Eur Radiol (2015) 25:2547–2557
DOI 10.1007/s00330-015-3679-2

CHEST

Computed tomography of acute pulmonary embolism: state-of-the-art

Long Jiang Zhang · Guang Ming Lu · Felix G. Meinel · Andrew D. McQuiston · James G. Ravenel · U. Joseph Schoepf

Received: 13 January 2015 / Accepted: 17 February 2015 / Published online: 13 March 2015
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Abstract Multidetector computed tomography (CT) plays an important role in the detection, risk stratification and prognosis evaluation of acute pulmonary embolism. This review will discuss the technical improvements for imaging peripheral pulmonary arteries, the methods of assessing pulmonary embolism severity based on CT findings, a multidetector CT technique for pulmonary embolism detection, and lastly, how to avoid overutilization of CT pulmonary angiography and overdiagnosis of pulmonary embolism.

Key Points

- *We describe clinical prediction rules and D-dimers for pulmonary embolism evaluation.*
- *Overutilization of CT pulmonary angiography and overdiagnosis of pulmonary embolism should be avoided.*
- *We discuss technical improvements for imaging peripheral pulmonary arteries.*
- *Pulmonary embolism severity can be assessed based on CT findings.*
- *We discuss multidetector CT techniques for pulmonary embolism detection.*

Keywords Pulmonary embolism · Tomography · X-ray-computed · Angiography · Prognosis · Low radiation dose

L. J. Zhang (✉) · G. M. Lu · U. J. Schoepf
Department of Medical Imaging, Jinling Hospital, Medical School of Nanjing University, Nanjing, Jiangsu 210002, China
e-mail: kevinzhlj@163.com

F. G. Meinel · A. D. McQuiston · J. G. Ravenel · U. J. Schoepf
Department of Radiology and Radiological Science, Medical University of South Carolina, Ashley River Tower, MSC 226, 25 Courtenay Dr, Charleston, SC 29401, USA

Introduction

Acute pulmonary embolism (PE) is a life-threatening disease, ranking as the third most common acute cardiovascular disorder after myocardial infarction and stroke [1]. It is reported that PE is fatal in up to 30 % of patients [2, 3]. One recent study showed that a delay (>1.5 hour) in the direct communication of an acute PE diagnosis was significantly correlated with delayed treatment initiation and higher risk of death within 30 days [4]. Thus, timely and accurate diagnostic management is required for patients with suspected PE.

Computed tomography pulmonary angiography (CTPA) plays a pivotal role in the detection, risk stratification, prognosis evaluation and follow-up of acute PE, and is now the accepted reference standard for PE evaluation and one of the most important steps in diagnostic algorithms of PE [5, 6]. However, CTPA is adding considerably to the population ionizing radiation burden [7]. A combination of pre-test prediction evaluation and D-dimer testing permits for optimal use of resources and minimisation of population radiation burden [6, 8]. In recent years, dual-energy CT has emerged to further improve the detection of PE [9]. However, with the increasingly widespread use of this test, overutilization of CTPA and overdiagnosis of PE are becoming more tangible considerations. Guidelines for appropriate use of CTPA have been developed to address these concerns [10]. This review will discuss the current prediction rules, the latest developments, and the limitations and appropriate place for CTPA in the assessment of patients with suspected acute PE.

Clinical prediction rules and D-dimer testing

Although clinical presentations of PE are nonspecific, a combination of signs, symptoms and risk factors has been used to assess the pre-test probability for PE. The Wells rule and the

revised Geneva rule are the most widely used clinical prediction rules (see Tables 1 and 2) [5, 6]. Use of either of these rules is recommended in the guidelines [5, 6]; this is also a necessary step in the diagnostic workflow of PE (Fig. 1).

D-dimers are frequently used in the diagnostic workup of acute PE [5, 6, 11]. D-dimer assays have a high negative predictive value; however, they have low specificity. It has been demonstrated that it is safe to rule out PE on the basis of a normal D-dimer test result and an unlikely pre-test clinical probability [12–14]. Because D-dimer levels increase with age, the new age-dependent D-dimer cutoff is recommended, which is defined as a patient's age x 10 μg/l in patients over 50 years of age [15], rather than the previously used "standard" of 500 μg/l in all patients [11].

Appropriate use of CTPA

CTPA is increasingly used in patients with suspected PE. Although CTPA can also confirm or rule out alternative diagnoses in patients with suspected PE, this consideration may not justify the increasing use of CTPA. Arguably, a negative CTPA will expedite discharge and prevent a patient with suspected PE from undergoing further downstream testing, and more importantly, from receiving unnecessary anticoagulation with the associated risk of complications [16]. However, it is undeniable that more stringent adherence to guidelines is needed to preserve the (comparative) effectiveness of this test [10]. Adherence to recommendations by the PIOPED II investigators for the appropriate use of CTPA is one option to reduce the number of CTPA examinations [17]. Curbing overutilization and inappropriate use is also the most important component of a population-based

Table 1 Wells rules for pulmonary embolism

Items	Clinical decision rule points	
	Original version	Revised version
Previous PE or DVT	1.5	1
Heart rate≥100 beats/minutes	1.5	1
Surgery or immobilization within the past four weeks	1.5	1
Haemoptysis	1	1
Active cancer	1	1
Clinical signs of DVT	3	1
Alternative diagnosis less likely than PE	3	1
Clinical probability		
Three-level score		
Low	0-1	N/A
Intermediate	2-6	N/A
High	≥7	N/A
Two-level score		
PE unlikely	0-4	0-1
PE likely	≥5	≥2

DVT=deep vein thrombosis; PE=pulmonary embolism

Table 2 Revised Geneva rules for pulmonary embolism

Items	Clinical decision rule points	
	Original version	Revised version
Previous PE or DVT	3	1
Heart rate		
75–94 beats/minute	3	1
≥95 beats/minute	5	2
Surgery or fracture within the past month	2	1
Haemoptysis	2	1
Active cancer	2	1
Unilateral lower limb pain	3	1
Pain on lower limb deep venous palpation and unilateral oedema	4	1
Age>65 years	1	1
Clinical probability		
Three-level score		
Low	0-3	0-1
Intermediate	4-10	2-4
High	≥11	≥5
Two-level score		
PE unlikely	0-5	0-2
PE likely	≥6	≥3

DVT=deep vein thrombosis; PE=pulmonary embolism

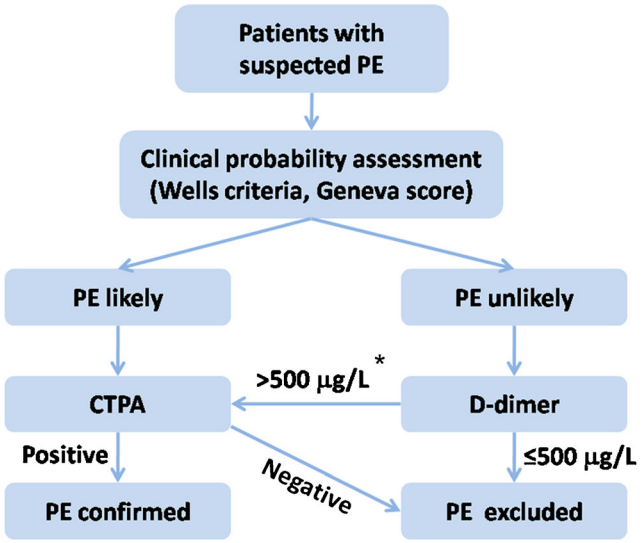

Fig. 1 Recommended diagnostic algorithm for clinically suspected acute PE. PE=pulmonary embolism; CTPA=CT pulmonary angiography. * D-dimer cut-off of patients' age x 10 μg/l is recommended in patients aged over 50 years

approach towards reducing collective radiation exposure from medical imaging.

Risk-factor assessment should always be the first step in evaluating suspected PE patients. Current guidelines [6, 18] agree that assessment of pre-test probability is essential and that CTPA is unnecessary when pre-test probability is low and a sensitive D-dimer test result is negative. If pre-test probability indicates "PE likely" or if D-dimer levels are elevated above the threshold, the patient should be referred for CTPA and further managed according to CTPA result (Fig. 1) [18, 19]. Using this algorithm, CTPA can be avoided in 20–30 % of suspected PE patients [19].

While in the earlier days of CTPA it has been argued that too many small PE may be missed, concerns of overdiagnosis and overtreatment of PE are now being voiced, resulting from the widespread use of advanced CT techniques with ever increasing sensitivity for small, peripheral emboli. Increased PE incidence with minimal change in overall mortality and no significant change in 7-day or 14-day mortality has been observed since the introduction of CTPA [10, 20]. Smaller subsegmental emboli are more frequently detected with advanced CTPA techniques that include the computer-aided diagnostic (CAD) system and dual-energy CTPA.

"Overdiagnosis" is a concept that is currently quite liberally applied to a variety of tests, mainly in the realm of imaging [21]; however, this term is ill defined. Stein et al. [22] believe that it is safe to withhold treatment of subsegmental emboli if the pulmonary–respiratory reserve is good, there is no evidence of deep venous thrombosis on serial testing, the major risk factor for PE was transient and is no longer present, there is no history of central venous catheterization or atrial fibrillation, and the patient is willing to return for serial venous ultrasound. Further research is needed in this field, ideally in the form of a prospective randomized controlled trial.

Assessment of PE severity

Cardiac measurements of right heart strain

Accurate risk stratification based on CTPA findings is essential in patients with PE. CT findings in acute PE used for risk stratification include right ventricular (RV) dilatation, interventricular septal bowing, embolus burden (Figs. 2 and 3), and right heart embolus in transit (Fig. 4) [2, 23, 24]. Among all above-mentioned parameters, RV dilatation is the most important prognostic factor for PE [2, 23, 24]. An international prospective cohort study demonstrated that RV dysfunction assessed by CTPA was an independent predictor for in-hospital death or clinical deterioration in the overall population and in haemodynamically stable patients [25]. Recent meta-analyses also support the above-mentioned findings [26, 27]. This supports the notion that CTPA can serve as a single procedure to diagnose PE and to assess the short-term risk of death, and thus guide the level of aggressiveness of management and treatment.

The RV/left ventricle (LV) ratio is the most commonly used marker for assessing RV dilatation in CTPA. Two methods have been proposed. One is to obtain multiplanar-reconstructed CT images, with the aim of emulating the true four-chamber view of echocardiography and cardiac MRI [28, 29]. The other is to measure heart chambers on standard transverse images [30, 31]. The RV and LV diameters from inner wall to inner wall at their widest point are measured on transverse sections at the level of the tricuspid and mitral valves (Fig. 5), respectively [31]. Thus, RV/LV diameter ratio can be calculated. Generally, patients with an RV/LV ratio>1.0 on transverse CT images or an RV/LV ratio>0.9 on true four-chamber reformatted views are regarded as having RV dysfunction [28–32].

Another method for evaluating RV dysfunction is calculating RV/LV volume ratio. Retrospective electrocardiogram (ECG)-gated CT acquisition was proposed to quantitatively evaluate RV and LV volumes. Using retrospective ECG-gated acquisition, triple-rule-out CT can simultaneously evaluate the presence of aortic dissection, acute PE and acute myocardial infarction. However, retrospectively ECG-gated CTPA can deliver more radiation exposure to the patients, which needs be carefully weighted when adopting this technique. RV volume measurements based on non-ECG-gated CT acquisition was also recommended. One study by Kang et al. showed that a RV/LV volume ratio>1.2 on non–ECG-gated chest CT is a predictor of early death in patients with acute PE, independent of clinical risk factors and comorbidities [29].

Embolic burden measurements

Several semi-quantitative algorithms to measure the degree and location of vascular obstruction in CTPA have been developed to evaluate PE severity. The most widely used algorithms include the Quanadli score (known as the pulmonary artery obstruction index) and the Mastora score [33, 34], measured on transverse images for everyday practitioners. Additionally, tools for quantitative blood embolus volume measurement on CTPA have been developed to calculate embolus burden [35]. However, the role of embolus burden assessment in CTPA as an indicator of short-term mortality is debated. Recently, one meta-analysis [36] indicated that localization of emboli in the central pulmonary arteries was associated with an increased risk of 30-day mortality, but no association between pulmonary artery obstruction index and 1-month or 3-month mortality was observed. In the clinical setting, these embolus burden scoring systems are rather complex and require an expert practitioner in the field of PE to perform the evaluation. Thus, to date they are rather unsuitable for emergency settings requiring rapid risk stratification.

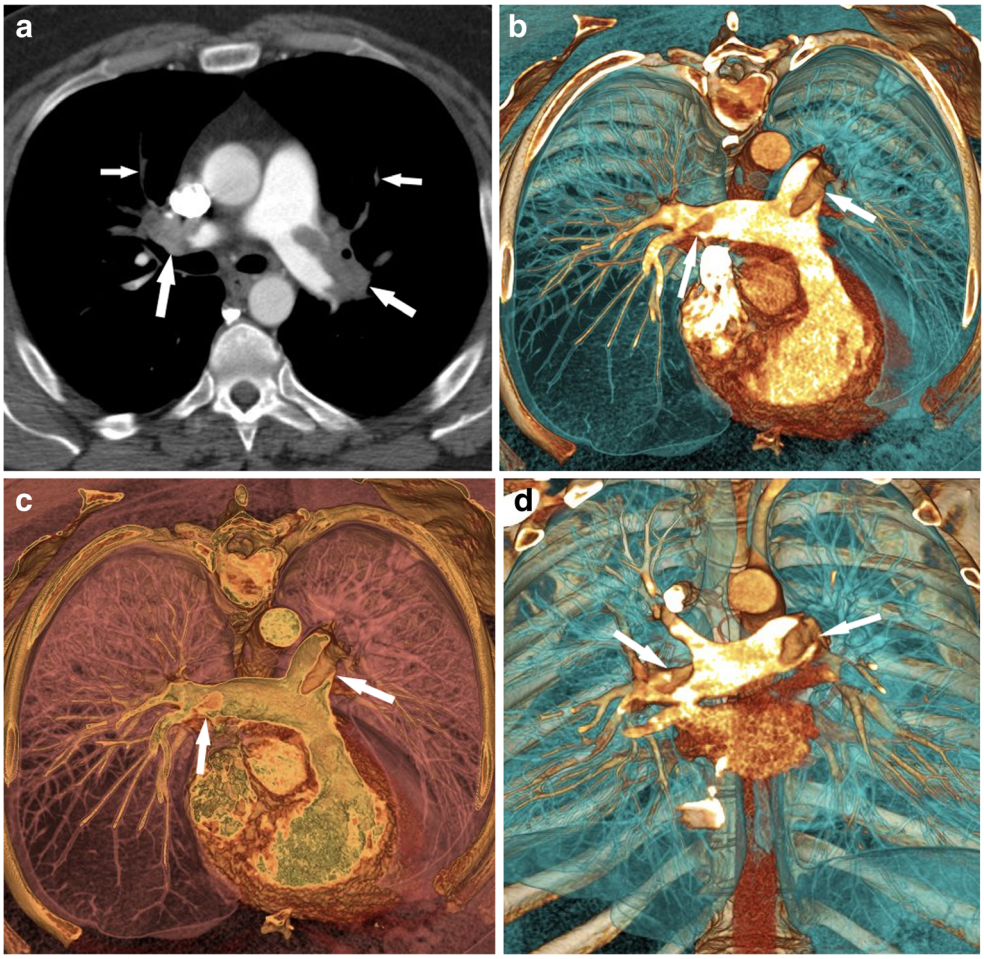

Fig. 2 Central pulmonary embolism in a 35-year-old man. CTPA shown as transverse CT image (**a**) and slab volume-rendered images in oblique transverse (**b**, **c**) and coronal (**d**) orientation demonstrates filling defects in both main pulmonary arteries extending into lobar, segmental and subsegmental pulmonary arteries (*arrows*)

Fig. 3 Isolated subsegmental pulmonary embolism in a 48-year-old woman. Transverse contrast-enhanced CT image shows filling defect in the right lower pulmonary artery (*arrow*)

Dual-energy CT perfusion scoring

Analysis of the extent of perfusion impairment on dual-energy CT appears to be a rational method to evaluate the hemodynamic significance of PE, because some non-obstructive emboli do not cause hemodynamic changes [37–41]. Two perfusion scoring methods have been proposed: grading the degree of perfusion defect per lobe [37–39], and estimating the volume of perfusion defects relative to the total lung volume [40, 41]. These studies showed good correlations between perfusion impairment and CT features of RV dysfunction, suggesting that perfusion defects might be a predictor of clinical outcome. However, further studies with larger cohorts are needed to confirm the correlation between perfusion scores and clinical outcome. In addition, simpler algorithms should be developed to render perfusion scoring feasible in the emergent setting. Meinel et al. [42] have proposed one such algorithm involving automated pulmonary perfused blood volume quantification at dual-energy CTPA, for assessment of the severity of acute PE. They found this algorithm to be capable of quantifying global pulmonary perfused blood volume in acute PE patients, which was inversely correlated with thrombus load,

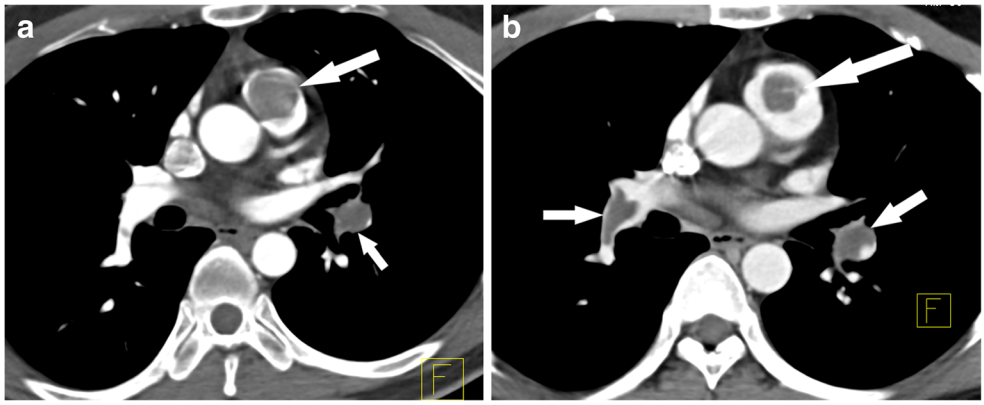

Fig. 4 Pulmonary embolism and right ventricular thrombus in a 31-year-old man. **a**) Transverse contrast-enhanced CT sections show emboli in the outflow tract of the right ventricle (*long arrow*) and left pulmonary artery (*short arrow*). **b**) Another transverse contrast-enhanced CT study acquired 13 days later shows the emboli in the outflow tract of the right ventricle (*long arrow*) and both pulmonary arteries (*short arrow*), indicating embolus in transit

laboratory parameters of PE severity, and the necessity for intensive care unit admission [42].

Detection of peripheral PE

Although the clinical significance of peripheral PE, especially isolated subsegmental PE, remains unclear, some clinical observations have indicated that subtle PE can progress into massive PE if no treatment is administered [43]. In patients with risk factors for PE, the following are implicated for peripheral PE progression into more severe disease: inadequate cardiopulmonary reserve, the presence of coexistent deep venous thrombosis, a history of PE, and the extent of symptoms [5].

Computer-assisted detection

CAD systems for PE have been developed to help detect endovascular emboli, especially in peripheral pulmonary arteries (Fig. 6). Mostly used as a second reader, CAD can help detect small emboli that are initially missed, increasing inexperienced reader's sensitivity for the detection of peripheral emboli [44–46]. One recent study [47] demonstrated that CAD correctly identified 77.4 % cases of acute PE previously missed in clinical practice. For inexperienced practitioners, utilizing CAD as a second reader can improve inter-observer agreement and diagnostic confidence [44, 45]. However, the high rate of false-positive detection marks per study (average 3.8–11.4), depending on the image quality of CTPA, remains a major concern [44–47]. Image quality degradation can result from suboptimal contrast enhancement of the pulmonary arteries, respiratory or cardiac motion, and high image noise. Additionally, incorrect pulmonary vein identification, and airway or parenchymal abnormality adjacent to a pulmonary artery branch, can result in false positive PE markings [48]. Although most false-positive CAD candidates are easily identified, this increases the time required for image interpretation. It was reported in Wittenberg et al.'s study [44] that reading time was extended by a mean of 22 seconds with the use of CAD. Due to the limited available evidence and the risk of false positive results, we do not recommend the routine use of CAD systems for PE detection. However, CAD use can be considered as an aid for inexperienced readers, and in cases with a strong clinical suspicion of PE initially interpreted as negative by a radiologist [10, 48].

CT-based lung perfusion and/or ventilation/perfusion imaging

The feasibility of evaluating lung perfusion based on CT techniques has long been recognized [40, 43, 49, 50]. More recently, the potential of dual-energy CT to improve peripheral PE visualization has been demonstrated in many experimental and clinical studies (Fig. 7) [51–57]. However, abnormalities such as small-airways disease and Takayasu's arteritis can result in lung perfusion defects that mimic PE [9, 23, 58]. Dual-energy CT ventilation/perfusion imaging appears to alleviate this problem, in analogy to ventilation/perfusion imaging in nuclear medicine [59, 60]. Zhang et al.'s study demonstrated the feasibility of dual-energy CT ventilation/perfusion imaging performed for detecting PE, and demonstrated a greater ability to detect small pulmonary emboli when compared with conventional CTPA (Fig. 8) [60]. Dual-energy CT perfusion imaging can become widely available even in single-source CT systems, which can be used in patients with clinically suspected PE; however, Xenon-enhanced dual-energy CT ventilation imaging is complex and not routinely available because of high radiation dose, complexity of acquisition, special equipment requirements, high cost and potential side effects of Xenon gas [61].

Dual-energy CT lung vessel applications

Dual-energy CT-based "lung vessel" applications have been developed to highlight iodine within small pulmonary vessels

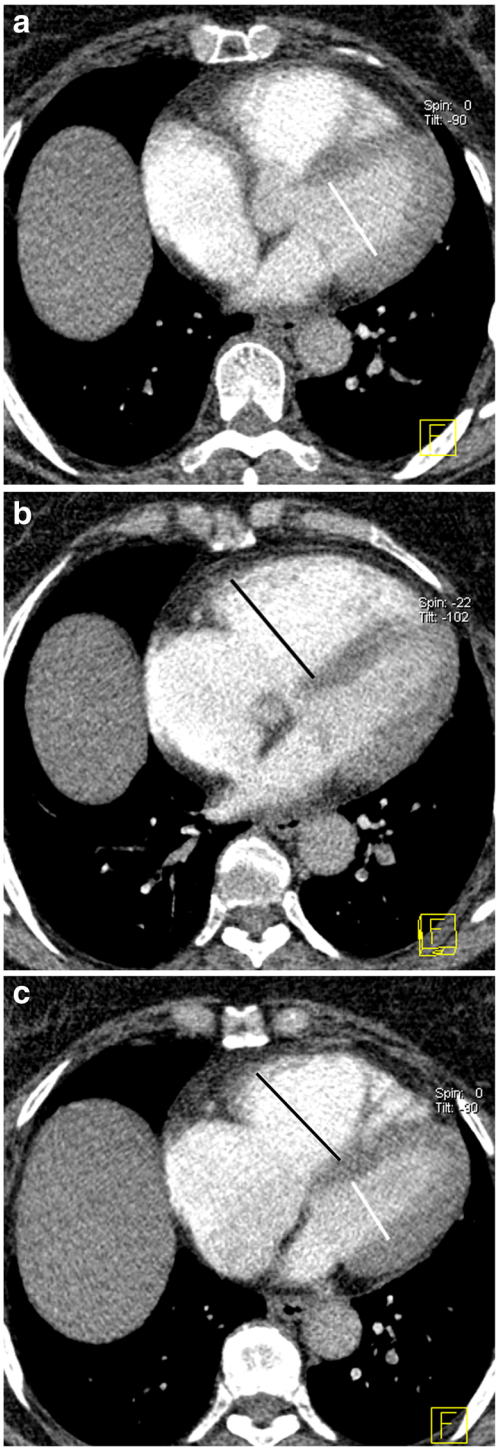

Fig. 5 Measurements of right ventricle and left ventricle diameters in a 68-year-old woman with multiple pulmonary emboli. **a** and **b**) Regular contrast-enhanced transverse CT images illustrate the measurements of right and left ventricular diameters in two different sections. **c**) Reformatted true four-chamber CT image illustrates measurements of the right and left ventricular diameters in one plane

and eliminate the ambiguity of low HU values caused by intravascular emboli, low contrast enhancement, and partial volume effects [62–64]. Some clinical and experimental studies have demonstrated that this technique can discriminate enhanced from non-enhanced peripheral pulmonary arteries (Fig. 7c), improving the visualization of small emboli [62–65]. A recent experimental study [65] indicated that this application had higher sensitivity for detecting subsegmental pulmonary emboli than conventional CTPA. However, this came at the price of decreased specificity and positive predictive value. Thus, such application should be further refined to improve accuracy and decrease the number of false positives on CTPA.

Multidetector CT technique for PE detection

Reduced radiation dose strategies

Due to the increasingly prevalent use of CT worldwide, concerns have been voiced over radiation exposure from CT and the stochastic risk of subsequent cancer induction. Thus, lowering radiation dose is at the forefront of new developments in medical imaging. Technical strategies of dose savings include tube current modulation, individualized tube voltage selection, high-pitch scan modes, iterative reconstruction (IR), scan length adjustment and collimator shutter action to avoid z-axis overscanning in CTPA studies [66, 67].

Lowering tube voltage is one of the most common and effective radiation reduction methods [68–72]. Substantial dose reduction can be achieved by reducing tube voltage to 100, 80 or 70 kVp in adult patients compared with the standard of 120 kVp in CTPA studies (Fig. 9); however, image quality and diagnostic accuracy were preserved. Automated tube voltage selection algorithms have been developed to select the most dose-efficient kVp setting for an individual patient based on the patient's anatomy, as determined by the planning range acquisition [73]. However, lowering tube voltage is not recommended for patients with a body mass index≥ 30 kg/m^2 because of high image noise and decreased image quality.

Employing high-pitch acquisition is another radiation dose reduction strategy in CTPA that is available on newer dual-source CT systems [74]. Again, the high-pitch acquisition technique is typically limited to normal-weight and mildly overweight individuals. This is because X-ray tubes have technical limits in the tube current they can provide, and may not allow the emission of sufficient photons during the very short acquisition time of high-pitch protocols to achieve good image quality in obese patients. Compared with a standard-pitch protocol, Hou et al. [74] showed that a 47 % radiation dose reduction can be achieved with high-pitch CTPA. In addition to reducing radiation dose, high-pitch image acquisition also improves temporal resolution, making it possible to image patients unable to complete a sufficient

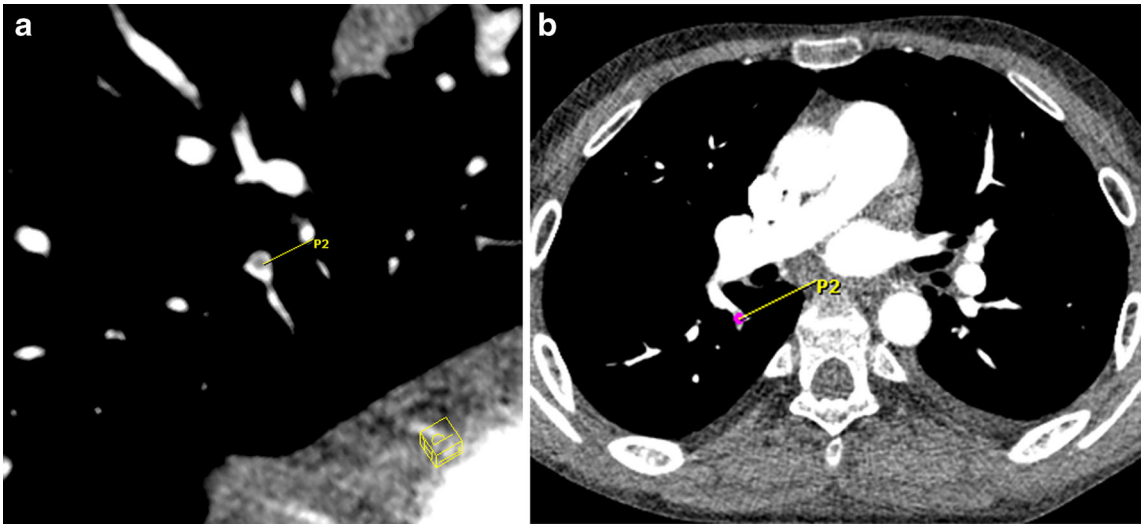

Fig. 6 Computer assisted detection for pulmonary embolism in a 20-year-old man. **a** and **b**) The computer assisted detection system indicates a filling defect in a right lower lung lobe segmental pulmonary artery (P2)

breath hold, reducing motion artefacts, and improving diagnostic evaluation of cardiovascular structures [75]. However, use of high-pitch technique will increase image noise; thus, IR is recommended when using this technique.

Combining low tube voltage, high-pitch scan modes and other dose-saving techniques such as IR, tube current modulation technique, automatic tube voltage selection, and optimized scanning range will further lower radiation dose while maintaining diagnostic image quality in patients with a body mass index<30 kg/m^2. However, it should be noted that the combined use of low tube voltage and high-pitch techniques can substantially increase image noise and lead to deterioration in image quality, especially in larger patients. This can be remedied by employing the most recent generation of dual-source CT systems with substantially increased x-ray tube power, or with the use an IR algorithm to reduce image noise [76]. Our data show that 80 kVp high-pitch CTPA with IR can reduce radiation dose by 50.3 % without image quality deterioration compared to 100 kVp standard-pitch CTPA with filtered back projection (Fig. 9) [75].

Reduced contrast medium volume

Although recent controlled studies have demonstrated that the risk of contrast-induced nephropathy with intravenously injected contrast media at CT may be greatly overstated [77, 78], lowering the volume of iodinated contrast material is desirable to further minimize this potential risk. A lower tube

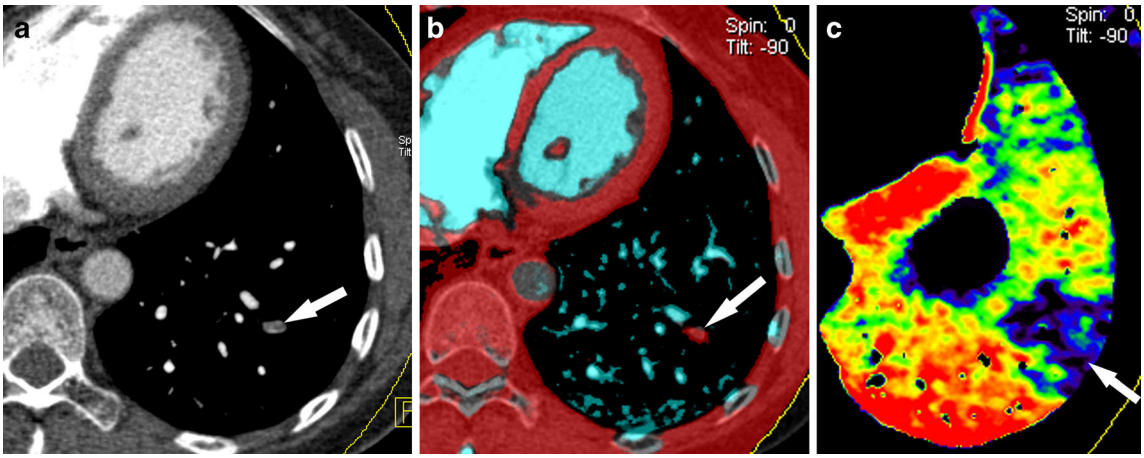

Fig. 7 Dual-energy CT lung perfusion imaging and lung vessels application in a 54-year-old woman with suspected pulmonary embolism. **a**) Transverse contrast-enhanced CT image shows filling defect in a subsegmental pulmonary artery (*arrow*) in the left lower lobe. **b**) Transverse lung vessels application image shows that the corresponding pulmonary artery is color-coded as red (*arrow*), indicating the dual-energy tissue signature of thrombotic material. **c**) The dual-energy CT lung perfusion image shows the corresponding perfusion defect (*arrow*) in the left lower lobe

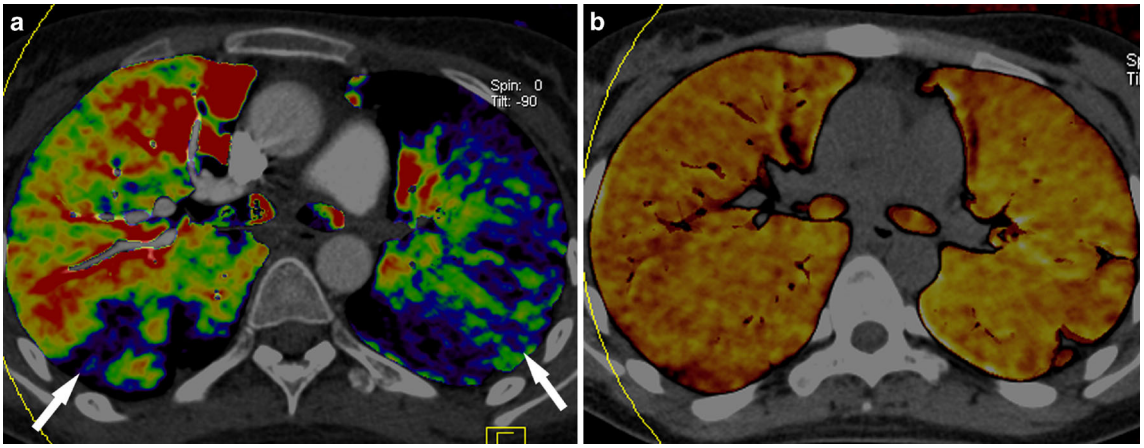

Fig. 8 Dual-energy CT lung ventilation/perfusion imaging in a 19-year-old woman with suspected pulmonary embolism. **a**) Transverse dual-energy CT lung perfusion image shows multiple perfusion defects in the right lower lobe and the left lung (*arrows*). Multiple filling defects within pulmonary arteries were present but not shown in this image. **b**) Transverse dual-energy CT lung ventilation image shows the nearly normal xenon distribution indicating normal ventilatory function

voltage increases the attenuation of iodine resulting in increased contrast enhancement. This can be attributed to decreased tissue penetration and higher photoelectric effect of lower energy x-rays, thus providing the potential to reduce contrast material volume [79, 80]. However, lowering tube voltage should be employed on a per-patient basis according to patient body mass index or by means of automated tube voltage selection systems, in order to avoid a significant

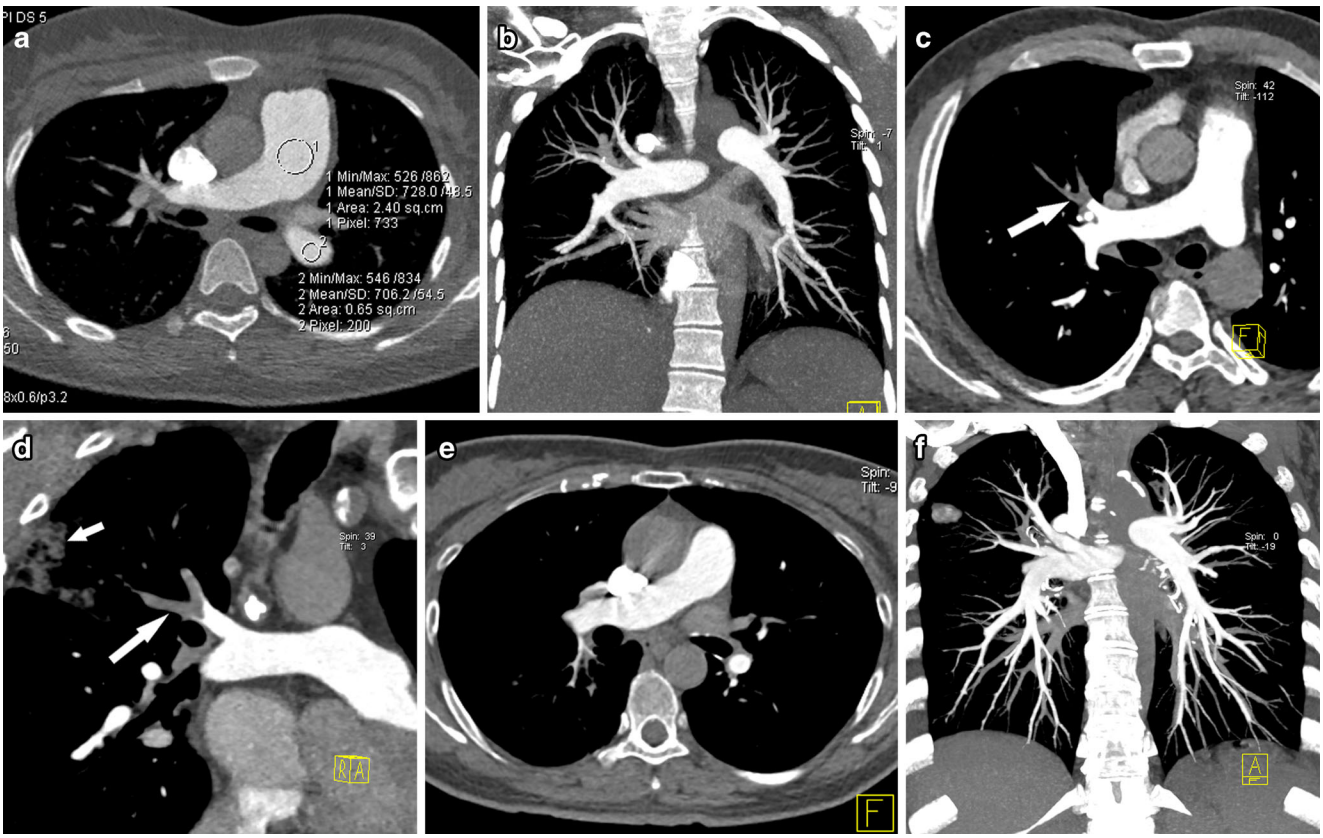

Fig. 9 Comparison of 70, 80 and 100 kVp CT pulmonary angiography in three patients. **a**) Transverse contrast-enhanced CT image and **b**) oblique maximum intensity projection images acquired with 70 kVp and high pitch scan mode (2) in a 26-year-old woman. **c**) Transverse contrast-enhanced CT image and **d**) coronal reformatted CT image acquired with 80 kVp and high pitch scan mode (2) in a 76-year-old man. Note the filling defect in a right upper lobe pulmonary artery (*arrow in Panel c and long arrow in Panel D*) and corresponding lung infarct (*short arrow in Panel d*). **e**) Transverse contrast-enhanced CT study and *F*) maximum intensity projection of study generated with 100 kVp and standard pitch factor (1.2) in a 42-year-old woman. These images were acquired with a second-generation dual-source CT system

increase in image noise [75, 81, 82]. Increasing pitch provides an additional opportunity for iodine load reduction, as acquisition of the entire chest takes only 1 sec or less. As little as 20 ml of contrast material can be used to achieve sufficient image quality if combined with IR (Fig. 9) [75]. Using dual-energy CT, iodine load can be reduced when virtual monochromatic imaging extrapolated to photon energies of 50 or 70 keV is used [83–85]. Saade et al. reported that appropriate contrast material volume can be acquired with use of a patient-specific approach; however, this approach is complex in the clinical setting, because it requires the calculation of contrast material volume according to the equation [86]. Thus, it is recommended that a combination of automatic tube voltage selection and high pitch technique is used to reduce contrast material volume in routine clinical practice.

Conclusions

Multidetector CTPA can be performed in dual-energy mode, and thus simultaneously enables morphological assessment of the heart-lung axis and provides functional information on pulmonary perfusion and ventilation. Multidetector CT systems employ various strategies that have substantially decreased radiation dose and contrast material volume required for CTPA, while maintaining image quality. Overutilization of CTPA resulting in potential overtreatment of clinically insignificant PE is an increasing concern, and requires adherence to and refinement of established clinical prediction rules and algorithms for the appropriate use of this imaging test.

Acknowledgments The scientific guarantor of this publication is Long Jiang Zhang. The authors of this manuscript declare relationships with the following companies: UJS is a consultant for and receives research support from Bayer, Bracco, GE, Medrad, and Siemens. The other authors have no conflicts of interest to declare. This study has received funding by Program for New Century Excellent Talents in University (NCET-12-0260 to L.J.Z.). No complex statistical methods were necessary for this paper. Institutional Review Board approval was not obtained because this is a review paper. Written informed consent was not obtained because this is a review paper. No study subjects or cohorts have been previously reported. Methodology: performed at one institution.

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