Abnormal S' of this region could help to confirm the presence of RV dysfunction in acute PE with very limited sensitivity for this diagnosis but was inferior to classic measures of RV systolic function with m-mode TAPSE for 30-day prediction of adverse outcome [13, 14].

TDI assessment of RV mid and apical segments and averaged RV free wall myocardial velocity does not help to predict PE in patients with high clinical probability of PE. As stand-alone parameters they also do not enable mortality risk stratification in patients with acute PE.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/polish_heart_journal.

Article information

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