

Right ventricular wall thickness indexed to body surface area as an echocardiographic predictor of acute pulmonary embolism in high-risk patients

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INTRODUCTION

The abnormalities in acute pulmonary embolism (PE) observed in a transthoracic echocardiographic examination (TTE) are ascribed to the right ventricular (RV) pressure overload and dysfunction evoked by PE, but those findings can also be present in the absence of acute PE and may occur due to concomitant cardiac or respiratory diseases [1, 2]. The recommendations for TTE use in PE diagnostics present a general approach without standard individualization to the patients' body size [1].

This study aimed to assess the usefulness of classic echocardiographic parameters indexed to the height and the body surface area (BSA) for prediction of acute PE in patients with a high clinical probability of PE referred for computed tomography pulmonary angiography (CTPA).

METHODS

Study group

This was a cross-sectional observational single-center study including consecutive patients referred for CTPA at an Internal Medicine Department with a high clinical probability of PE, from August 1, 2018 to June 11, 2019. The diagnostic algorithm and treatment regimens were adopted from the guidelines of the European Society of Cardiology [1, 3]. Exclusion criteria and echocardiographic assessment methodology are described in the Supplementary material. 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

Statistical analysis was performed with the R Project for Statistical Computing version 3.6.3 (R Foundation for Statistical Computing, Free Software Foundation Inc., Vienna, Austria). Categorical variables were presented as absolute frequencies or relative percentages, while continuous variables as median with interquartile range (IQR) or as mean with standard deviation (SD). Categorical variables were compared using the χ^2 test or the Fisher test.

The normality of distribution was investigated with the Shapiro-Wilk test. For quantitative variables and normal distribution, the t-test was applied. For the non-normal distribution, the Mann-Whitney test was used. Two-sided *P*-values <0.05 were considered statistically significant. Calculated *P*-values were not adjusted for multiple testing. Detailed statistical analysis is described in the Supplementary material.

RESULTS AND DISCUSSION

The study comprised 108 consecutive patients, 5 of whom had contraindications to CTPA and were transferred to another unit for further diagnostics. Another 9 patients had echocardiograms of poor quality that were excluded. Three patients had nondiagnostic CTPA. Finally, 91 individuals were eligible to

be enrolled in the survey. Baseline characteristics of these patients are presented in the Supplementary material, *Table S1*. As many as 49 patients had PE confirmed in CTPA; 22 subjects had central PE (44.9%), whereas 27 individuals (55.1%) had peripheral PE: segmental — 18 (36.7%) or subsegmental — 9 (18.4%). Forty-two patients had no radiological signs of PE.

Clinical and biochemical variables

Considering clinical data, there were no differences in sex, age, body size, clinical prediction rules for PE, or in most comorbidities. The individuals with PE had less often coronary artery disease (CAD) and chronic heart failure (CHF, Supplementary material, *Table S1*). In the analysis of laboratory tests results, they had only a higher concentration of D-dimer (Supplementary material, *Table S2*). The calculated cut-off value for D-dimer as a single predictor of PE, with a sensitivity of 57% and specificity of 80% in the study group, was 4.891 ng/ml.

Classic TTE parameters

The only parameter that was different in the groups of patients with and without PE was the right ventricular wall thickness (RVWT, average values of 4.97 [0.77] vs. 5.58 [1.75] mm; $P = 0.046$) (Supplementary material, *Table S3*). There were no significant differences regarding the severity of valvular defects between the groups.

Indexation of echocardiographic parameters to height

The left atrial end-diastolic area (LA EDA) indexed to height and RVWT indexed to height were significantly lower in the group with PE (Supplementary material, *Table S1*).

Indexation of echocardiographic parameters to BSA

Indexation to BSA revealed the differences between patients with and without PE in the left ventricle (LV) and the left atrium (LA) sizes. The indexed derivatives of left ventricular end-diastolic diameter (LVEDd), the left ventricular transverse diameter (LVTD), the left atrium diameter parasternal window — long-axis views (LAd PLAX), LA EDA — were decreased in the group with PE. RVWT indexed to BSA was also lower in patients with PE (Supplementary material, *Table S3*).

Specific echocardiographic signs of PE

The only specific TTE sign for PE, i.e. a mobile thrombus in the right atrium or right ventricle, was more frequently observed in the PE group (Supplementary material, *Table S4*).

Clinical and echocardiographic predictors for PE

In the univariate logistic regression the variables significantly associated with the PE diagnosis comprised (1) CAD, CHF (occurrence of both lowered the chances for PE); (2) serum D-dimer concentration (positively correlated with PE);

(3) RVWT; (4) LAd PLAX indexed to BSA; (5) LVEDd indexed to BSA; (6) pulmonary artery (PA) indexed to BSA; (7) LA EDA indexed to BSA; (8) RVWT indexed to BSA (all negatively correlated with PE). In the multivariable analysis, the factors independently positively associated with PE included the absence of CAD, higher D-dimer concentration, and lower RVWT indexed to BSA (Supplementary material, *Table S5*).

Clinical significance

To evaluate a possible clinical utility of RVWT indexed to BSA, we performed receiver-operating characteristic (ROC) analysis and calculated the optimal cut-off value. The obtained area under the curve (AUC) was 0.68 (95% confidence interval [CI], 0.56–0.80; $P = 0.002$), the upper cut-off value of 3.19 mm/m² with accuracy of 60% predicted acute PE. Its sensitivity was 0.14 (95% CI, 0.06–0.27) and specificity was 0.69 (95% CI, 0.53–0.82; Supplementary material, *Figure S1*). To enhance the predictive potential of RVWT indexed to BSA, we combined it with D-dimer levels in the multiple regression model. ROC and model statistics are shown in the Supplementary material, *Figure S2*. In this model AUC equaled 0.776 (95% CI, 0.669–0.883; $P < 0.001$), with sensitivity of 0.76 (95% CI, 0.60–0.89) and specificity of 0.68 (95% CI, 0.50–0.82).

Echocardiography is an underutilized tool in PE diagnostics and outcome prognosis. RV dysfunction on TTE is associated with an increased risk of short-term mortality even in an initially hemodynamically stable patient with PE [4–6]. TTE may also help to identify possible candidates for early thrombolytic treatment, thus TTE should be widely used in clinical practice in all patients with PE [7, 8]. In the presented study, nearly 50% of subjects had a negative result for PE in CTPA. It stresses the urgent need for the search for additional predictive factors. Our results of RVWT indexed to BSA confirm the usefulness of TTE and its potential in this area.

Indexing of heart cavities size to BSA is becoming a standard in echocardiography [9]. Nevertheless, indexation of ventricular wall thickness (WT) to BSA has an emerging role. Left ventricular wall thickness (LVWT) showed significant relation with BSA. Indexed LVWT was similar in men and women, but it differed among races and was associated with decreased hypertrophic cardiomyopathy diagnoses [10–12].

The only biochemical and clinical variables independently associated with PE diagnosis were D-dimer concentration and CAD. The current algorithms use D-dimer testing in patients with low/moderate clinical probability of PE to rule out PE [1]. Our findings should stimulate future research on D-dimer in PE diagnostics.

Due to low accuracy and sensitivity, RVWT indexed to BSA is not useful as a single indicator of PE. An open question remains about possible associations between RVWT and other RV indices and their diagnostic utility for PE diagnosis, which is beyond the scope of this article but requires future research. Standard indexation of TTE param-

eters reveals differences between the groups of patients of high clinical probability of PE with and without acute PE. The factors independently associated with PE include the absence of CAD, higher D-dimer concentration, and lower RVWT indexed to BSA.

Supplementary material

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

Article information

Conflict of interest: None declared.

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