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Prognostic implications of computed tomographic right ventricular dilation in patients with acute pulmonary embolism

Keum-Ju Choi [a], Seung-Ick Cha [a,*], Kyung-Min Shin [b], Jaekwang Lim [b], Seung-Soo Yoo [a], Jaehee Lee [a], Shin-Yup Lee [a], Chang-Ho Kim [a], Jae-Yong Park [a], Won-Kee Lee [c]

[a] Department of Internal Medicine, Kyungpook National University School of Medicine,Daegu, Korea
[b] Department of Radiology, Kyungpook National University School of Medicine, Daegu, Korea
[c] Department of Preventive Medicine, Kyungpook National University School of Medicine, Daegu, Korea

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ABSTRACT

Introduction: Whether right ventricular (RV) dilation on computerized tomography (RVD-CT) is a useful predictor for clinical outcomes of acute pulmonary embolism (PE) remains debatable. Furthermore, data regarding the best combination of prognostic markers for predicting the adverse outcome of PE are limited.
Materials and Methods: The authors retrospectively reviewed 657 consecutive patients hospitalized at a tertiary referral center with a diagnosis of PE based on multi-detector row CT scan.
Results: Patients were allocated into an adverse outcome group (11% [n = 69]) or a low risk group (89% [n = 588]). Multivariate analysis showed that RVD-CT (RV/left ventricle [LV] diameter ratio ≥ 1), high pulmonary embolism severity index (PESI) score (class IV-V), high N-terminal-pro-B-type natriuretic peptide (NT-proBNP,≥1,136 pg/ml), and elevated troponin I (≥ 0.05 ng/ml) significantly predicted an adverse outcome (odds ratio [OR] 6.26, 95% confidence interval [CI] 2.74-14.31, $p < 0.001$; OR 4.71, 95% CI 2.00-11.07, $p < 0.001$; OR 2.71, 95% CI 1.15-6.39, $p = 0.023$; and OR 3.00, 95% CI 1.27-7.07, $p = 0.012$, respectively). The addition of RVD-CT to PESI, NT-proBNP, troponin I or their combinations enhanced the positive predictive values and positive likelihood ratios of an adverse outcome.
Conclusions: RVD-CT could be an independent prognostic factor of adverse outcomes in patients with acute PE, and provides additional prognostic value when combined with other prognostic factors.

Introduction

Mortality rates of acute pulmonary embolism (PE) vary from less than 5% in clinically stable patients to more than 30% in hemodynamically unstable patients [1–4]. The main cause of early mortality is right ventricular (RV) failure, whereas most late deaths are caused by underlying diseases, such as cancer [5–7]. Risk stratification is pivotal for determining the therapeutic strategy for acute PE. To reduce PE-related mortality, high risk patients with hypotension and patients requiring more aggressive therapy than standard anticoagulation, such as thrombolytic therapy, should be promptly identified.

The first step in clinical decision-making involves consideration of clinical variables, such as PE severity index (PESI) [8]. This index provides a validated means of making clinical predictions and is useful for identifying low risk patients suitable for outpatient therapy, but not for identifying high risk patients [9]. Furthermore, although RV dysfunction is directly associated with PE-related mortality, it is not incorporated in the PESI scoring system [9]. Therefore, it has been suggested that prognostic factors suggestive of RV dysfunction should be considered to improve predictability in high risk patients [10]. Recent studies on prognostic assessment of PE have focused on RV dysfunction and myocardial injury [10]. Furthermore, B-type natriuretic peptide (BNP) or N-terminal-pro-BNP (NT-proBNP) and troponin I or T, which are blood biomarkers of RV dysfunction, have been used in clinical research and practice [10]. At present, echocardiography remains the reference standard for assessing RV dysfunction in PE patients [11–13], but it is of limited availability in many institutions, and occasionally its imaging quality is poor. Because the majority of patients with PE are diagnosed by multi-detector row computed tomography (MDCT), CT is a more accessible diagnostic method than echocardiography for detecting RV dysfunction in clinical practice [9]. Many reports have studied the utility of CT as a predictor of mortality in these patients [14–17], and of the various CT measurements examined, RV/left ventricle (LV) diameter ratio is the most promising [17]. However, whether RV dilation on CT (RVD-CT) is a useful predictor of poor prognosis remains debatable. Furthermore, combinations of prognostic factors, such as PESI, blood biomarkers, and CT parameters, are likely to be more predictive than any single factor. However, data regarding the best

* Corresponding author at: Department of Internal Medicine, Kyungpook National University Hospital, 130 Dongdeok-Ro, Jung-Gu, Daegu 700–721, South Korea. Tel.: +82 53 200 6412; fax: +82 53 426 2046.
E-mail address: sicha@knu.ac.kr (S.-I. Cha).

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combination of prognostic factors for the prediction of mortality in PE are limited [18].

Thus, the aim of the present study was to assess whether RVD-CT could be used to predict clinical outcome in patients with PE. In addition, we investigated whether combinations of RVD-CT and other well-known markers could be used to improve prognostic value in terms of predicting adverse outcomes.

Methods

Study Population

We retrospectively identified 657 consecutive patients hospitalized at Kyungpook National University Hospital (KNUH), a tertiary referral center, in Daegu, South Korea between March 2003 and December 2012 with a MDCT-based diagnosis of PE. Patients were allocated based on clinical outcome to an adverse outcome group or a low risk group. This study was approved by the Institutional Review Board of the KNUH, which waived the requirement for written informed consent because of the retrospective nature of the study.

Clinical Outcome

PE-related in-hospital death was defined as in-hospital death fulfilling the following criteria: if there were objective evidences of death directly caused by PE or if death could not be attributed to other causes and PE could not be excluded. Adverse outcome was defined as PE-related in-hospital death or serious clinical conditions, including infusion of vasopressors because of persistent hypotension, refractory hypoxia (impending respiratory failure or mechanical ventilation), or cardiopulmonary resuscitation, which is similar to the definitions used in previous studies [19,20].

Data Collection

Demographic patient data, including age, gender, and body mass index (BMI) at presentation were checked, and risk factors of venous thromboembolism (VTE) and comorbid conditions were reviewed. Unprovoked PE was defined as the absence of reversible provoking risk factors, such as surgery, trauma, active cancer, pregnancy and puerperium within 3 months of the event, or immobilization (bed rest within past month for most of the day for $\geq$3 consecutive days) [21]. The presence of symptoms, hypotension (systolic blood pressure <90 mm Hg), and tachycardia (heart rate >110/min) were also recorded. PESI was retrospectively calculated by a pulmonologist (C.K.J.) [8]. PESI score was obtained by summing each patient's age (years), male (10 points), cancer (30 points), heart failure (10 points), chronic lung disease (10 points), pulse rate $\geq$110/min (20 points), systolic blood pressure <100 mmHg (30 points), respiratory rate $\geq$30/min (20 points), temperature <36 °C (20 points), altered mental status (60 points), and arterial oxygen saturation <90% (20 points). Each patient's score correspond with the following risk classes: $\leq$65, class I (very low risk); 66–85, class II (low risk); 86–105, class III (intermediate risk); 106–125, class IV (high risk); >125, class V (very high risk).The usage of thrombolytic agents, VTE recurrence, and length of hospital stay were also checked.

Blood levels of NT-proBNP and troponin I were checked, and arterial blood gas analysis (ABGA) data, including partial pressure of oxygen in arterial blood (PaO_2), partial pressure of carbon dioxide in arterial blood ($PaCO_2$), inspired oxygen fraction (FiO_2), and PaO_2/FiO_2 ratio were recorded. Eletrocardiographic (ECG) changes were reviewed for the presence of T-wave inversion on precordial leads, Q1S3T3, and right bundle branch block. Transthoracic echocardiographic findings including the presence of RV dysfunction and RV systolic pressure (RVSP) were also reviewed. RV dysfunction was defined echocardiographically as RV free wall hypokinesia, and RVSPs were calculated using TR flow velocity as determined by Doppler echocardiography [22].

Radiological Evaluation

CT scans were performed using a MDCT with 16 or 64 detector rows (Light Speed 16, General Electric, Milwaukee, WI, USA; or Aquilion 64, Toshiba Medical Systems, Japan). As described in an earlier study [23], PE was diagnosed on CT images as a sharply delineated pulmonary arterial filling defect present in at least two consecutive image sections, either located centrally within the vessel or with acute angles at its interface with the vessel wall. RV diameter was measured in the transverse section that showed the tricuspid valve at its widest from the inner wall to the inner wall [15]. Left ventricle (LV) diameter was measured on the transverse image that showed the mitral valve at its widest like the diameter of RV. The RV/LV diameter ratios were calculated (Fig. 1). The most proximal sites of pulmonary arteries where pulmonary emboli were observed were also recorded.

Statistical Analysis

Statistical analysis was performed using SPSS, version 12.0 (SPSS Inc., Chicago, IL, USA). Data were expressed as medians with interquartile ranges (IQR) for continuous variables and numbers with percentages for categorical variables. The Mann–Whitney *U* test was used to compare continuous variables between the adverse outcome and low risk groups, and chi-squared test or Fisher's exact test was used to compare categorical variables. When continuous variables were converted to categorical variables, cut-off values were determined using receiver operating characteristic (ROC) curves. To identify predictors of adverse outcomes, forward stepwise multiple logistic regression analysis was used using variables of $p < 0.05$ in univariate analysis. A goodness-of-fit test used to assess the fit of logistic regression models was the Hosmer–Lemeshow test. In addition, we calculated sensitivities, specificities, positive predictive values, negative predictive values, positive likelihood ratios, and negative likelihood ratios for prediction of adverse outcomes. MedCalc, version 12.0 (MedCalc Software, Ostend, Belgium) was used for analysis of ROC curve. P-values <0.05 were considered to indicate statistical significance.

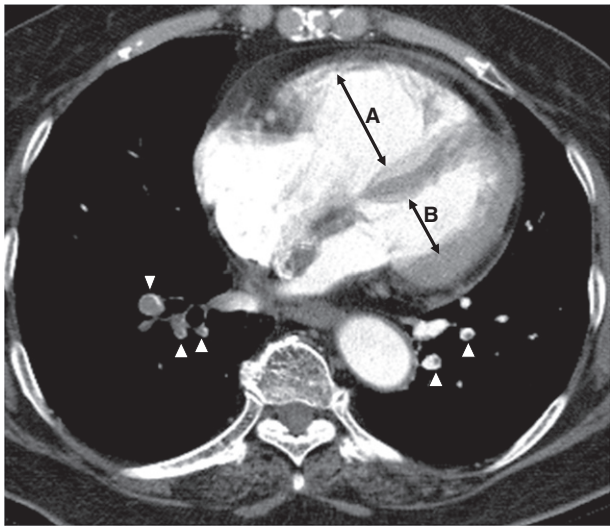

Fig. 1. Measurement of right ventricle (RV)/left ventricle (LV) diameter ratio on computed tomography image. The RV (A) and LV (B) diameters were measured on the transverse section in which their diameters were greatest from the inner to the inner wall. Multiple pulmonary emboli (arrowheads) were noted at segmental pulmonary arteries.