



## EDITORIAL COMMENT

# Pulmonary CT angiography in pulmonary embolism: Beyond diagnosis<sup>☆</sup>

## Angio-TC pulmonar no tromboembolismo pulmonar: para além do diagnóstico

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Right ventricular dysfunction (RVD) is the most common cause of short-term mortality in patients with acute pulmonary embolism (PE).<sup>1</sup> Shock and hemodynamic instability, defined as systolic blood pressure below 90 mmHg or a fall of more than 40 mmHg, is a clinical marker of high risk and identifies patients who may benefit from early thrombolysis.<sup>2</sup> However, in PE patients without hemodynamic compromise, the cost/benefit ratio of fibrinolytic therapy is less clear. In order to determine the therapeutic strategy in such patients, a more detailed and accurate stratification is essential, based on early detection of RVD.

The pathophysiology of RVD in PE is thought to be due to a sharp increase in right ventricular (RV) afterload caused by both mechanical pulmonary arterial obstruction and pulmonary vasoconstriction mediated by neurohumoral factors.<sup>3</sup> Although compensatory mechanisms to maintain RV systolic function come into play, including catecholamine-induced tachycardia and recruitment of preload reserve via the Frank-Starling mechanism, cardiac output from the RV decreases, resulting in reduced left ventricular (LV) filling. Increased wall stress and decreased oxygen supply can trigger ventricular ischemia, which in turn leads to systolic dysfunction and hemodynamic instability. Depending on clinical conditions, including comorbidities and clot burden, this vicious cycle may prove rapidly fatal, particularly

in untreated patients. Thus, early accurate diagnosis and effective treatment are of the utmost importance in PE.

The prognostic value of confirming RVD in PE by echocardiography or multidetector computed tomography (CT) pulmonary angiography has only been demonstrated in relatively small studies.

While CT angiography has a central role in diagnosis of PE, its usefulness in determining prognosis has been less well studied. CT studies have analyzed various parameters of RV dilatation, including RV/LV ratio >1 determined on the basis of transverse or reconstructed 4-chamber images,<sup>4–6</sup> but its prognostic value is relatively limited in patients with hemodynamically stable PE.<sup>7</sup> Other pulmonary CT criteria have been proposed as markers of RVD, such as interventricular septal bowing, ratio of pulmonary artery to aortic diameters, coronary sinus, azygos vein and superior vena cava diameters, and reflux of contrast into the inferior vena cava. More recent studies have demonstrated that three-dimensional assessment of ventricular volumes is superior to measurement of diameters in diagnosing RVD.<sup>8,9</sup>

However, most of these studies are retrospective, clinical presentation is not consistently defined and there are considerable differences in terms of interobserver reproducibility.

Besides signs of RV overload and dilatation, PE severity as determined by clot burden scores on pulmonary CT angiography has been suggested as a predictor of RVD. An obstruction index of 40–60% is associated with intermediate or high-risk PE in patients who present without hypotension.

The CT criterion used to diagnose PE consists of direct visualization of nonocclusive endoluminal thrombus or of

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complete occlusion by thrombus in normal-sized or enlarged vessels. In the study by Qanadli et al.<sup>10</sup> that served as the basis for defining a clot burden score, the arterial tree of each lung was regarded as having 10 segmental arteries (three to the upper lobes, two to the middle lobe and to the lingula, and five to the lower lobes). The presence of embolus in a segmental artery was scored 1 point, and emboli in the most proximal arterial level were scored a value equal to the number of non-visualized segmental arteries. To provide additional information on residual perfusion distal to the embolus, a weighting factor was assigned depending on the degree of obstruction (0 – no thrombus; 1 – partially occlusive thrombus; 2 – total occlusion). Thus, the maximal CT obstruction index was 40 per patient. The percentage of vascular obstruction was calculated by dividing each patient's score by the maximum score  $\times$  100.

It is important to analyze the relationship between a CT obstruction index and parameters of RV dilatation, since the presence of RVD indicates a high probability of recurrence of potentially fatal PE, even with anticoagulation.<sup>11,12</sup> At the same time, the degree of pulmonary vascular obstruction is the most important factor in RV response to PE.

The study by Rodrigues et al. in this issue of the *Journal* demonstrates the value of analyzing the correlation between a previously validated angiographic clot burden score (the Qanadli score – QS) and clinical, electrocardiographic, laboratory and echocardiographic parameters of RVD. The authors showed through careful analysis of 107 patients admitted with intermediate/high-risk PE that clot burden assessment by pulmonary CT angiography based on the QS can have considerable clinical impact by enabling better stratification and selection for thrombolytic therapy. Higher QS was associated with greater prevalence of syncope/lipothymia, RV abnormalities on ECG suggestive of pressure overload, lower creatinine clearance and  $PO_2/FiO_2$  ratio, and higher troponin I. The study also suggests that the CT obstruction index can predict RV dilatation. These results are consistent with data reported in other studies.<sup>10,13</sup> In the study by Rodrigues et al.,  $QS \geq 18$  points was independently associated with RVD.

In terms of echocardiographic parameters, there were no significant differences in pulmonary artery systolic pressure between patients with  $QS \geq 18$  or  $<18$ , as found in previous studies,<sup>10,13</sup> which is to be expected in the context of acute RV overload and dysfunction in an unselected population, as the presence of preexisting comorbidities such as pulmonary disease was not an exclusion criterion. A limitation of the study is that echocardiographic parameters of RVD were not systematically analyzed and compared.

Nevertheless, higher clot burden scores correlated linearly with parameters of RVD assessed by pulmonary CT angiography, including RV, superior vena cava, azygos vein and coronary sinus diameters, RV/LV and pulmonary artery/aorta ratios, reflux of contrast into the inferior vena cava and interventricular septal bowing. These findings are important, as they demonstrate the potential of pulmonary CT assessment of clot burden in terms of RV function. Previous studies have documented significant interobserver differences in CT findings of RVD in PE patients, suggesting that volumetric analysis of the RV/LV ratio is less observer-dependent and more reproducible. Interobserver variability was not analyzed in the study presented here.

Type B natriuretic peptide (BNP) and its N-terminal fraction (NT-proBNP) have been shown to be markers of RVD with considerable short- and medium-term prognostic value in patients with PE, as demonstrated by a study recently published in the *Journal*<sup>14</sup> that retrospectively analyzed consecutive patients admitted for PE over a period of three and a half years.

Elevated NT-proBNP levels identified PE patients with worse short-term prognosis, and showed excellent power to predict 30-day all-cause mortality. This and other studies suggest that BNP and NT-proBNP may have an important role in the initial evaluation of patients with PE, adding valuable prognostic information. It would have been interesting if these biomarkers had been included in the study by Rodrigues et al.

In-hospital mortality was independent of clot burden scores. However, the association between clot burden and medium- and long-term mortality in patients admitted for PE has not been determined and further prospective studies should be performed.

## Conflict of interest

The author has no conflicts of interest to declare.

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