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COMMENTARY

Refining Risk Stratification in Nonmassive Acute Pulmonary Embolism

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Continuing advances in diagnosis and therapy have been regarded as the driving forces behind the recent decrease in mortality rates due to pulmonary thromboembolism. Estimates from European countries between the years 2010 and 2015 revealed a significant drop in age-standardized annual pulmonary thromboembolism–related mortality from 12.8 to 6.5 deaths per 100 000 inhabitants (1). On the other hand, the higher sensitivity of CT pulmonary angiography for the diagnosis of pulmonary thromboembolism may have substantially contributed to an apparent increase in the disease incidence. This phenomenon raised significant concerns about overdiagnosis and potential negative downstream ramifications of anticoagulation therapy, including costs associated with hospital admissions and adverse events (2). Therefore, algorithms for patient management should be aligned along maximization of therapy efficacy, while minimizing the collateral effects on the lower risk population.

In this issue of *Radiology: Cardiothoracic Imaging*, Rotzinger et al (3) shed light on the prognostic value of the CT obstruction index (CTOI), originally proposed by Qanadli et al (4), for determining mortality risk in patients with pulmonary thromboembolism. This well-conducted study examined the 30-day and 3-month mortality in 690 patients with pulmonary thromboembolism who underwent CT pulmonary angiography at the time of diagnosis, which excluded those who required thrombolytic therapy or mechanical thrombectomy. This cohort was stratified according to the presence or absence of preexisting cardiopulmonary comorbidities, including cardiovascular diseases, chronic obstructive pulmonary disease, and malignancies. Not surprisingly, mortality was higher in patients with comorbidities at both 30-day and 3-month time points when compared with their counterparts without comorbidities (30-day mortality: 14.6% vs 7.0%, respectively, $P = .001$; 3-month mortality: 17.8% vs 8.1%, respectively, $P = .001$). While the prognostic use of CTOI was not supported by the statistical analysis in patients with comorbidities, the authors found that CTOI cutoffs set at 20% and 40% could stratify mortality risk in those without cardiopulmonary comorbidities. In this subgroup, 30-day and 3-month mortality in patients with CTOI < 20% were substantially lower, with odds ratios of 0.39 (95% confidence interval [CI]: 0.17, 0.92) and 0.47 (95% CI: 0.21, 0.99), respectively. In contrast, a CTOI ≥ 40% was associated with increased mortality, with odds ratios of 2.9 (95% CI: 1.17, 6.83) and 4.47 (95% CI: 2.07, 9.81), respectively.

Many authors have previously noted the potential role of CT pulmonary angiography as an ancillary tool for determining patient prognosis in pulmonary thromboembolism, which goes beyond its traditional diagnostic role. Bankier et al (5) were the first to adapt two conventional angiography clot burden indexes (ie, Walsh and Miller indexes) to spiral CT, finding heterogeneous correlation between these semiquantitative indexes and the severity of disease based on clinical parameters. In a later study, Qanadli et al (4) proposed an obstruction index specifically designed for CT pulmonary angiography, which assigns a unitary value to each segmental pulmonary artery with thromboembolism, multiplied by a weighing factor (1 for partial obstruction or 2 for complete obstruction). For scoring purposes, the upper lobes are subdivided into three segments, the right middle lobe and lingula into two segments, and lower lobes into five segments. More proximal vessels are scored according to the number of distal branching segments. As a later modification that was used by the authors in the current article, the total CTOI is calculated as the sum of the individual scores per artery, divided by the maximum possible total score (ie, 40) and converted to a percentage. The CTOI and the Miller index were shown to be significantly correlated ($r = 0.87$, $P < .0001$) in patients who underwent both CT pulmonary angiography and conventional angiography (4). In a small study of 59

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See also the article by Rotzinger et al in this issue. Conflicts of interest are listed at the end of this article.

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patients with pulmonary thromboembolism, Wu et al (6) found that CTOI was an independent predictor of mortality with an odds ratio of 2.32 (95% CI: 1.28, 4.18), even after adjustments for other variables (age, sex, preexisting malignancy, cardiac disease, or hypercoagulability). Mastora et al (7) described another semiquantitative clot burden index on CT pulmonary angiography similar to the CTOI, which also correlates with presence of pulmonary hypertension and cor pulmonale on echocardiography. Most importantly, all of these semiquantitative obstruction indexes were shown to be significantly correlated with each other in patients with pulmonary thromboembolism (8).

Of note, additional parameters extracted from CT pulmonary angiography have also emerged as prognostic factors in thromboembolism. For instance, increased right ventricular–to–left ventricular diameter ratio is an established marker of right ventricular strain that is associated with mortality in these patients (8). Moreover, iodine maps obtained from dual-energy CT pulmonary angiography can be used as surrogates of lung perfusion, allowing for quantification of perfusion defects caused by pulmonary thromboembolism. Semiquantitative and quantitative methods for assessing lung perfusion based on dual-energy CT pulmonary angiography were shown to be significantly correlated with the CTOI, and similarly associated with worse clinical outcomes (9–11).

Many factors influence the incorporation of any of these prognostic factors into clinical practice. First, there is the need for robust data to support their validity across multiple centers. Second, the tool should rely on available technology, easiness of use, and reproducibility. Last, the importance of such tool should be measured against its impact on clinical management and decision making. In their article, Rotzinger et al (3) help to advance the knowledge in this field by confirming the prognostic value of CTOI in a large cohort of patients, paving the way for future incorporation of this parameter into the clinical decision-making process. This is particularly relevant when considering the current guidelines for venous thromboembolic disease therapy. In particular, patients considered to have low-risk pulmonary thromboembolism, under specific conditions, could receive antithrombotic therapy at home or be discharged earlier in the course of treatment (level of evidence: 2B) (12). Therefore, the CTOI has the potential to fulfill this role as an objective imaging marker of disease severity. In the near future, part of the laborious component of the CTOI score could be facilitated by embracing automation pipelines based on artificial intelligence. As an example, automatic segmentation and volumetric quantification of clot burden using a deep convolutional neural network was shown to produce values that are significantly correlated with both CTOI (r = 0.82, $P < .001$) and Mastora score (r = 0.87, $P < .001$) (13).

Noticeably, Rotzinger et al (3) also provide insight about some of the limitations of their study. Primarily, the CTOI did not have an independent prognostic role in patients with preexisting cardiopulmonary diseases. This fact underscores the necessity for incorporating the full clinical picture into the risk equation. Future investigation about the effects of integrating multiple clinical and imaging parameters may hopefully show that the accuracy of risk predictions can be actually improved. Notwithstanding, we congratulate the authors for their important contribution to the field.

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