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Pulmonary Embolism in Oncologic Patients

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Abstract

Interest in diagnosis and treatment of pulmonary embolism (PE), a potentially fatal disease, is always high, especially among oncologic patients. In fact, not only tumors but also chemotherapy increases the risk to develop thromboembolic events in these particular patients. Moreover, nowadays, it frequently happens to detect incidental PE by imaging examinations performed for other purposes and, as oncologic patients are surely the ones who undergo the most of the diagnostic procedures, they are also the ones that more often are found to be affected by incidental, asymptomatic, pulmonary embolism.

Keywords: Pulmonary embolism; Diagnostic imaging; Multidetector computed tomography; Pulmonary artery; Neoplasms

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Diagnostic Imaging

Granted that, in patients with hemodynamic stability, the diagnosis of PE should follow a sequential diagnostic work-up consisting of clinical probability assessment, D-dimer testing and, only if necessary, imaging procedures, it is a sure thing that, at present, diagnostic imaging plays a primary role in the routinely management of patients with suspected PE [1].

Evaluation of suspected PE is possible with different kind of examinations; namely: pulmonary angiography, ventilation-perfusion scanning, computed tomography (CT), and in more recent years, magnetic resonance. Among these techniques, however, it is surely CT, even from the first-generation machines, that has clearly revolutionized the diagnostic approach to this pathology [2, 3]. In fact CT, and in particular multidetector CT (MDCT) with its high sensitivity (83-100%) and specificity (89-97%) is widely considered the gold standard to rule out this tricky pathology [4-7].

New generations of MDCT, with 64 to 320 and more detectors' rows, are characterized by a higher spatial resolution that allows to diagnose even small emboli in sub-segmental arteries (sub-segmental pulmonary embolism – SSPE) and a higher temporal resolution that allows to identify PE not only in examinations performed with CT angiography protocol but even in chest CT examination performed with standard protocols [8]. However, the CT scan technique and in particular the slice thickness play an essential role in the diagnosis of pulmonary embolism so that a constraint on the slice thickness (<2 mm) is mandatory to correctly evaluate filling defects in pulmonary arteries [8, 9]. In presence of PE, conventional CT-angiography examination is able to estimate the clot burden; this estimation could be replaced by the analysis of the extent of perfusion impairment on dual-energy CT examinations [10]. It is also to underline that, nowadays, CT-angiography protocols based on the injection of a small volume (<50 ml) of high concentrated contrast media at low voltage (80-100 kVp) makes possible to confidently diagnose/rule out PE with a very low radiation dose to the patient [11, 12]. Among the advantages of CT imaging there is also the possibility to give additional information to predict patient's outcome; in particular, the major determinant of patient's outcome is the presence of right ventricular dysfunction, easily detectable by CT imaging [3, 13, 14].

Due to both MDCT technical features and the increasing skill of radiologists, the detection of pulmonary emboli in asymptomatic patients who undergo MDCT for other purposes, mainly for oncologic staging or follow-up, is more and more frequent [8, 15].

Oncologic Patients

Oncologic patients, a growing wide world population, are a particularly delicate subgroup of patients, many being the issues concerning acute pulmonary embolism among them. First of all, it is well known that malignancy as well as chemotherapy and radiotherapy are predisposing factors for venous thromboembolism. In fact, the risk of thrombosis among oncologic patients is reported to be about 4-6 times higher than in the general population and even more increased (about 6.7-fold) in patients treated with chemotherapy [16-20]. Furthermore, the

risk varies with the kind of malignancy and the stage of disease, being much higher in patients with advanced stage of cancer [18-24]. Moreover, the risk of PE recurrence and death from PE is higher in oncologic patients in comparison to general population [1, 18, 25]. Many authors report, in fact, a twofold higher incidence rate of central PE in patients with malignancy than in patients without, probably due to the pro-coagulant activity of cancer [19, 26]. That is why, even considering the potential hemorrhagic risk of anticoagulation therapies, patients with cancer are candidate for indefinite anticoagulation, with periodic reassessment of the risk-benefit ratio; some authors even suggest prospective clinical trials of primary thrombo-prophylaxis for some types of cancer due to their biological aggressiveness [1, 19, 22, 24, 27].

Nowadays, it frequently happens to incidentally detect acute, even massive, PE in asymptomatic, often oncologic, patients: it is, hence, believed that most fatal PE are not suspected clinically and not treated [7, 18, 28]. The early diagnosis could surely help to prevent fatal PE but we think that differences in patients symptoms and/or in the entity of venous thromboembolism should be taken into consideration. On one hand, regarding the detection of asymptomatic pulmonary embolism in oncologic patients, many authors, even if there is no complete agreement, suggest that clinical outcomes appear to be similar to symptomatic PE [18, 29-31]. On the other hand, there is surely a difference in the clinical significance of the incidental detection of central or lobar pulmonary embolism compared to small sub-segmental disease.

Pulmonary Embolism Burden

As stated before, the detection of filling defects in pulmonary arteries in patients undergoing CT not to rule out/confirm pulmonary embolism happens with increasing frequency. However, while patients with massive, central or lobar pulmonary embolism, even if asymptomatic, are going to be considered as well as symptomatic patients and treated with anticoagulation therapies, what to do in cases of detection of small peripheral pulmonary emboli is object of discussion [32-34]. It is also to be considered that while the detection of large pulmonary emboli is somewhat easy even in CT performed not with angiographic protocol, the possibility of false positive results in the detection of small pulmonary emboli particularly in case of lack of vessel opacification or motion artifacts is real and we think that radiologists must know what this involve. Anticoagulation therapy, in fact, carries a higher risk of hemorrhagic complications as demonstrated by the 3% of treated patients developing every year a major bleeding event requiring medical care [1, 34]. The incidence of isolated small segmental pulmonary emboli is between 5% and 15%, depending on the population studied [34]. Nielsen et al. found no differences in the outcome of patients with asymptomatic PE treated compared to those untreated [35, 36]. Moreover, O'Connell et al. demonstrated that the detection of SSPE in oncologic patients, if not associated with symptoms or clinical and laboratory specific parameters, has no impact on clinical conditions or any adverse impact on survival [31, 34]. However, on the other hand, SSPE could be an early manifestation of hyper-coagulable state, associated to pro-coagulant potential and so the question is whether the risk of anticoagulation can outweigh the benefits. Concerning this, Zompatori et al. in a recent review on SSPE suggest that a model of multi-parametric scoring for isolated SSPE, based on CT results and other clinical and laboratory parameters, could be helpful to identify which patients should benefit from a specific therapy. Regardless of these controversies and of the cancer, there are three clinical scenarios in which most would agree that even a small embolus requires treatment: (a) in patients with small embolus and inadequate cardiopulmonary reserve; (b) in patients who have a small embolus and coexisting acute DVT, and (c) in patients who have recurrent small embolus possibly due to thrombophilia, to prevent chronic PE and pulmonary artery hypertension [7, 37].

In conclusion, pulmonary embolism in oncologic patients is a topic of growing importance due to the increasing diagnostic performance of MDCT and the consequent increase in the incidental detection of pulmonary arteries filling defects. Considering the reduced specificity of a high D-dimer level, the predisposing role of cancer itself, chemo and radiotherapies, attention should be paid to the CT detection of emboli in patients with malignancy. However the role of SSPE and its clinical significance is still uncertain and has to be clarified.

Conflict of Interest

None

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