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Canadian Society of Thoracic Radiology/ Canadian Association of Radiologists Best Practice Guidance for Investigation of Acute Pulmonary Embolism, Part 1: Acquisition and Safety Considerations

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Abstract

Acute pulmonary embolism (APE) is a well-recognized cause of circulatory system compromise and even demise which can frequently present a diagnostic challenge for the physician. The diagnostic challenge is primarily due to the frequency of indeterminate presentations as well as several other conditions which can have a similar clinical presentation. This often obliges the physician to establish a firm diagnosis due to the potentially serious outcomes related to this disease. Computed tomography pulmonary angiography (CTPA) has increasingly cemented its role as the primary investigation tool in this clinical context and is widely accepted as the standard of care due to several desired attributes which include great accuracy, accessibility, rapid turnaround time and the ability to suggest an alternate diagnosis when APE is not the culprit. In Part 1 of this guidance document, a series of up-to-date recommendations are provided to the reader pertaining to CTPA protocol optimization (including scan range, radiation and intravenous contrast dose), safety measures including the departure from breast and gonadal shielding, population-specific scenarios (pregnancy and early post-partum) and consideration of alternate diagnostic techniques when clinically deemed appropriate.

Résumé

L'embolie pulmonaire aiguë (EPA) est une cause bien connue d'atteinte, voire de défaillance du système circulatoire qui représente souvent un défi diagnostique pour le médecin. La difficulté diagnostique est principalement due à la fréquence des présentations indéterminées, ainsi qu'à plusieurs autres maladies qui peuvent avoir des présentations cliniques similaires. Cela oblige souvent le médecin à poser un diagnostic définitif en raison des conséquences potentiellement graves de cette affection. L'angiographie pulmonaire par TDM s'est de plus en plus établie comme l'outil d'investigation principal dans ce contexte clinique; elle est largement admise en tant que norme de soins en raison de plusieurs caractéristiques recherchées, notamment sa grande précision, son accessibilité, le retour d'information rapide et son aptitude à suggérer un diagnostic autre quand l'EPA n'est pas en cause. Dans la 1re partie de ce document d'orientation, une série de recommandations mises à jour est proposée au lecteur concernant l'optimisation des protocoles d'angiographie TDM (notamment l'étendue de l'examen, la dose d'irradiation et la dose de contraste intraveineux), les mesures de sécurité incluant le départ depuis les seins et la protection des gonades, des scénarios

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propres à certaines populations (grossesse et post-partum précoce) et la prise en compte d'autres techniques de diagnostic lorsque cela est jugé cliniquement approprié.

Keywords
acute pulmonary embolism, computed tomography, radiation dose reduction, intravenous contrast, pregnancy

Introduction

Acute pulmonary embolism (PE) is an important cause of cardiovascular morbidity and mortality in Canada.[1-4] It is a difficult clinical diagnosis to make and thus leads to thousands of computed tomography pulmonary angiogram (CTPA) studies being performed every year in patients in emergency departments and on inpatient wards.[5,6] CTPA plays a vital role in the diagnosis of acute PE while also helping to guide management due to its ability to identify imaging features that confer worse outcomes such as right heart enlargement and strain and central distribution of pulmonary emboli.[3,7-14] Additional benefits of accessibility, accuracy, identification of alternate diagnoses and rapid reporting turn-around time have helped establish CTPA as the current standard of care imaging for acute PE. Multiple societies and organizations including the Canadian Society of Thoracic Radiology endorse and highly recommend the need for imaging to rule out acute PE be based on pre-test likelihood using clinical prediction scores such as the Wells,[15] modified Geneva score,[16] and the Pulmonary Embolism Rule-out Criteria (PERC) (Figure 1).[17-22] The PERC score should be limited to the outpatient setting as it is only validated for use in the emergency department in low pre-test likelihood populations to safely exclude acute PE without the need for D-dimer testing or imaging[16,23] The use of age-adjusted D-dimer levels is now recommended in major society guidelines for patients with a non-high clinical probability of PE.[18,19]

In an effort to reduce unnecessary CTPAs through the emergency departments, recent research from a Canadian group evaluated the safety of increasing the age-adjusted D-dimer thresholds (to 1000 ng/ml) that would trigger imaging in low pre-test likelihood populations.[7] They demonstrated nearly 20% reduction in the number of CTPAs performed for low pre-test likelihood patients using this diagnostic algorithm, and recorded no adverse events or outcomes at 90-day follow-up. This requires further validation across multiple centers and thus has not yet been implemented in Canadian emergency departments. If CTPA is contraindicated, ventilation/perfusion (V/Q) scanning or magnetic resonance angiography (MRA) may be considered alternatives.

The goal of this document is to provide current and practical recommendations to help radiologists and radiology departments achieve high quality CTPA studies at the lowest radiation dose and to avoid some of the pitfalls that impair image quality and limit diagnostic certainty during interpretation. Part 1 of this document covers the essentials of optimal CTPA acquisition techniques including radiation dose reduction strategies and intravenous contrast considerations. We have incorporated recommendations in response to recent shifts in practice such as the move away from using breast and gonadal shields. Part 1 also briefly discusses population-based guidance relating to pregnant and early post-partum patients who are suspected of having acute PE. In an era of constant technologic advancement, the requirements to achieve diagnostic CTPA studies while avoiding technical and imaging interpretation pitfalls have also evolved. Part 2 describes the common technical and image interpretation pitfalls that range from contrast timing and bolus interruption issues, motion and beam hardening artifact, interpretation pitfalls secondary to a post-surgical state or acute PE mimics such as chronic PE, neoplasms, tumor emboli and vasculitis. Part 2 also highlights emerging technologies such as dual energy CT and its potential future role in the imaging of acute PE. In the supplement, we provide a CTPA reporting template to draw attention to the key elements that should be included in the radiology report. Accurate description of the location of single or multiple filling defects within the pulmonary artery tree (segmental versus subsegmental etc.) is emphasized due to the potential impact on management.

This guidance document is very timely and extremely relevant. Achieving high-quality CTPA studies and issuing complete and accurate reports has never been more crucial as we are deeply entrenched in a devastating global COVID-19 pandemic where acute PE due to an associated pro-thrombotic state is a well-known complication.[24-26]

Where relevant, we quote data to support evidence-based practice and promote a culture of continuous quality improvement by highlighting areas of current controversy where further research is warranted. We recognize that this guidance document will require future modification as new evidence emerges and best practice guidelines evolve over time.

CT Pulmonary Angiogram Acquisition Protocols

CTPA aims to achieve optimal contrast opacification of the pulmonary arteries while minimizing patient radiation exposure and contrast volume. Optimal timing of imaging post contrast injection is critical for maximizing image quality and accurate study interpretation.

Parameters of Imaging Acquisition

- Multidetector CT (MDCT) with 16- detector rows or greater. 64-detector MDCT or greater is preferable.
- Selection of scan parameters optimized for individual CT scanners and patient body habitus
- Use of the smallest detector width
- Thin sections (1.25 mm or less)

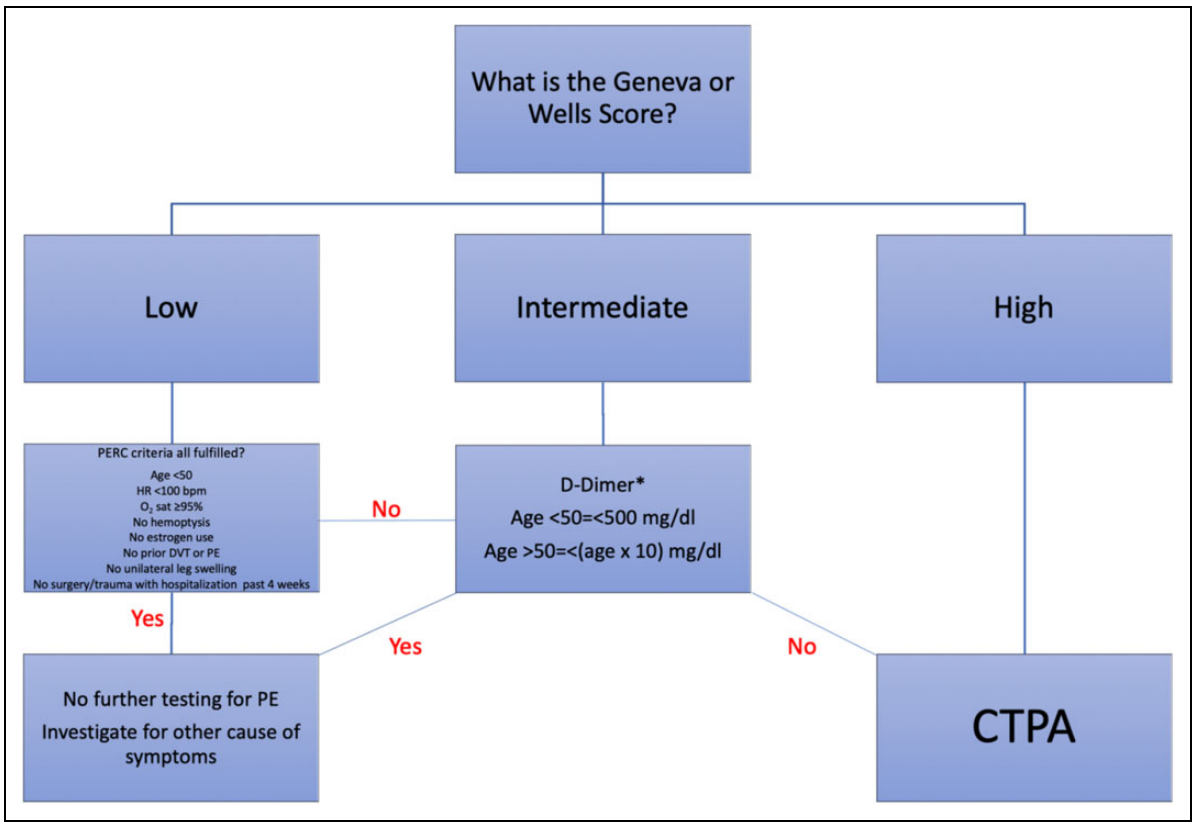

Figure 1. Algorithm for determining when to perform CTPA in patients with suspected acute pulmonary embolism. Criteria have been supported by the ASH, ESC/ERS, ACR, CADTH, and Thrombosis Canada. *High sensitivity D-dimer (ELISA or ELISA-derived).

- Field of view: from lung apex to the diaphragm including the entire lungs (widest rib-to-rib distance)
- Single inspiratory breath-suspension for the duration of image acquisition
- Cranio-caudal direction of scan acquisition is preferable.

Contrast Injection Protocol

- Intravenous (IV) access in antecubital fossa or forearm vein with appropriately sized catheter (18-20 gauge or larger in adults). A right arm injection is preferable. Central venous catheters can be used if approved for power injection
- Use of power injection device to program volume and flow rate of contrast injection
- Rapid bolus injection of sterile saline is advised prior to CTPA to ensure adequacy of IV access for power injector
- Parameters including volume of contrast, injection rate and scan delay will depend on the scanner system used and patient's characteristics including body habitus. Scanners with wider detectors or the use of high-pitch technique typically require less contrast and higher injection rates.
- Non-ionic contrast media (at least 350 mg/mL concentration)
- 50 to 80 mL of IV contrast 3 at a rate of 4.5 to 6 ml/s, followed by saline flush (30 ml) at the same rate to allow washout of contrast from the superior vena cava (SVC) thus minimizing streak artifact.

Contrast timing can be determined using bolus tracking with region of interest (ROI) in the main pulmonary artery, or bolus tracking:

- Bolus tracking technique involves a region of interest (ROI) placed in the main pulmonary artery on an axial image that is scanned repeatedly after contrast injection to monitor when the threshold is reached (100-150 HU), which in turn determines the start of the scan. CTPA scan is initiated automatically or manually, typically with a short time delay (4-8 s) to ensure imaging at peak contrast opacification. Bolus tracking has the advantage of using overall lower iodine dose as it does not include the test bolus. It is less technologist-dependent, more reproducible within and across centers and faster to perform.
- Test bolus (or timing bolus) involves IV injection of small bolus of contrast material (10-15 mL) at the desired rate, followed by acquisition of sequential stationary CT images at the level of the main pulmonary artery. A time-attenuation curve is generated and the peak of the curve is used to determine the scanning time (delay). An additional delay of 4 to 6 seconds is added to

the peak time to allow time for scanner to move to the start position and to account for the larger amount of contrast material used in the actual study.

Assessment of Image Quality

- Optimal opacification requires a minimum of 250-300 Hounsfield units (HU) pulmonary artery enhancement measured with ROI in the main pulmonary artery.
- Review of CTPA with axial views reconstructed with mediastinal window settings (window width 400HU, window level 40HU) and/or with PE-specific window settings (600HU/100HU).
- Sagittal and coronal reformats (1.25-3 mm) and coronal maximum intensity projection (MIP) images (7-8 mm)
- Additional reconstructions along the longitudinal axis of the pulmonary artery may be used in difficult cases.

Safety Considerations

Radiation Safety

Technological advances have alleviated some of the concern regarding the use of ionizing radiation and the theoretical risk of cancer. Moreover, there is a significant benefit-to-risk ratio of CTPA when accounting for the mean lifetime attributable risk of cancer mortality.[27]

Radiation dose reduction is particularly important for pregnant patients to minimize radiation exposure to both mother and fetus. Radiation exposure to the fetus from CTPA is low (<1 mGy) and fetal radiation exposure is lower with CTPA than ventilation/perfusion (V/Q), especially in the first trimester.[28] However, CTPA delivers a larger effective dose to the breast tissue than V/Q scan (10-70 mGy for CT *vs.* <1.5 mGy for V/Q).[28] Customization of scan length via limitation of the craniocaudal extent along the Z-axis, for example stopping the scan at the right hemidiaphragm, has received recent interest to limit fetal exposure.[29] Emboli within small pulmonary arterial branches have a limited impact on mortality and morbidity and therefore could be omitted from the scan in order to reduce fetal radiation exposure with little clinical impact.

The use of bismuth breast shields in no longer recommended in any clinical scenario.[30] The use of abdominal lead shielding for pregnant patients is still practiced at some institutions. This practice has been recently challenged.[31] Studies have shown that most radiation to the fetus during CTPA occurs from internal scatter.[32] Although abdominal lead shielding might reduce external fetal scatter,[33] it may in fact increase internal scatter radiation to the fetus. In addition, improper positioning of the lead shield may result in artifacts and obscuration of anatomy. Use of automatic exposure control in the presence of gonadal shields has been shown to increase absorbed radiation dose to the stomach and colon and unshielded ovaries in female pediatric patients.[34] Nonetheless, abdominal shielding may alleviate the pregnant patient's anxiety regarding radiation exposure to the fetus[35] and the habit of shielding may prove difficult for some departments to abandon.[36,37] It is thus important to address patient concerns prior to the examination and offer evidence-based practice. The use of in-plane bismuth shielding is also not favored due to resultant mild to moderate artifacts. Instead, the more modern approach of global tube current and voltage adjustment should be adopted.

Contrast Medium Safety

Contemporary protocols involve a lower volume of contrast material due to the use of contrast agents with higher iodine concentration and faster scan times. Iodinated contrast agents are avoided in patients with extremely low glomerular filtration rate (e-GFR <30) per current guidelines.[38,39] Recent studies have demonstrated that the risk is probably overestimated in many clinical scenarios.[38,40,41] In the setting of severe nephropathy, careful assessment of risk and benefit is critical.

Anaphylactoid reactions, related to intravenous iodinated contrast for modern low-osmolar and iso-osmolar contrast materials are extremely infrequent, ranging from 0.2% to 0.7% with fatal reactions occurring in 1 out of 170,000 injections.[42] Additionally, most departments have pre-procedural regimens to lessen the severity of such reactions with steroid therapy prior to the scan. Such protective measures may not be possible in the acute setting. If a definitive history of significant life-threatening contrast allergy is established, an alternative imaging modality should be considered.

Dose Reduction Strategies

Radiation dose reduction has been a focus of radiology research for many years. There has been considerable progress in radiation dose reduction through technological advances in hardware as well as postprocessing. Even better, this has been achieved without sacrificing diagnostic accuracy or image quality.[43,44] Modern strategies for dose reduction include limiting peak tube voltage, use of modern post-processing techniques, high-pitch scanning, tube current modulation, scan range customization for pregnant patients[45,46] and reducing contrast material injection.

Lowering Peak Tube Voltage

Peak tube voltage (kVp) is readily adjustable with increments ranging from 80 to 140 kVp. Radiation dose is proportional to the kVp (CTDIvol) when all other parameters are kept constant. Hence, lowering the peak tube voltage translates into an effective dose reduction strategy.[47-51] For instance, lowering peak kilovoltage from 120 to 100 kVp for a CT examination of the thorax can result in greater than 30% reduction in radiation dose.[52] Although lowering kVp results in less photon transmission and hence higher image noise, due to the maintenance of contrast to noise ratio, image quality is often preserved.[51,53] However, significant tube voltage reduction in larger patients should be avoided to circumvent excessive image noise.[54,55] Some vendors offer automated tube voltage selection systems

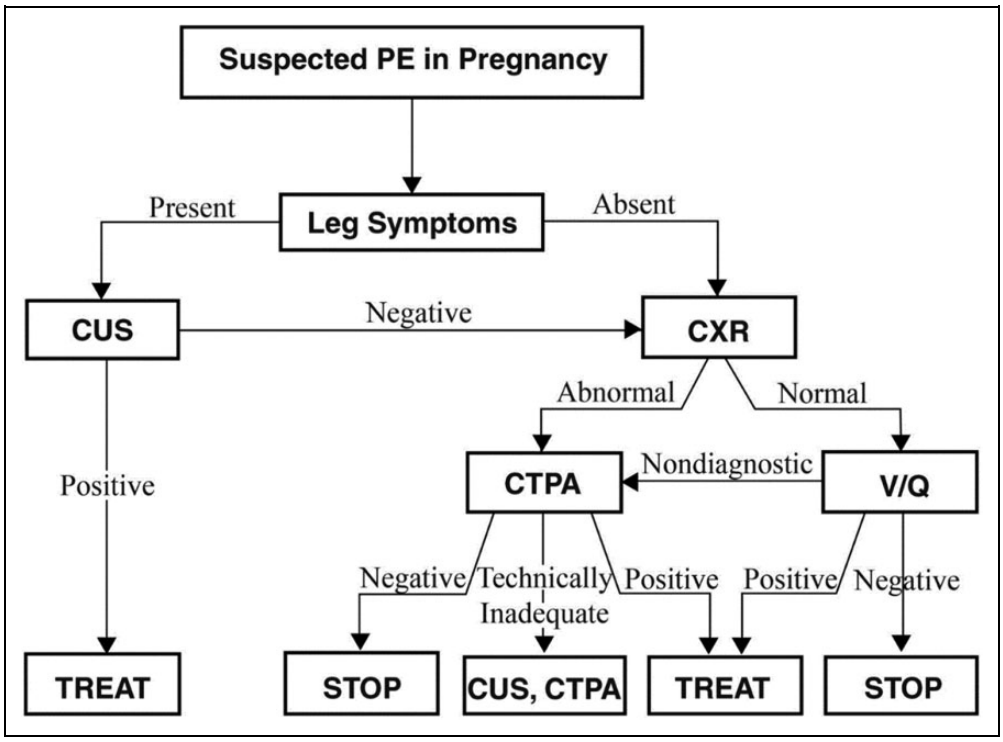

Figure 2. Diagnostic algorithm for suspected PE in pregnancy. From Leung A et al. Radiology 2012; 262:635-646 with permission.

which assist in achieving an equilibrium between radiation dose and image quality.[56-58] Lowering the kVp also results in higher attenuation of intravascular contrast material as the beam energy reaches the k-edge of iodine (33 keV). Effectively, this allows for lesser volume of intravenous contrast material required.[33,59] This is of particular benefit to patients with renal deficiency.

Postprocessing Algorithms

Iterative reconstruction (IR) in statistical, model or hybrid forms are now widely accessible. Modulation of tube current and voltage were previously avoided in clinical practice to circumvent excessive image noise. This has been mitigated by employing modern IR algorithms. Today's low-dose CTPA protocols, when combined with IR are comparable to conventional standard dose CTPA in terms of image quality.[60] One study showed that a high-pitch 80-kV CTPA combined with IR offered similarly diagnostic images as a standard-pitch 100-kVp pulmonary CTA with filtered back projection at half the dose.[57]

High-pitch Scanning

High-pitch scanning offers multiple benefits including reduction in radiation dose, higher temporal resolution and the ability to reduce the volume of intravenous contrast material. This is of particular importance when scanning subjects with renal insufficiency and for subjects who are unable to tolerate breath-holding. A welcomed by-product of higher temporal resolution is less motion artifact and hence the potential for simultaneous assessment of cardiovascular structures.[54,57] Since image noise increases with higher-pitch acquisitions, the use of IR is of paramount importance to maintain image quality.[54,57,61,62] Sub-second low-tube-voltage pulmonary CTA examinations are now possible with as little as 20-40 mL of intravenous with an effective delivered dose of less than 1 mSv in select patients.[57,63,64] With on-going technological advances, extending such modified techniques to all patients irrespective of body size may eventually become a reality.[65]

Low Tube Current (mA)

The ability to lower the tube current without compromising image quality is achievable using IR reconstruction techniques. Newer-generation dual source CT scanners are increasingly able to yield higher quality images in large patients at low tube potential. This is achieved by channeling lower individual tube mA and allocating the dose between 2 tubes operating at the same kVp.[29] These "large body habitus" mode protocols are becoming popular and offer dose reduction even in larger patients.

Investigation of Acute Pulmonary Embolism in Pregnancy

Acute pulmonary embolism is often suspected in pregnant women due to overlap in acute PE symptoms (shortness of breath, tachycardia etc.) with the normal physiologic changes of pregnancy. However, acute PE is uncommon in pregnant

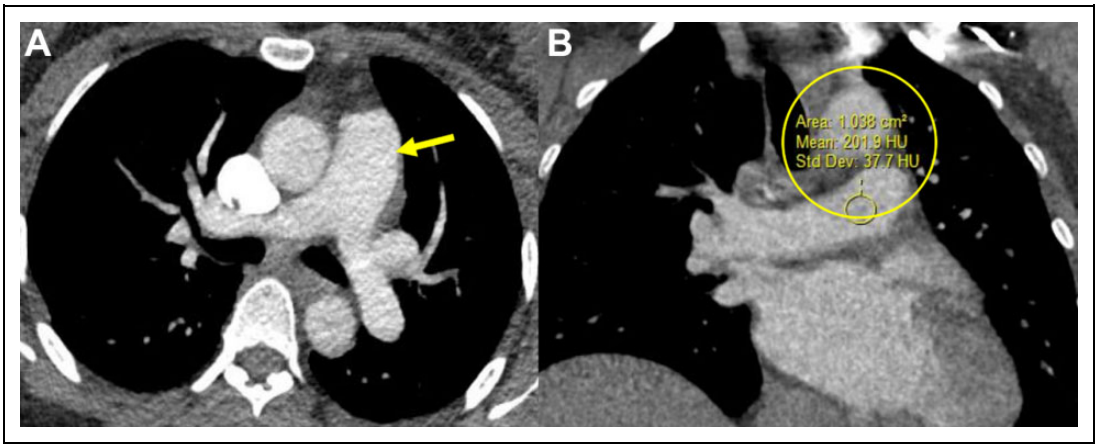

Figure 3. CTPA in a 40-year-old woman 3-days post-partum. A, Axial image, mediastinal window, shows suboptimal contrast opacification of the pulmonary arterial tree (arrow). B, Coronal reformat with density measurement in the main pulmonary artery (circle) is approximately 200 HU, below the target of 300 HU. Nevertheless, the study was diagnostic and there were no filling defects to suggest acute PE.

women, occurring in only 3-9% of those suspected of having acute PE.[66-68] Despite this low prevalence, mortality from acute PE is considered a significant cause of maternal death during pregnancy. Therefore, ruling out acute PE in pregnant women poses a diagnostic challenge for both acute care physicians and radiologists.

Clinical scoring systems such as the Wells score[69] or the Geneva score[16,70] have not been validated in pregnant women.[70] Leg swelling is a common pregnancy related complaint but also one that may suggest deep venous thrombosis (DVT). One study showed only 10% of women had DVT in the presence of concerning clinical features.[67] Despite this, the most widely used guideline for investigation of acute PE in pregnancy includes compression ultrasound early in the diagnostic algorithm to avoid ionizing radiation in the event of a positive ultrasound result (Figure 2). However, it is recognized that the diagnostic yield of compression ultrasound is low in the absence of leg symptoms. This is reflected in the alternate pathway involving chest radiographs as the first imaging test when there are no leg symptoms to suggest DVT. In the setting of a normal chest radiograph, V/Q scanning is suggested as the next imaging modality and usually only the perfusion component is completed, often at reduced dose. In the case of non-diagnostic V/Q or an abnormal chest radiograph (which increases the rate of indeterminate result on V/Q scan), CTPA is the recommended imaging modality.

Several studies have reported comparable accuracy of CTPA and low dose perfusion scanning for detection of acute PE in pregnant women but the mean maternal and fetal radiation doses have been reported to be lower with low dose perfusion scanning (no ventilation component).[68,71] Small perfusion defects should be interpreted with caution in pregnant patients with a known history of asthma. In these instances, the ventilation component should be completed or further evaluation with CTPA if it remains unclear whether small perfusion defects are due to acute PE or matched defects due to asthma.

Following a non-diagnostic CTPA, in addition to performing leg ultrasound or repeat CTPA with correction of technical factors, a V/Q scan could also be considered to rule out PE.

However, in practice, V/Q scanning may not be performed as per the suggested guidelines due to lack of availability outside regular working hours but this will vary across institutions. In these instances, CTPA is often performed in the acute care setting irrespective of chest radiographic results.

With regard to CTPA technique, the volume and injection rate of iodinated contrast should be increased to achieve optimal opacification of the pulmonary arteries due to the expanded blood volume that results during pregnancy. Increasing the iodinated contrast volume may be considered for women in the early post-partum period as well (i.e., within the first week) because the physiologic changes of pregnancy have yet to normalize (Figure 3).

Due to lack of consensus on D-dimer thresholds for normal versus abnormal levels in pregnant women, high prevalence of elevated D-dimer in pregnancy[72] and case reports of false negative results,[73] the D-dimer is generally omitted from the diagnostic algorithm. Another suggested algorithm includes the use of D-dimer followed by compression ultrasound in those with positive D-dimer level or high clinical suspicion based on a modified Geneva score.[74] This particular diagnostic algorithm is not widely adopted at most institutions.

Lactating/Breastfeeding Post-partum Women

Lactating breasts are more radiation sensitive due to increased mitotic rate.[75-77] The amount of iodinated contrast excreted into breast milk is extremely small. Therefore, women who are breastfeeding should continue to do so even if they have received iodinated contrast agents for CT scans according to current guidelines.[78]

Alternatives to CTPA

CTPA has been firmly established as the first-line imaging study for the work-up of acute pulmonary embolism. However, alternate imaging may be considered in the setting of severe allergy to CT intravenous contrast agents, significant renal impairment, patient refusal to radiation exposure, lack of or poor IV access and CT equipment failure. It is therefore important to be aware of the strengths and weaknesses of the alternative modalities.

Ventilation/Perfusion Scan

V/Q scan is the best alternative diagnostic tool for investigating acute pulmonary embolism. However, V/Q scanning is not universally accessible across Canada. V/Q is also preferred by some as the initial imaging test for young female patients due to lower radiation dose to the breasts and for pregnant women.[79] Moreover, a perfusion scan only approach (no ventilation component) could be considered in patients with a normal chest X-ray in an aim to further reduce radiation dose.

The efficacy of the V/Q scan has been validated through randomized prospective trials showing that it is safe to withhold anticoagulant therapy in patients with a normal perfusion scan.[80] A major limitation of V/Q scanning is the relatively high frequency of inconclusive results leading to additional diagnostic testing. A study showed VQ scintigraphy was diagnostic in only 30-50% of emergency patients with suspected PE.[15] Also, a high-probability V/Q scan is not sufficient to confirm PE in patients with a low pre-test probability.[15] This highlights the importance of adhering to assessment of pre-test probability. Nonetheless, patients with a non-diagnostic V/Q scan and low clinical probability of PE have a low prevalence of confirmed PE,[81] and the negative predictive value of this combination is further enhanced by the absence of a DVT on a lower-limb compression ultrasound (CUS). The Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis (PISAPED) showed a low rate of inconclusive tests by this combination albeit the ability to exclude PE was shown to be inferior to CTPA.[82]

Multiple studies have proposed single-photon emission CT (SPECT) imaging, with or without low-dose CT, to lower the rate of inconclusive tests.[83-85] Unfortunately, most of these studies were limited by their retrospective design. Only one study used a validated diagnostic algorithm.[86] There is scant literature on outcome studies and optimization of scanning protocols. The time it takes to perform SPECT imaging ranges between 15-30 minutes, and this may also be unacceptable in the emergency setting. In summary, large-scale prospective studies are still required to validate SPECT techniques.

Magnetic Resonance Angiography

Due to its lack of ionizing radiation, magnetic resonance angiography (MRA) has received much attention in the last 2 decades through technique and protocol optimization. Unfortunately, it remains in the investigative stages as large-scale studies[87,88] have shown low sensitivity and an unacceptable rate of inconclusive results. MRA has a reasonable ability to exclude proximal emboli but detection is limited at the segmental and subsegmental level. Investigations on whether MRA in conjunction with other tests such as compression ultrasound can safely exclude clinically relevant PE are on-going. One such multi-center outcome study is the US National Clinical Trial number 02059551.

Accessibility to MRA remains an obstacle at some institutions, particularly in the acute setting. MRA using gadolinium-based contrast agents for ruling out PE during pregnancy is also not recommended due to the reported association of rheumatologic, inflammatory and infiltrative skin conditions that occur after delivery and increased risk of stillbirth and neonatal death.[89]

Compression Ultrasound

Ultrasound has a sensitivity >90% and a specificity of ~95% for detecting thrombus in symptomatic legs.[90,91] A meta-analysis advocated for ultrasound as a diagnostic strategy for patients with CT contraindications and symptomatic legs.[92] Since the probability of a positive proximal ultrasound in suspected PE is higher in patients with signs and symptoms related to the leg veins than in asymptomatic patients,[90,91] resorting to this modality is advocated in patients who have leg symptoms. A positive ultrasound test in a patient suspected of having PE is considered sufficient for initiation of anticoagulant treatment without further testing.[92] Such patients should still undergo risk assessment for PE severity.

Conclusion

The objective of this guidance document is to provide current and practical recommendations on how to achieve high quality diagnostic CTPA studies while avoiding the most common technical and interpretation pitfalls. It is intended to remain relevant to radiologists and radiology departments nationwide and across a wide spectrum of health care practice settings. As new data emerges from ongoing and future research studies, we will revise the document accordingly.

Key Points

1. CTPA should not be performed unless pre-test clinical prediction rules have been applied and a D-dimer has been performed in the low or intermediate risk patients.
2. Achieving high quality diagnostic CTPA studies at the lowest possible radiation dose requires careful optimization of technical parameters including the intravenous contrast bolus.
3. Breast and gonadal shields are not recommended.

Abbreviations

CTPA	Computed Tomography Pulmonary Angiogram
DVT	Deep vein thrombosis
HU	Hounsfield units
IR	Iterative reconstruction
MDCT	Multi-detector CT
MIP	Maximum intensity projection
MRA	Magnetic Resonance Angiography
PE	Pulmonary embolism
PERC	Pulmonary Embolism Rule-out Criteria
ROI	Region of interest
SVC	Superior vena cava
V/Q	Ventilation/perfusion scanning

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