Title:

Investigation and diagnostic imaging of suspected pulmonary embolism during pregnancy and the puerperium: A review of the literature

Running Title:

Diagnostic imaging of PE during pregnancy

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Abstract

Pulmonary embolism (PE) is a leading cause of maternal mortality with women at increased risk of PE during pregnancy and the early postpartum period. Clinical assessment of suspected PE during pregnancy is challenging as signs and symptoms associated with PE overlap with physiological changes of pregnancy. Clinical tests and rules commonly used to assess pre-test probability of PE were historically not well validated in the pregnant population.

The challenges of clinical assessment in the pregnant and postpartum population result in a lowered threshold for diagnostic imaging. Computed-tomographic pulmonary angiography (CTPA) and nuclear medicine lung scintigraphy or ventilation/perfusion (V/Q) scans are the main types of diagnostic imaging for suspected PE. Both methods are associated with small levels of ionising radiation exposure to mother and fetus. Accuracy of the diagnostic imaging tests are paramount. Haemodynamic changes of pregnancy, including increased heart rate, increased blood volume, and altered flow velocity in the pulmonary arteries, may influence the quality of imaging.

This comprehensive review examines the literature and evidence for the investigation and diagnostic imaging of suspected pulmonary embolism during pregnancy with CTPA and V/Q. Clinical decision-making tools, biomarkers, and diagnostic imaging during pregnancy and postpartum will be considered with a focus on diagnostic accuracy and yield, radiation dose exposure (maternal-fetal), and protocol modifications. Current practice guideline

recommendations and recent literature on diagnostic pathways are also presented.

Keywords: computed-tomographic pulmonary angiography, lung scintigraphy, pregnancy, pulmonary embolism, radiation.

Introduction

Pulmonary embolism (PE) is a leading cause of maternal mortality in the developed world, with women being at increased risk during both pregnancy and the early postpartum period.[1] Physiological changes associated with pregnancy and the puerperium, including venous stasis, vascular damage, pelvic compression, and hypercoagulability, contribute to an increased risk of venous thromboembolism (VTE).[1] In the United States, PE accounts for 9-20% of maternal deaths.[2, 3] In Australia where the incidence of maternal mortality is relatively low at 6.8 deaths per 100,000 women giving birth, pulmonary thromboembolism is the most frequent cause of direct maternal deaths.[4] Timely and accurate diagnosis of PE during pregnancy and the postpartum period is required for adequate therapeutic management to reduce associated maternal mortality.

Clinical assessment of suspected PE during pregnancy is challenging. Signs and symptoms classically associated with PE, such as shortness of breath, tachycardia and leg swelling, can also occur with physiological changes of healthy pregnancy.[1] Furthermore, clinical tests and rules commonly used to assess pre-test probability of PE are not well validated in the pregnant population.[5, 6] Together, these factors lower the threshold for diagnostic imaging in pregnant and postpartum women.

Diagnostic imaging for investigation of suspected PE includes computed tomographic pulmonary angiography (CTPA) and nuclear medicine lung scintigraphy or ventilation/perfusion (V/Q) scans. Both modalities are associated with radiation exposure.[1, 7] Accuracy of the diagnostic tests is paramount as a missed PE due to a false-negative result may be fatal. Conversely, false-positive results leading to an incorrect diagnosis of PE in pregnant women results in unnecessary anticoagulant therapy, may alter delivery plans, and impacts future contraceptive options.[1] The need for a correct diagnosis outweighs the radiation risks associated with diagnostic investigations.[7]

In this review, we present the current evidence for the investigation and diagnostic imaging of suspected pulmonary embolism during pregnancy, including clinical decision-making tools, biomarkers, current practice guidelines, diagnostic yield of imaging techniques, and both maternal and fetal radiation dose exposure.

Methods

During March 2019, PubMed and Medline OVID were searched for relevant articles. MeSH terms included “pregnancy” and “pulmonary embolism” and “radiation” or “electromagnetic radiation”. Studies published in English were included. The searches identified 232 publications for consideration and review. Reference lists of selected articles were reviewed for additional relevant literature. After studies were excluded (duplicates, languages other than English, case reports, correspondence, letters, and editorials), abstracts of the remaining 105 publications were considered for inclusion (Figure 1). Literature published within the last decade was focused on to take into account current practice and technologies, however widely referenced, high quality older publications also considered.

Discussion

Clinical decision-making tools in pregnant patients with suspected PE

Clinical assessment of suspected pulmonary embolism during pregnancy is challenging. Clinical decision-making tools developed to determine the pre-test probability of PE often excluded[6] or limited number of pregnant patients in the original datasets.[5]

The application of these tools for suspected PE during pregnancy have produced variable results. Two small retrospective studies suggested a role for a modified Wells score (MWS) in identifying women at low risk of PE.[8, 9] This finding, however, has not been consistently supported in retrospective research.[10]

More recently, the prospective DiPEP study investigated the use of clinical features, decision-making rules and biomarkers in selecting pregnant or postpartum women with suspected PE for imaging. In contrast to previous results, authors of this extensive study concluded neither the Wells score or revised Geneva score to be valid or reliable tools in assessing risk of PE during pregnancy or postpartum.[11]

D-dimer tests in pregnant patients with suspected PE

In the non-pregnant population, D-dimer is a simple, inexpensive, well-validated biomarker that can aid in the exclusion of PE. Current guidelines lack consensus on the role of D-dimer during pregnancy.[12] Levels of D-dimer increase during normal pregnancy and peak around delivery, making interpretation challenging during this period.[13] Despite attempts to define alternative D-dimer thresholds in pregnant patients to reflect the physiological increase, a recent review concluded the evidence for recommending a certain threshold remains poor.[14]

D-dimer levels were also investigated in the DiPEP study. Sensitivity and specificity of D-dimer was 88.4% and 8.8% using a hospital laboratory threshold, and 69.8% and 32.8% using predefined gestation-specific thresholds, respectively.[11, 15] These results suggest no role for the use of D-dimer alone in selecting pregnant or postpartum women with suspected PE for imaging.

The challenge of clinical assessment in this population results in most women with suspected PE during the pregnant and postpartum period requiring diagnostic imaging. A lower diagnostic rate demonstrates this reduced threshold to imaging; prevalence of positive PE diagnosis after imaging in pregnant populations is reportedly 5% or less compared with a rate of 15-20% in non-pregnant women.[16]

Diagnostic management pathways

The recent publications of the CT-PE Study and Artemis Study have provided new diagnostic algorithms to guide imaging and management of suspected PE during pregnancy, demonstrating reductions in the number of women requiring imaging.[16, 17]

The CT-PE-Pregnancy Group reported the safety of a diagnostic algorithm based on an assessment of pre-test clinical probability using the revised Geneva score, a highly sensitive D-dimer test, bilateral compression ultrasonography (CUS), CTPA, and a V/Q scan if results of CTPA were inconclusive. With 395 women included in the study, the 3-month thromboembolic rate was 0.0%. PE was ruled out in 11.6% based on the combination of low-intermediate probability and a negative D-dimer result. Furthermore, PE was diagnosed in 1.8% patients through use of CUS with identified proximal deep vein thrombosis (DVT), thus avoiding need for CTPA in both groups.[17]

The Artemis Study assessed a pregnancy-adapted YEARS diagnostic algorithm using three criteria (clinical signs of DVT, haemoptysis, and PE as most likely diagnosis) combined with a high-sensitivity D-dimer level. The D-dimer level and presence or absence of YEARS criteria guided clinicians in ruling out PE, performing CTPA for diagnosis, or initiating anticoagulant. In difference to the previous study, CUS was only performed if clinical signs of DVT were present (19% of cohort). The 3-month incidence of VTE was low (0.21%) with one diagnosis of proximal DVT and no diagnoses of PE. Based on the algorithm, CTPA was not indicated in 39% of women, thus avoiding associated radiation exposure. The algorithm was most efficient in the first trimester with CTPA not indicated in 65% of subjects compared to 32% in the third trimester.[16]

Both prospective studies experienced protocol violations, 9.6% (38/395) and 7% (36/494) for the CT-PE Pregnancy Group and Artemis study, respectively, highlighting challenges in developing and adhering to protocols and diagnostic workup in the pregnant population.[16, 17] This is consistent with reports of pregnancy being the greatest factor for inappropriate diagnostic management of suspected PE.[18]

In using different algorithms, both studies demonstrated the potential to safely avoid diagnostic imaging in a select group of pregnant women with suspected PE. With CUS having a low diagnostic yield, its use only in women who have clinical signs of DVT is a warranted approach with benefits to resource allocation.

Diagnostic Imaging with CTPA and VQ

The main imaging modalities for diagnosis of suspected PE are CTPA and V/Q scans. In the general population, CTPA is the imaging test most commonly used for investigation of PE, being widely available and with the potential to provide alternate diagnoses (Figure 2).[19] In non-pregnant populations, CTPA is associated with a high negative predictive value (NPV) and low rates of inconclusive or non-diagnostic CTPA results.[20] However, there is concern that CTPA during pregnancy is associated with increased rates of non-diagnostic studies. Normal haemodynamic changes of pregnancy such as increased heart rate and blood volume, as well as altered flow velocity may dilute contrast medium in the pulmonary arteries causing poor vascular opacification and suboptimal imaging for PE detection (Figure 3).[21, 22] Furthermore, difficulties with breath-holding may contribute to motion artifact and decrease diagnostic accuracy of CT imaging.[23] Conversely, V/Q scans are associated with higher non-diagnostic rates in the general population but are found to have improved diagnostic accuracy in the pregnant population.[24] As a cohort, pregnancy women are younger and healthier than the general population, with reduced baseline lung disease that contributes to abnormal ventilation scans.[25]

During pregnancy, international guidelines generally recommend use of V/Q scans in women with normal chest x-rays, with CTPA as an alternative or second line option (Table 1&2).[3, 7, 26-30] These recommendations are primarily based on historically reported increased maternal breast radiation dose and higher indeterminate rates associated with CTPA than scintigraphy in pregnant populations.[12] A lack of prospective studies in the area limit the strength of guidelines with recommendations based largely on expert opinion and retrospective studies.[19] Furthermore, advances in CT technology and CTPA protocol modifications aimed at decreasing radiation dose and non-diagnostic rates may not be adequately reflected in current guideline recommendations.[31]

Diagnostic Accuracy and Yield

Two recently published systematic reviews aimed to collate published data about diagnostic imaging for PE during pregnancy. A Cochrane Review assessed diagnostic accuracy and non-diagnostic rates of CTPA and lung scintigraphy, while Tromeur and colleagues reviewed radiation exposure in addition to diagnostic outcomes.[19, 32] Meta-analyses were not performed due to heterogeneity and low methodological quality of included studies. The reviews reported similar accuracy of CTPA and V/Q during pregnancy but differing rates of non-diagnostic results (Table 3). The two reviews concluded both CTPA and lung scintigraphy are appropriate for exclusion of PE during pregnancy, with limitations in the results and quality of studies noted.[19, 32]

The conflicting non-diagnostic rates may be due to several factors. Large differences in the number of studies included may have contributed to the discrepancy in reported rates. Gestation age may also impact on the quality of CTPA image with increased rates of suboptimal studies having been observed in later pregnancy compared to earlier pregnancy.[33] Different definitions of nondiagnosis within the studies may have also contributed. In Tromeur and colleague's review, a non-conclusive CTPA result was defined as suboptimal contrast opacification and respiratory motion artifact that did not allow for inclusion or exclusion of PE. Non-diagnostic results of V/Q scanning were consistent with PIOPED criteria as low or intermediate probability scan results.[32] The Cochrane review did not provide its definition of non-diagnostic tests, however, a number of the included studies only used intermediate probability as non-diagnostic and low probability as normal scans which may reflect the differences reported.[19, 32]

Low-dose perfusion only scanning (LDQ) has lower maternal radiation exposure than CTPA and is effective in excluding PE in pregnant patients. Sheen and colleagues reported findings of a retrospective cohort study of 322 pregnant women who underwent imaging for PE with LDQ or CTPA in the largest series of perfusion-only imaging to date.[34] The study was published after the release of the Cochrane review. The NPV was 100% and 97.5% for LDQ and CTPA, respectively. The non-diagnostic rates of CTPA (9.3%) and LDQ (9.3%) were higher than those recognised in the Cochrane review. Authors suggested the higher rates may have been due to a high prevalence of asthma within the study population. Limitations of the study include its retrospective design, potential for information bias and being insufficiently powered to detect small differences in negative rates between imaging methods.[34] It is recognised however, to achieve such level of would require very large study numbers and is unlikely to occur.

Maternal and Fetal Radiation Exposure

Both CTPA and V/Q diagnostic imaging raise concern of potential harm to the mother and fetus through exposure to ionising radiation and intravenous contrast enhancement material.[19, 32] Studies investigating radiation associated with CTPA and V/Q have produced variable results in radiation dose exposure (Table 4).[35-46]

While the fetal radiation dose exposure associated with both CTPA and V/Q is well below the reported 100milliGray (mGy) threshold for inducing deterministic effects such as fetal malformation[47], concern remains with a small increased risk of childhood cancer. During normal pregnancy, the natural background radiation to a fetus during pregnancy is approximately 1mGy.[48] The impact of additional low-level radiation is difficult to quantify but it is known that exposure to radiation in utero is associated with increased risk of malignancy.[49] A fetal radiation dose exposure of 10mGy is associated with a relative risk of 1.4 but the overall individual risk remains low due to underlying low incidence of childhood cancer; the absolute risk of cancer at ages 0-15 is reported at about one excess cancer death per 1,700.[47]

The major concern with CTPA and maternal radiation exposure is the potential to increase the lifetime risk of breast cancer. Breast tissue is recognised to be even more radiosensitive than previously thought, with the ICRP recently doubling its tissue weighting factor.[50] It is hypothesised that during pregnancy and lactation, the proliferating breast tissue may be even more sensitive to radiation.[7] Importantly, a recent study reported the risk of early-onset breast cancer to be similarly low after exposure to V/Q scanning or CTPA during pregnancy or postpartum, supporting the notion that both imaging modalities are a valid option.[51] Ongoing research into longer-term effects are required.

Maternal and fetal radiation dose exposure associated with CTPA and V/Q lung scintigraphy were reviewed by Tromeur and colleagues.[32] Of 22 studies included, 11 compared CTPA and/or V/Q lung scans in human clinical studies while the remaining studies assessed CTPA radiation exposure in phantom females. The fetal/uterus absorbed dose ranged from 0.2 to 0.7mGy with V/Q scanning and 0.002 to 0.51mGy CTPA. The reported mean maternal effective radiation dose for CTPA and V/Q ranged from 0.23-9.7milliSievert (mSv) and 0.9-5.85mSv, respectively.[32] However, the maternal effective dose range was skewed by a study that included radiation doses of both the monitoring and diagnostic components of CTPA.[43] Accordingly, the lowest maternal effective dose for CTPA reported in Tromeur's work did not reflect a diagnostic scan. The female phantom studies of CTPA demonstrated mean maternal effective dose range of 2.5mSv to 4.9mSv, with fetal/uterus absorbed dose ranging from 0.003mGy to 0.73mGy.[32]

Wide variations between studies in equipment, protocols, and methodologies for calculating radiation dose meant comparisons for the different imaging methods were not performed. Heterogeneity of CTPA data studies included wide variation in CT scanner type, protocol variation such as kilo-voltage, tube current, pitch, and contrast injection rates limited comparisons. Similarly, V/Q studies included both SPECT and planar imaging in addition to variation in dosing protocols limiting utility of pooled results. Furthermore, the studies generally did not elaborate on gestation age at exposure or predicted differences in radiation exposure across gestational ages.[32] The radiation doses reported are consistent with values previously published; with CTPA delivering lower fetal but higher maternal radiation doses compared to V/Q scans.[3, 7] Reassuringly, all maternal and fetal radiation exposure doses for both techniques were reported to be below safety threshold.[32] These differences highlight the need for understanding individual, institutional practice regarding imaging and radiation dose exposure for suspected PE during pregnancy.

Organ-specific radiation dose, particularly to breast, deserves further consideration. The largest study within both reviews involved a sample size of 991 patients imaged for suspected PE during pregnancy across 24 sites in the UK.[35] The study reported estimated typical organ-specific radiation dose to breast and fetus. For scintigraphy, breast and fetus radiation dose was calculated to be approximately 0.28 and 0.2mGy, respectively. CTPA radiation dose ranged from 2 to 14mGy and 0.002 to 0.02mGy for breast and fetus, respectively.[35] Wide variations in CTPA radiation dose were observed across study sites, further demonstrating the importance of understanding institutional practice.

Typically, CTPA imaging involves three components: a patient topogram, a contrast-monitoring scan, and a diagnostic scan. It has not been well described in the previous studies if the CTPA radiation doses reported are attributable to the entire CTPA imaging or only to the diagnostic component of CTPA. While contrast monitoring contributes little to total Dose Length Product (DLP), which is commonly used to estimate radiation dose, contrast monitoring techniques may account for 27% of overall breast dose in CTPAs of pregnant women.[43] Consideration of the individual components of CTPA and their influence on breast radiation dose may be warranted.

Protocol modifications and other techniques to reduce radiation

Reduction in radiation exposure may be achieved through protocol modification and other techniques including protective garments, dosing variation and reduced scan length. Low dose CTPA protocols incorporating reduced voltage and reduced scanning area of aortic arch to diaphragm dome can result in a lower maternal effective dose of 1mSv and a breast dose of 2mGy.[35] A large prospective study currently underway is evaluating low-dose CTPA for suspected PE in a pregnant population and may provide further insight into optimised protocols, safety, image quality and associated breast-radiation dose, however with an estimated study date completion in 2024, it will be some time before results are available.[31]

Non-lead (high-Z) based protective garments are variably used to shield organs outside of the primary field of radiation. A 2018 review of 11 studies evaluated the use of high Z patient shielding for fetal dose reduction in CT.[52] Uterus doses, used as a surrogate marker for fetal exposure during first trimester, ranged from 60 to 660μGy. The use of high-Z garments was associated with a relative dose reduction to the uterus of 20-56%. Authors of the same review then compared dose reduction outcomes associated with high-Z garments to radiation dose estimates of CT protocols with scan length reduction using recognised Monte-Carlo simulations. Uterus radiation dose exposure could be reduced by up to 24% for chest imaging with CT when scan length was decreased by 1-3cm.[52]

Hendriks and colleagues also recently evaluated the effect of scan length optimisation of CTPA during pregnancy reporting significant reductions in fetal radiation dose exposure as well as maternal effective dose reduction.[53] Two length reduction approaches were used, including a fixed 10% length reduction as well as individualised optimised scans, both of which demonstrated reduced radiation dose exposure. Importantly, after scan length optimisation, no previously diagnosed PE cases were missed. Previous reports have suggested breast radiation exposure from CTPA may be reduced by approximately 50% with the use of thin bismuth radio-protective shielding to breasts.[54] The adoption of a combination of these different methods may reduce radiation dose exposure of CTPA during pregnancy.

For lung scintigraphy, perfusion-only scanning is associated with reduced fetal radiation dose and minimised maternal breast radiation dose if ventilation tracers are not administered.[55] A two-step protocol for commencing with LDQ-scan only has been proposed for pregnant women.[32, 56] In the younger pregnant population where there is a low prevalence of co-morbid pulmonary disorders, PE can be excluded in many cases based on a normal perfusion pattern. In the case of abnormal perfusion images, ventilation scans should be performed.[32, 56] The European Association of Nuclear Medicine and Molecular Imaging (EANM) recommendations extend this protocol over two-days with perfusion-only scanning on day one with subsequent ventilation scan the next day only if indicated.[57]

The derived mean radiation adsorbed doses of LDQ from a recent study were estimated to be 0.16, 0.47, 0.02mGy to maternal breast, maternal whole body, and fetus, respectively.[34] These findings support reduced maternal and fetus radiation doses of LDQ. It should be noted, however, that radiation dose measurements were not a primary focus of this study. Interestingly, it has been argued that for a minimal reduction in fetal dose radiation the 2-day protocol leaves the potential for a delayed diagnosis of PE and the associated risk of delayed or inadequate treatment.[58]

Conclusion

With ongoing challenges in the use of conventional risk assessment tools and non-invasive assessment for suspected PE during pregnancy, the role of diagnostic imaging for suspected PE currently remains paramount. The recent publications of diagnostic algorithms to guide imaging and management of suspected PE during pregnancy may lead to reduced numbers of women requiring imaging, however the threshold to image will likely remain lower than the general population.

As PE is a leading cause of maternal mortality, timely diagnosis through imaging is essential. The literature supports diagnostic equivalence of CTPA and lung scintigraphy in diagnosing PE in pregnant women. Accordingly, maternal-fetal radiation exposure should be an important consideration in diagnostic tests. Guidelines support the use of V/Q scans in the pregnant population with normal chest x-rays with recognition of the maternal radiation dose associated with CTPA. These guidelines, however, are based on data that may have less relevance with advancements in technology and imaging protocols. Furthermore, these studies have not well described the investigation during the postpartum period. With few prospective studies investigating the role of diagnostic imaging of PE during pregnancy and in the absence of long term follow-up after maternal and fetal radiation exposure during pregnancy, retrospective studies can provide understanding into current practice.

The variability of radiation dose exposure amongst studies may reflect differences in imaging practices, protocols, equipment and radiation reduction methods used within institutions. These differences highlight the importance of understanding individual, institutional practice regarding imaging and radiation dose exposure for suspected PE during pregnancy. Understanding local practice of diagnostic imaging in the investigation of suspected PE during pregnancy and puerperium and the associated radiation exposure may allow for optimisation of clinical protocols and provide information to guide clinician-patient discussion about the investigations.

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Table 1 - Summary of recommendations on CTPA and V/Q from relevant guidelines of CTPA/VQ use ACOG (American College of Obstetricians and Gynaecologists), SOMANZ (Society of Obstetric Medicine of Australia and New Zealand), ASTH (Australasian Society of Thrombosis and Haemostasis), EANM (European Association of Nuclear Medicine), RCOG (Royal College of Obstetrician and Gynecologists), CXR (chest x-ray), DVT (deep vein thrombosis), PE (pulmonary embolism), V/Q (ventilation/perfusion), CTPA (computed tomography pulmonary angiography)

International Guidelines	Summary of Recommendations	Level of evidence
American Thoracic Society/Society of Thoracic Radiology Clinical Practice Guideline (endorsed by ACOG)	In pregnant women with suspected PE and a normal CXR, we recommend lung scintigraphy as the next imaging test rather than CTPA	Strong recommendation, low quality evidence
Australian and New Zealand Guidelines (endorsed by SOMANZ and ASTH)	V/Q scanning is preferred investigations in pregnant or postpartum women with suspected PE who have a normal CXR. CTPA should be used in women with an abnormal CXR or where V/Q scanning is inconclusive or not available The fetal and maternal radiation dose with either V/Q scanning or CTPA is within acceptable limits, and neither should be withheld in a pregnant woman who has clinical symptoms that raise the suspicion of PE	Group Consensus Level 1
EANM Guidelines 2009	In pregnancy, particularly during the first trimester, a 2-day protocol starting with a perfusion-only scan followed if necessary, by a second day ventilation study	Level IV Grade C
European Society of Cardiology 2019	D-dimer measurement and clinical prediction rules should be considered to rule out PE during pregnancy or the post-partum period. In a pregnant patient with suspected PE (particularly if symptoms of DVT), venous CUS should be considered to avoid unnecessary radiation. Perfusion scintigraphy or CTPA (low-radiation dose protocol) should be considered to rule out suspected PE in pregnant women; CTPA should be considered as the first-line option if the CXR is abnormal	Class IIa Grade B Class IIa Grade B Class IIa Grade C
RCOG Green-top Guideline 2015	In women with suspected PE without symptoms and signs of DVT, V/Q lung scan or a CTPA should be performed When the CXR is abnormal and there is a clinical suspicion of PE, CTPA should be performed in preference to a V/Q scan Alternate or repeat testing should be carried out where V/Q scan or CTPA is normal but the clinical suspicion of PE	Grade C Grade D

	remains	
		Grade C
	Women with suspected PE should be advised that, compared with CTPA, V/Q scanning may carry a slightly increased risk of childhood cancer but is associated with a lower risk of maternal breast cancer; in both situations, the absolute risk is very small	Grade D
Society of Obstetricians and Gynaecologists of Canada 2014	In pregnant women, a V/Q scan is the preferred test	III-B

Table 2 - Australian Guidelines and recommendations for investigating suspected PE during pregnancy SOMANZ (Society of Obstetric Medicine of Australia and New Zealand), ASTH (Australasian Society of Thrombosis and Haemostasis), CXR (chest x-ray), DVT (deep vein thrombosis), PE (pulmonary embolism), V/Q (ventilation/perfusion), CTPA (computed tomography pulmonary angiography)

Australian Guidelines	Summary of Recommendations
Australian and New Zealand Guidelines (endorsed by SOMANZ and ASTH) 2012	All pregnant or postpartum women with clinical suspicion of PE should have appropriate imaging D-dimer testing is not recommended for the evaluation of suspected DVT or PE in the pregnancy or early postpartum period V/Q scanning is preferred investigations in pregnant or postpartum women with suspected PE who have a normal CXR. CTPA should be used in women with an abnormal CXR or where V/Q scanning is inconclusive or not available The fetal and maternal radiation dose with either V/Q scanning or CTPA is within acceptable limits, and neither should be withheld in a pregnant woman who ha clinical symptoms that raise the suspicion of PE
Thrombosis and Haemostasis Society of Australia and New Zealand (THANZ) 2019	In pregnant women, given the absence of contrast combined with studies showing that the proportion of diagnostic V/Q scans is high, V/Q scan is the preferred diagnostic investigation

Table 3. Comparison of two recent reviews evaluating diagnostic imaging of suspected PE during pregnancy with CTPA and lung scintigraphy. Diagnostic accuracy was similar between the reviews, however different rates of non-diagnostic results were reported. *CTPA (computed tomography pulmonary angiography), V/Q (ventilation/perfusion), PE (pulmonary embolism).*

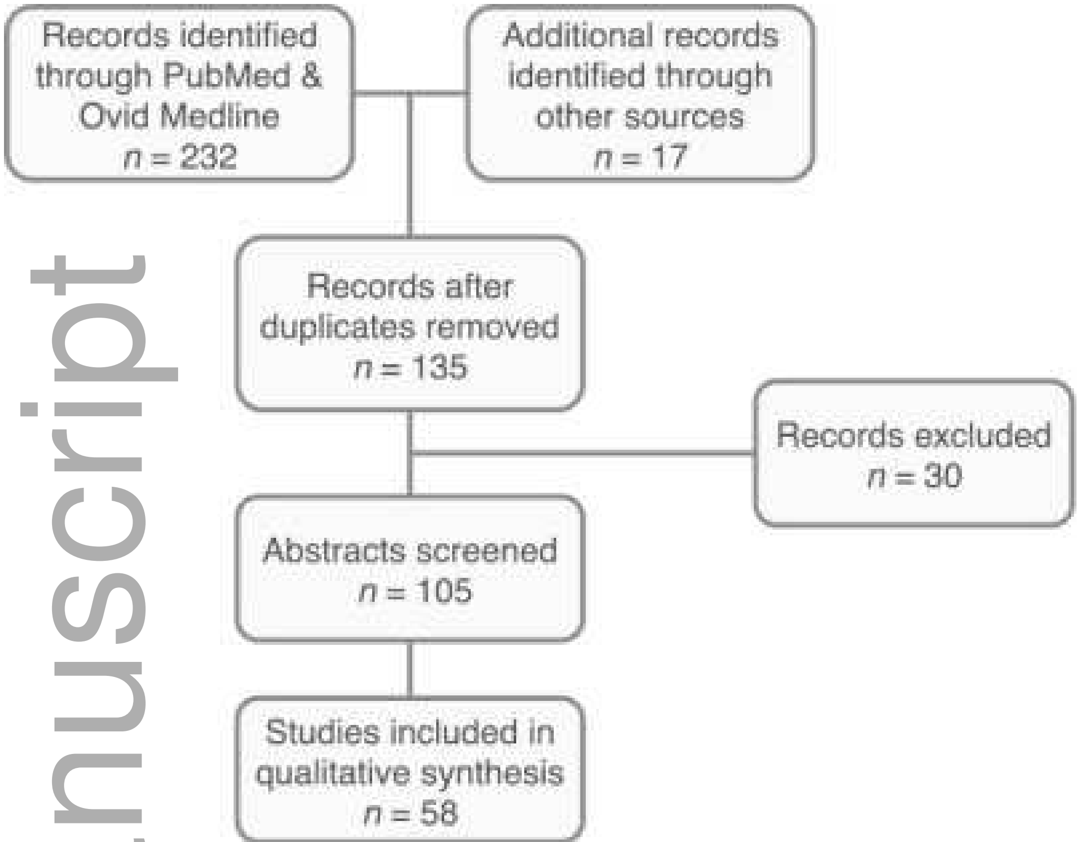
	Cochrane Review 2018	Tromeur et al 2019
Diagnostic Accuracy		
Total studies	11	13
V/Q subjects	665	1270
CTPA subjects	695	837
V/Q		
Negative Predictive Value	100%	
False Negative Rate		0%
CTPA		
Negative Predictive Value	100%	
False Negative Rate		0%
Non-Diagnostic Results		
Total studies	11	30
V/Q subjects	665	2535
CTPA subjects	695	1774
V/Q non-diagnostic rate	5.9%	14%
CTPA non-diagnostic rate	4.0%	12%
Prevalence of PE		
Median (range)	3.3% (0.0-8.7%)	4.1 (0-22.2%)

Table 4 - Overview of studies in real-life patients on radiation dose exposure from CTPA or V/Q lung scanning

CTPA (computed tomography pulmonary angiography), V/Q (ventilation/perfusion), DLP (dose length product), mSv (milliSievert), mGy (milliGray), µSv (microSieverts), kV (kilovolts), cm (centimetre)

Study	CTPA (contrast)					VQ Scan (Q+V)			
	Number of imaging tests	Maternal Effective Dose	Maternal Breast Dose	Foetal dose	DLP mean	Number of imaging tests	Maternal Effective Dose	Maternal Breast Dose	Foetal dose
Armstrong et al 2017	269 CTPA		2-14 mGy	0.02 – 0.002 mGy	217 mGy.cm	769 V/Q		0.28mGy	0.2mGy
Halpenny et al 2017	23 CTPA (old protocol)	1.66mSv			118.48 mGy.cm				

	45 CTPA (low dose protocol)	0.97mSv			69.34 mGy.cm						
Mitchell et al 2017	84 CTPA (120kV)		7.64mGy								
	15 CTPA (80kV)		3.65mGy								
Grüning et al 2016	23 CTPA	7.8mSv	20 mSv	110µSv		89 V/Q	1.6 mSv	0.56 mSv	77µSv		
Jordan et al 2015	50 CTPA	9.8mSV									
Bajc et al 2015									**3months**	**6months**	**9months**
						20 Q SPECT (50mBq)		0.25mGy	0.20 mGy	0.25 mGy	0.05 mGy
						14 V SPECT (30mBq)		0.2mGy	0.007 mGy	0.011 mGy	0.014 mGy
						93 Q SPECT (120mBq)		0.6mGy	0.48 mGy	0.60 mGy	0.48 mGy
Moradi et al 2015	27 CTPA (pregnant)				303.55 mGy.cm						
	17 CTPA (postpartum)				333.12 mGy.cm						
Astani et al 2014	30 CTPA	21.02 mSv	44.35 mGy	0.46 mGy		7 V/Q	1.29 mSv	0.37 mGy	0.40 mGy		
Browne et al 2014	70 CTPA				397.54 mGy.cm						
Ridge et al 2011	28 CTPA	5.3mSv									
	20 CTPA (low dose protocol)	4.8mSv									
Revel et al 2011	46 CTPA	7.3 mSv			405 mGy.cm	94 V/Q	0.9 mSv				
Litmanovich et al 2009	26 CTPA	1.79 mSv			105.65 mGy. cm						



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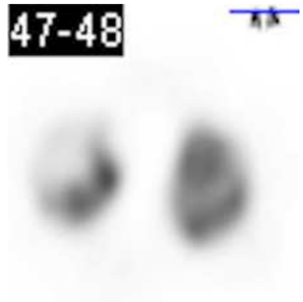

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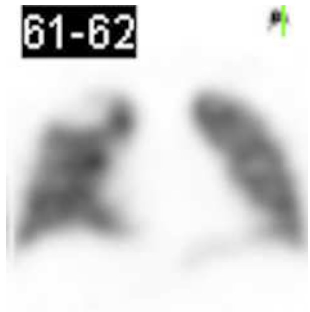

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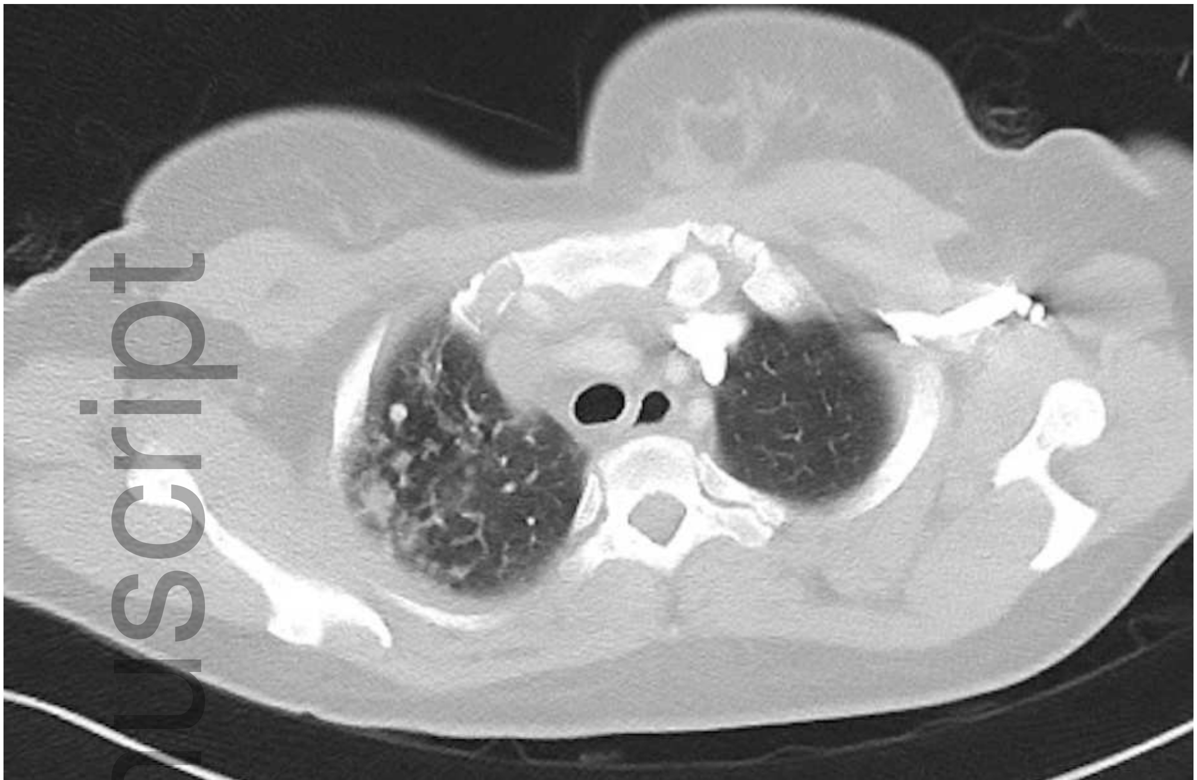

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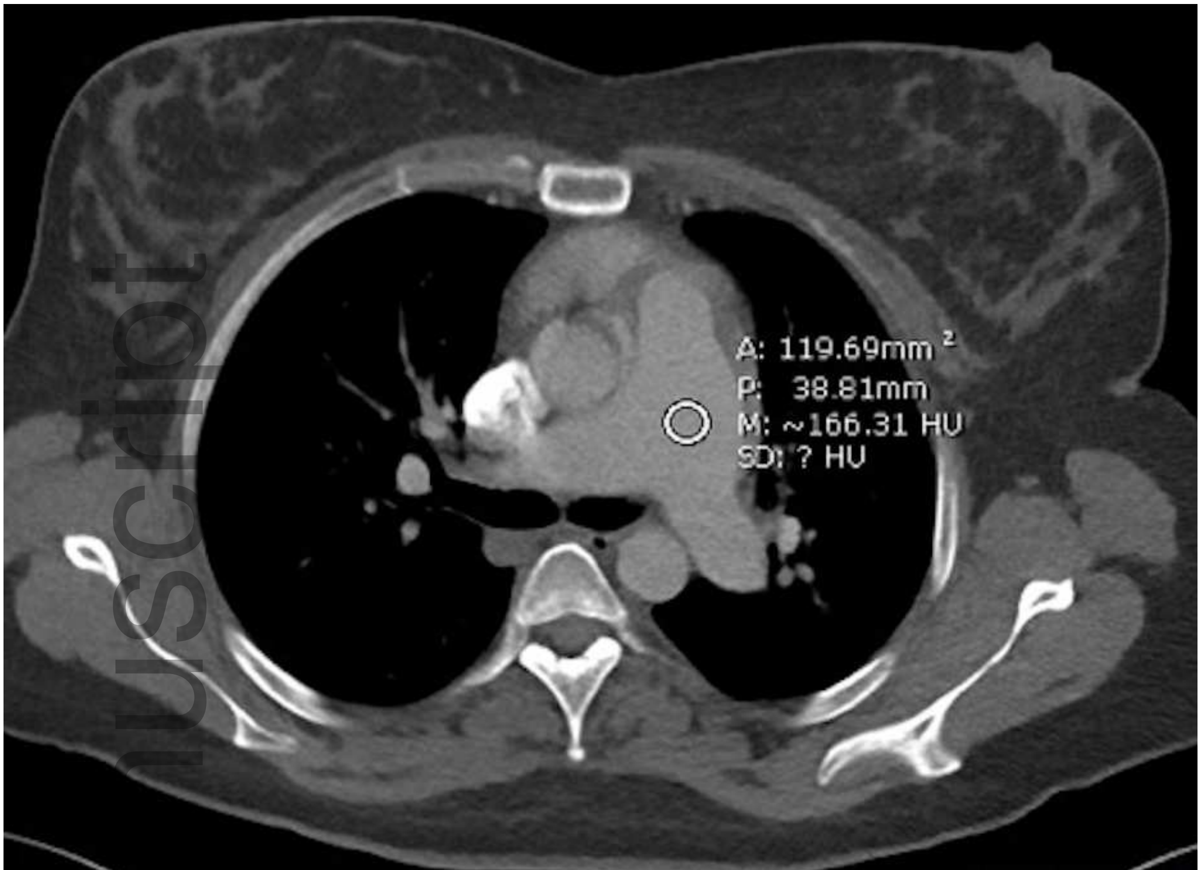

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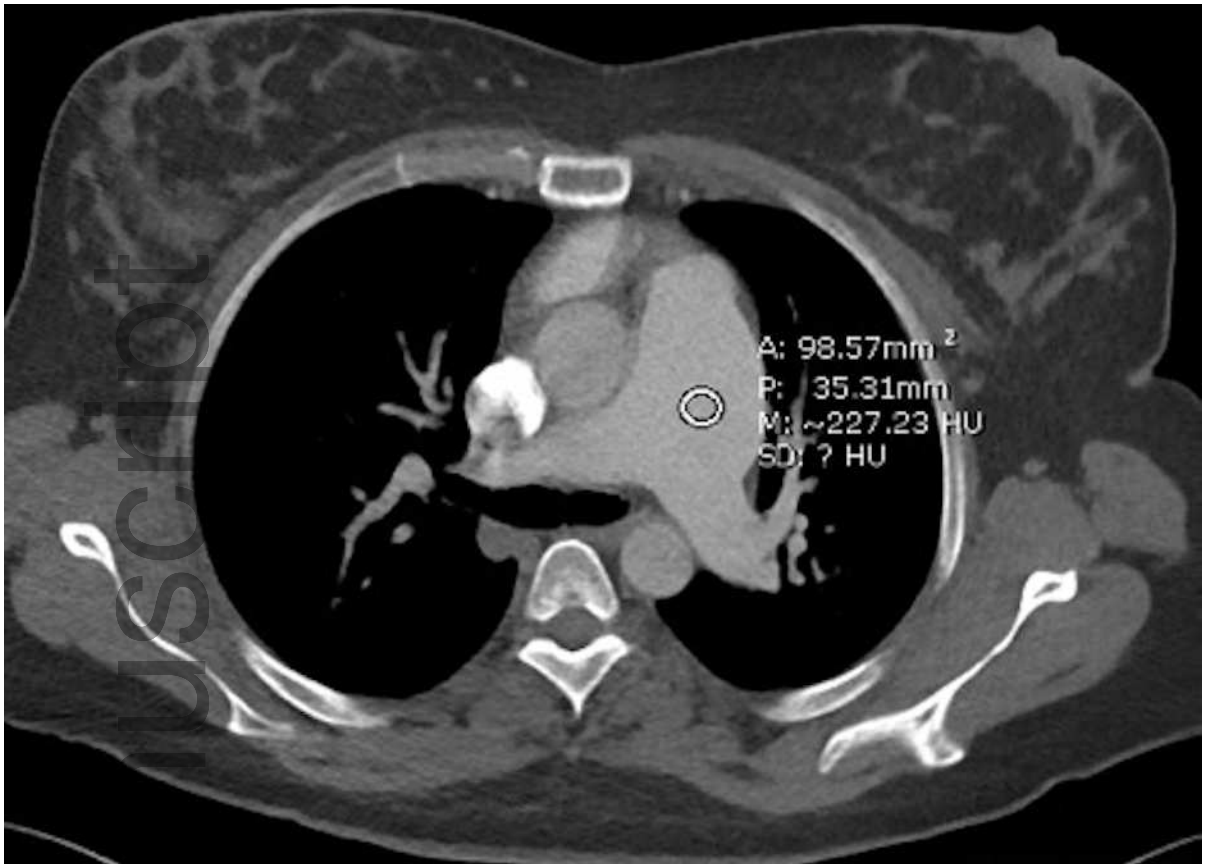

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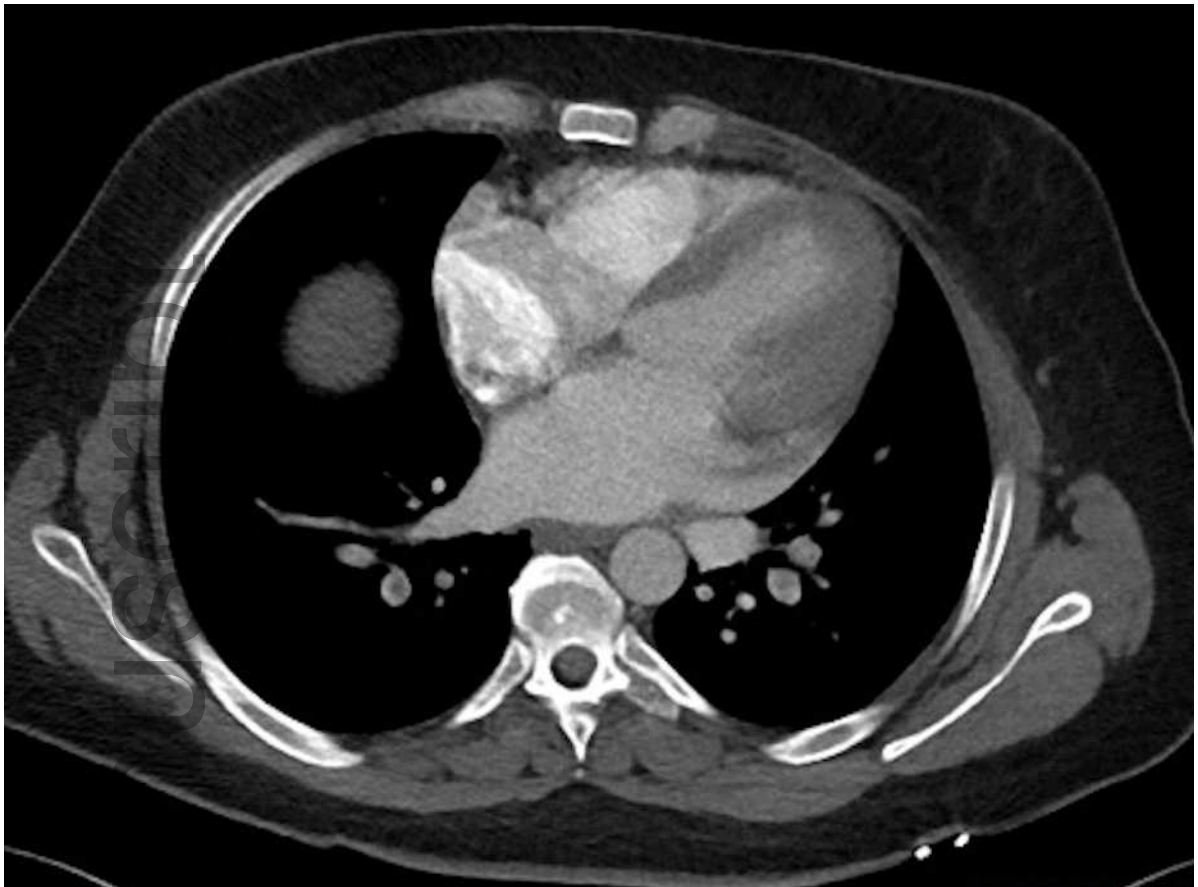

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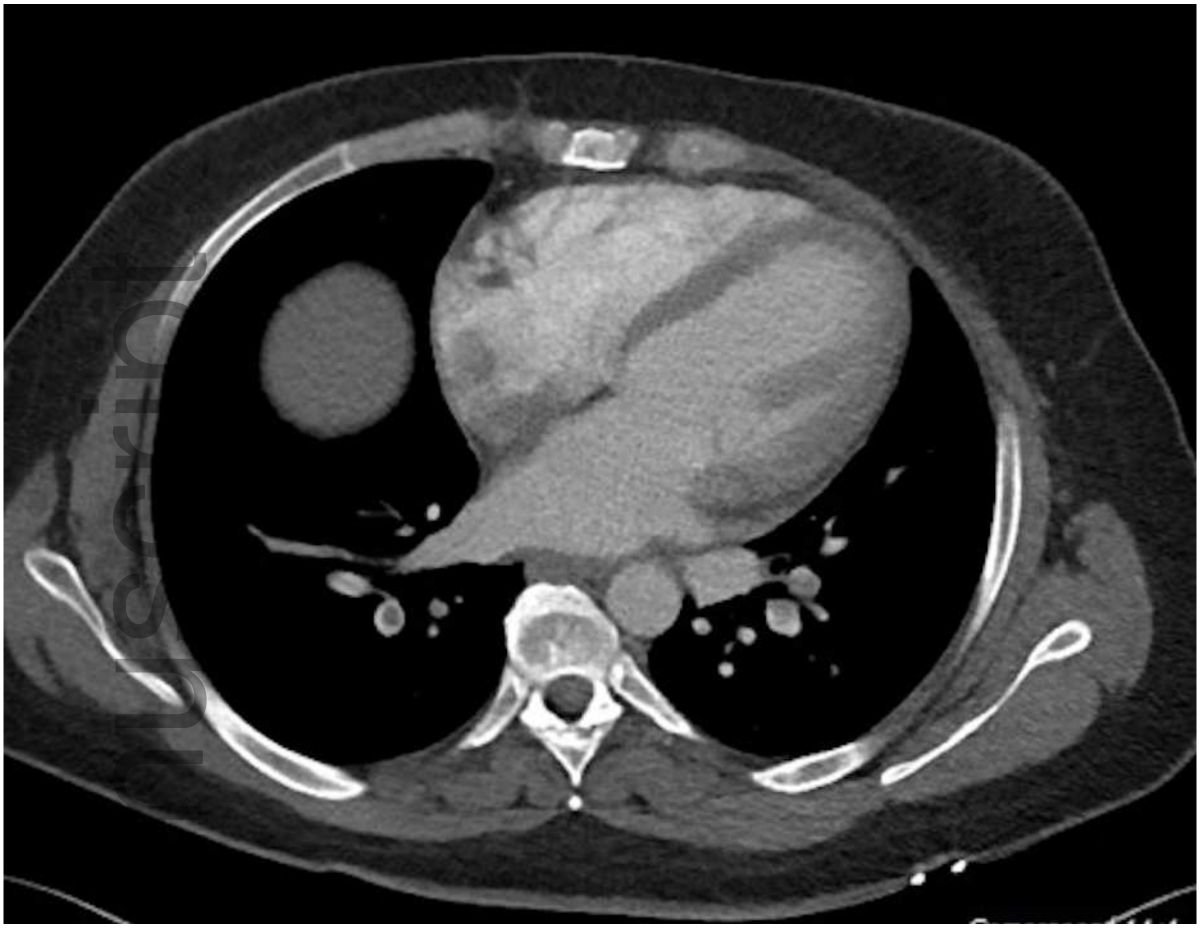

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