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Prognostic value of computed tomography pulmonary angiography indices in patients with cancer-related pulmonary embolism: Data from a multicenter cohort study

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Abbreviations: PE, pulmonary embolism; CT, computed tomography; CTPA, computed tomography pulmonary angiography; RV, right ventricle; LV, left ventricle; RV/LV, right ventricular to left ventricular ratio; IVS, interventricular septum; QI, Qanadli pulmonary arterial obstruction index; CPHT, chronic pulmonary hypertension; PA, pulmonary artery; AA, ascending aorta; IVC, inferior vena cava; SVC, superior vena cava; Az, azigos vein; CI, confidence interval; IQR, interquartile range; Std. Error, standard error; ROI, region of interest; HU, Hounsfield units; SaO_2, arterial oxygen saturation.

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ABSTRACT

Objective: To analyze the prognostic value of pulmonary artery obstruction versus right-ventricle (RV) dysfunction radiologic indices in cancer-related pulmonary embolism (PE).
Methods: We enrolled 303 consecutive patients with paraneoplastic PE, evaluated by computed tomography pulmonary angiography (CTPA) between 2013 and 2014. The primary outcome measure was serious complications at 15 days. Multivariate analyses were conducted by using binary logistic and robust regressions. Radiological features such as the Qanadli index (QI) and RV dysfunction signs were analyzed with Spearman's partial rank correlations.
Results: RV diameter was the only radiological variable associated with an adverse outcome. Subjects with enlarged RV (diameter > 45 mm) had more 15-day complications (58% versus 40%, $p = 0.001$). The QI correlated with the RV diameter ($r = 0.28$, $p < 0.001$), left ventricle diameter ($r = -0.19$, $p < 0.001$), right ventricular-to-left ventricular diameter ratio ($r = 0.39$, $p < 0.001$), pulmonary artery diameter ($r = 0.22$, $p < 0.001$), and pulmonary artery/ascending aorta ratio ($r = 0.27$, $p < 0.001$). A QI $\geq$ 50% was only associated with 15-day complications in subjects with enlarged RV, inverted intraventricular septum, or chronic cardiopulmonary diseases. The central or peripheral PE location did not affect the correlations among radiological variables and was not associated with clinical outcomes.
Conclusions: Right ventricular dysfunction signs in CTPA are more useful than QI in predicting cancer-related PE outcome.

1. Introduction

Venous thromboembolic disease is common in oncologic patients, with an annual incidence of around 12% [1]. Compared with patients without cancer, symptomatic pulmonary embolism (PE) has a poorer prognosis in the presence of active tumors. Clinical outcomes can vary from minimally symptomatic episodes to fatal events, which illustrates the importance of understanding its prognostic factors [2]. Initial evaluation is typically carried out by clinical examination, gasometry, electrocardiogram, and specific biomarkers. Moreover, transthoracic echocardiography can aid in assessing the hemodynamically unstable patient, thereby informing the management algorithm [3]. However, this procedure is not always available in emergency situations.

Computed tomography pulmonary angiography (CTPA) is the gold standard to diagnose symptomatic PE, with sensitivity and specificity values of between 96–100% and 89–98%, respectively [4]. Despite not performing electrocardiogram gated CTPA, acceptable concordance rates have been reported in the evaluation of right ventricular (RV) dysfunction between CTPA and echocardiography [5]. Several studies have attempted to correlate PE radiological features with different clinical traits (e.g., blood pressure or mortality), but the results have been inconsistent. Interestingly, the CTPA signs of RV dysfunction (increased ventricular diameter, altered right-to-left ventricle ratio, or anomalies of the interventricular septum such as flattening or inversion) are indicators of hemodynamic instability [6–10]. In contrast, the methods used to quantify the degree of pulmonary artery obstruction have yielded seemingly discrepant results [9–11], and increased vascular resistances do not necessarily lead to poor outcomes. In example, the scant clinical repercussion displayed by PEs located on main or lobar arteries has been striking, given that they comprise between 40 and 88% of the embolisms diagnosed incidentally on computed tomography (CT) scans [12,13], in a similar proportion as symptomatic PE [14].

In addition, most studies using CTPA have been performed in PE associated with a wide variety of disorders [6–11]. Nevertheless, to date, literature has paid less attention to address the comparison of radiological features that better predict the outcome in cancer-associated PE, despite reports of a worse prognosis in this population [2]. Only a limited number of studies have shown that pulmonary artery obstruction correlates poorly with the clinical repercussions observed in oncologic patients [15,16], but little is known at present about the prognostic value of other CTPA indices. Given the specific oncologic cardiovascular comorbidities, such complications deserve a separate research.

As reported by Starling in 1914, the obstruction of ventricular outflow causes ventricular enlargement, which in turn helps to overcome the increased ventricular afterload [17]. Our hypothesis is that RV dysfunction identified by CTPA is more useful than pulmonary obstruction indices in predicting the outcome of cancer-related PE, likely because it evaluates better the impact of the increased afterload on ventricular function, especially when the Starling mechanism fails in compensating the pressure against which the RV must pump the blood. The primary aim of this exploratory study was therefore to analyze the prognostic value of pulmonary artery obstruction versus right ventricular dysfunction radiologic indices in oncologic patients with pulmonary embolism (PE). We have also analyzed how the parameters of pulmonary artery obstruction alter ventricular morphology.

2. Patients and methods

2.1. Study design

We have performed a cohort study of individuals with acute PE evaluated by CTPA. Fourteen Spanish centers have participated in this research. The registry was approved by the respective Ethics Committees of the participating institutions and informed consent was attained from all subjects alive at the initiation of the study. Participants were enrolled between October 2013 and November 2014. The method of selection involved studying all consecutive patients with cancer and PE detected by CTPA over this period of time. A negative control group was also recruited (consecutive selection of patients from the same centers, with the same eligibility criteria except that the clinical suspicion of PE was excluded by CTPA) to evaluate the radiological and clinical characteristics in the absence of the effect of PE. CTPA studies used for the detection of PE were reanalyzed by 14 senior radiologists, one at each center, specialized in pulmonary radiology, with more than five years of experience. Data collection for patients with PE was prospective in 58% (n = 175) of the sample. We pooled these data with a retrospective cohort selected with the same eligibility criteria as the prospective cohort, in the same centers, from PE events detected from 2009 to 2013. When the acute PE occurred previously to the beginning of the study, the information was obtained from radi-