CHEST

Diagnosing Pulmonary Embolism During Pregnancy

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TOPIC IMPORTANCE: Pulmonary embolism (PE) is one of the leading causes of pregnancy-related deaths in high-income countries. Maternal mortality from PE has been attributed to delayed recognition and investigation. The diagnosis of PE may be challenging, as its early signs and symptoms may overlap with physiological changes of pregnancy. As such, promptly ruling out suspected PE using diagnostic testing is of paramount importance. This narrative review provides a contemporary overview of risk assessment tools, diagnostic modalities, counseling needs, and existing best practice guidance for the diagnosis of PE in pregnancy.

REVIEW FINDINGS: The revised Geneva score and the pregnancy-adapted YEARS algorithm are promising risk stratification methods that have been found to be safe and effective to support the diagnosis of PE in pregnancy. CT pulmonary angiography and ventilation perfusion scans have comparable safety and effectiveness profiles. Iodinated contrast agents administered for CT pulmonary angiography in pregnant patients with suspected PE are not associated with risks of neonatal adverse events. Pregnant patients may experience distress about fetal health during diagnostic testing, underscoring the importance of counseling to help in decision-making and improve the quality of care. Recent guidelines have supported the use of clinical prediction rules. Both imaging modalities are considered safe in pregnancy, with some guidance advising to choose between the 2 tests based on chest radiography results.

SUMMARY: The choice of diagnostic testing should be based on equipment availability, the ability to perform testing in a timely manner, clinical urgency, chest radiography results, and suspicion of alternative diagnoses.

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Pregnancy is associated with an increased risk of VTE, which includes pulmonary embolism (PE) and deep vein thrombosis (DVT).[1] PE is one of the leading causes of

ABBREVIATIONS: ARTEMIS = Pregnancy-Adapted YEARS Algorithm for the Diagnosis of Suspected Pulmonary Embolism; CTPA = CT pulmonary angiography; CT-PE = Diagnosis of Pulmonary Embolism During Pregnancy; CUS = compression ultrasonography; CXR = chest X-ray; DiPEP = Diagnosis of PE in Pregnancy; DVT = deep vein thrombosis; OPTICA = Optimized CT Pulmonary Angiography in Pregnancy; PE = pulmonary embolism; $\dot{V}/\dot{Q}$ = ventilation perfusion scan

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maternal mortality globally, which has been attributed to delayed recognition and investigations.[2,3] The diagnosis of PE may be challenging, as symptoms and signs of PE such as dyspnea, sinus tachycardia, and lower extremity edema are often present in pregnancy due to physiological changes.[4]

The diagnosis of PE can be established by using risk assessment tools and radiologic diagnostic modalities, including CT pulmonary angiography (CTPA) and lung ventilation perfusion ($\dot{V}/\dot{Q}$) scanning.[5] The current narrative review provides a contemporary overview of risk assessment tools, imaging and diagnostic modalities, and existing best practice guidelines for the diagnosis of PE in pregnancy.

Literature Search

We consulted with an information specialist to develop a search strategy. The MEDLINE database was searched for articles published in any language from database inception to November 25, 2024, combining the key words "pregnancy," "pregnant women," "ventilation-perfusion scan," "ventilation-perfusion ratio," "computed tomography angiography," "thorax," "lung," "pulmonary angiography," "chest CT," "chest cat scan," and "CT chest scan" used separately or in combination. Outsourcing and snowball sampling from article references were also used. Articles with information on risk assessment tools, imaging and diagnostic modalities, counseling needs, and existing best practice guidance for the diagnosis of PE in pregnancy were retained.

Evidence Review

Establishing Pretest Probability

D-dimers, used alongside other clinical factors, are well-established biomarkers for guiding further diagnostic imaging to rule out PE in the nonpregnant population.[6-8] D-dimer testing incorporated in risk assessment algorithms in pregnancy was evaluated in 2 prospective studies in 2018 and 2019: the Diagnosis of Pulmonary Embolism During Pregnancy (CT-PE) study and the Pregnancy-Adapted YEARS Algorithm for the Diagnosis of Suspected Pulmonary Embolism (ARTEMIS) study (Table 1).[9,10]

The CT-PE study involved 395 participants with suspected PE.[10] PE was ruled out in patients at low or intermediate pretest probability using the revised Geneva score with a D-dimer level < 500 μg/L.[10] When the pretest clinical probability was high or when the D-dimer level was ≥ 500 μg/L, a bilateral compression ultrasonography (CUS) of the lower extremities was performed; if no DVT was identified, a CTPA was performed. No VTE or deaths occurred during the 3-month follow-up (0.0%; 95% CI, 0.0%-1.1%). Chest imaging was avoided in 11.6% of participants. However, the single D-dimer cutoff level limits the utility of the revised Geneva score following the first trimester of pregnancy as D-dimer levels tend to increase from 1 trimester to another and peak around delivery.[11] In addition, the revised Geneva score comprises predictors that are generally not applicable to pregnant patients.[12] The Pregnancy-Adapted Geneva score, developed from the CT-PE study, excludes criteria that are less or unlikely to be relevant in pregnancy (eg, age > 65 years and malignancy).[13] Although the Pregnancy-Adapted Geneva score outperformed the Geneva score (area under the curve, 0.795 vs 0.684), it requires prospective validation.

The ARTEMIS study included 498 pregnant participants.[9] YEARS criteria were evaluated (clinical signs of DVT, hemoptysis, and PE as the most likely diagnosis) in conjunction with D-dimer levels. PE was excluded if no YEARS criteria were present and the D-dimer level was $< 1{,}000$ μg/L, or with ≥ 1 YEARS criteria with a D-dimer level < 500 μg/L. Patients with symptoms of DVT underwent CUS. Participants in whom PE could not be ruled out underwent a CTPA. During the 3-month follow-up period, a single case of

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TABLE 1] Establishing the Pretest Probability of PE

Parameter	CT-PE Study[10]	ARTEMIS Study[9]
Prevalence of PE in study population	7.1%	4%
Risk assessment algorithm used	Pretest clinical probability using the revised Geneva score, D-dimer testing, bilateral lower limb CUS, and CTPA	Pregnancy-adapted YEARS algorithm involving 3 criteria: (1) clinical signs of DVT; (2) hemoptysis; and (3) PE as the most likely diagnosis, with D-dimer level cutoffs based on number of criteria met
Results	Imaging was avoided in 11.6% of patients	Imaging was avoided in 39% of patients
Specificity	100%	100% (assuming no false-positive findings) (95% CI, 99.2-100; $P < .05$)
Sensitivity	100%	95.2% (95% CI, 77.3-99.2; $P < .05$)
Conclusion	A diagnostic strategy based on clinical probability, D-dimer, CUS, and CTPA can safely rule out PE in pregnant women	The pregnancy-adapted YEARS algorithm can safely rule out PE and reduce the need for CTPA in pregnant women
Limitations	Nonrandomized design Limited yield of certain tests such as CUS in the absence of DVT symptoms	Nonrandomized design Physicians occasionally knew the D-dimer results when evaluating the YEARS criteria, which could introduce bias in the assessment of PE as the most likely diagnosis

ARTEMIS = Pregnancy-Adapted YEARS Algorithm for the Diagnosis of Suspected Pulmonary Embolism; CTPA = CT pulmonary angiography; CT-PE = Diagnosis of Pulmonary Embolism During Pregnancy; CUS = compression ultrasonography; DVT = deep vein thrombosis; PE = pulmonary embolism.

popliteal DVT (adjusted OR, 0.21; 95% CI, 0.04-1.2) was diagnosed. The pregnancy-adapted YEARS algorithm allowed CTPA imaging to be avoided in 39% (95% CI, 35-44) of participants. The algorithm was most efficient in the first trimester and least efficient in the third trimester.[9]

Importantly, the ARTEMIS algorithm was externally validated using data from the CT-PE-pregnancy study.[14] Retrospective application of the YEARS algorithm in 371 participants showed that 21% of patients could have avoided imaging without missing any PE, resulting in a 0 of 77 (95% CI, 0.0-3.9) failure rate. The study therefore concluded by supporting the use of this clinical decision rule.

The Diagnosis of PE in Pregnancy (DiPEP) study, a mixed prospective and retrospective cohort study, included 324 pregnant or postpartum individuals with suspected PE and 198 pregnant or postpartum individuals with diagnosed PE.[8] In this study, clinical features, decision rules, and D-dimer levels lacked sufficient accuracy to rule out PE in pregnant or postpartum women with suspected or diagnosed PE. A secondary analysis of this cohort in 2019 assessed whether the Geneva score and pregnancy-adapted YEARS algorithm could effectively rule out suspected PE.[15] The subgroup analysis included 219 prospectively recruited pregnant participants with suspected PE who underwent D-dimer measurement and definitive diagnostic imaging. In this subset, while the revised Geneva score would have correctly excluded 46 of 219 patients with suspected PE, it would have incorrectly excluded 3 of 12 patients with a PE. The revised Geneva score yielded a sensitivity of 75.0% (95% CI, 42.8-93.3) and a specificity of 20.8% (95% CI, 15.6-27.1). While the pregnancy-adapted YEARS algorithm alone would have correctly excluded 96 (43.8%) of 219 patients, it would have incorrectly excluded 5 of 12 participants with a PE. The pregnancy-adapted YEARS algorithm yielded a sensitivity of 58.3% (95% CI, 28.6-83.5) and a specificity of 44.0% (95% CI, 37.1-51.0). As a result, the secondary analysis of the DiPEP study concluded that pregnancy-adapted clinical decision rules have a limited diagnostic accuracy.

Analyses of the DiPEP study cohort were affected by important methodologic challenges.[15] The cohort's use of both prospective and retrospective data, variable D-dimer tests, and anticoagulation prior to sampling introduced limitations.[16] The small sample size limits the study's reliability, and recommendations against D-dimer use should be interpreted cautiously.

A 2021 systematic review and meta-analysis, including the CT-PE study and the ARTEMIS study, evaluated the safety of using D-dimer to rule out VTE in pregnant patients with suspected PE and/or DVT.[17] The study found that D-dimer levels can safely exclude VTE in pregnant patients with a low or intermediate pretest probability of the condition. The analysis reported a sensitivity of 99.5% (95% CI, 95.0-100.0; $I^2 = 0\%$) and a negative predictive value of 100% (95% CI, 99.19-100.0; $I^2 = 0\%$). In addition, the 3-month thromboembolic event rate among pregnant women left untreated following a negative D-dimer result was 0.32% (1 of 312; 95% CI, 0.06-1.83).

In summary, this review found that the revised Geneva score and the pregnancy-adapted YEARS algorithm may be considered safe to help in the diagnosis of PE, and they are especially helpful in the first 2 trimesters. In addition, the pregnancy-adapted YEARS algorithm, more specific to pregnancy, has been externally validated.[14] As a result, the pregnancy-adapted YEARS algorithm may be considered for further use in clinical practice, although further research is needed.[18]

Accuracy of Diagnostic Imaging

Both CTPA and $\dot{V}/\dot{Q}$ scanning are associated with ionizing radiation exposure.[19] However, several advantages are associated with the use of CTPA. First, this imaging modality enables the visualization of alternative diagnoses in the absence of PE such as parenchymal and vascular pathologies, including aortic dissection and subtle infective changes.[20] Moreover, CTPA allows for an assessment of clot burden and anatomy, which may be used to guide percutaneous intervention.[21] Moreover, CTPA is widely available in hospitals, making it helpful in an emergency setting, and results can be promptly obtained and interpreted.[22] On the other hand, it is hypothesized that CTPA in pregnancy may lead to more nondiagnostic tests attributed to suboptimal vascular enhancement due to increased blood volume and timing issues.[1,5,23,24] Because most cases of PE missed in a 2017 Cochrane review involved patients with inconclusive scans, nondiagnostic testing is an important factor to consider.[25] One of the main advantages of $\dot{V}/\dot{Q}$ scanning is that it avoids the use of iodinated contrast material, which is relatively contraindicated in patients with renal insufficiency (estimated glomerular filtration rate < 30 mL/min per 1.73 m^2) or moderate to severe iodinated contrast allergy.[26]

Thus, choosing between CTPA and $\dot{V}/\dot{Q}$ scanning may be challenging. A 2019 systematic review and meta-analysis included articles published evaluating both modalities.[26] $\dot{V}/\dot{Q}$ scanning had a pooled proportion of false-negative scans of 0.0% (adjusted OR, 0; 95% CI, 0-0.4; $I^2 = 0.0$), as none of the 1,270 pregnant patients who underwent a $\dot{V}/\dot{Q}$ scan were diagnosed with PE or DVT during the 3 months' follow up. CTPA had a pooled proportion of false-negative scans of 0.0% (adjusted OR, 0.0; 95% CI, 0.0-0.16; $I^2 = 5.7$), with 3 of the 837 patients diagnosed with nonfatal PE following a normal CTPA result. The pooled frequency of nondiagnostic $\dot{V}/\dot{Q}$ scans and CTPA were 14% (95% CI, 10-18; $I^2 = 90.3\%$) and 12% (95% CI, 6-17; $I^2 = 93.86\%$), respectively. The negative predictive value and rates of nondiagnostic tests of $\dot{V}/\dot{Q}$ scanning and CTPA were comparable. The absolute numbers of inconclusive tests were also low for both modalities. These results align with a Cochrane review in which both modalities were found to be suitable for ruling out PE during pregnancy.[25]

The Optimized CT Pulmonary Angiography in Pregnancy (OPTICA) study, a prospective observational study, validated the safety, radiation dose, and image quality of a low-dose CTPA protocol optimized for pregnancy using an iterative reconstruction-enabled 128-slice CT system.[27] A bolus tracking technique was used with 60 mL of 350 mg/mL iodinated IV contrast at 4 mL/s. The OPTICA study yielded a 100% negative predictive value for CTPA (adjusted OR, 0.0; 1-sided 95% CI, 0.0-2.66). Adequate image quality and low radiation exposure were maintained. In total, 3% of tests were nondiagnostic and 5% were repeated, mainly due to obesity and issues with performing the Valsalva maneuver.

Importantly, the accuracy of both imaging modalities may be optimized. Bedside echocardiography can be used as an adjunctive diagnostic test in the acute setting to aid diagnosis and risk stratification.[28] Moreover, all patients should have a chest radiograph (CXR) to guide the imaging modality choice and help to look for alternative pathologies that could explain the patient's symptoms, such as consolidation or pneumothorax.[23] In a 5-year retrospective study of 304 pregnant or postpartum patients suspected of having PE, 280 patients underwent a CXR. In the subgroup of women with an abnormal CXR, nondiagnostic results were less likely with CTPA than with a $\dot{V}/\dot{Q}$ scan (adjusted OR, 0.4; 95% CI, 0.2-0.8; $P < .01$). As such, CTPA is favored in the presence of an abnormal CXR. To optimize the yield of CTPA, adjustments include

TABLE 2] Radiation Doses Associated With CTPA and $\dot{V}/\dot{Q}$ Scans

Parameter	CTPA	$\dot{V}/\dot{Q}$ scan	Background Exposure
Mean maternal effective doses			Baseline radiation exposure: around 2.4 mSv/year[35]
Tromeur et al, 2019[26]	0.23-9.7 mSv	0.9-5.85 mSv	
Tester et al, 2023[22]	4.7 ± 2.9 mSv	1.7 ± 0.8 mSv	
Gillespie et al, 2024[27]	1.4 ± 0.9 mSv	NA	
Fetal/uterus absorbed dose			Natural background radiation during pregnancy to fetus during pregnancy: approximately 1 mGy[19]
Tromeur et al, 2019[26]	0.002-0.51 mGy	0.2-0.7 mGy	
Tester et al, 2023[22]	"Low"	"Low"	
Gillespie et al, 2024[27]	0.1 ± 0.2 mGy	NA	

CTPA = CT pulmonary angiography; mSv = millisievert; mGy = milligray; NA = not applicable; $\dot{V}/\dot{Q}$ = ventilation perfusion scan.

increasing the contrast flow rate to 6 mL/s, boosting contrast volume by 25%, using 370 mg/mL contrast, and coaching patients to have shallow breathing and avoid the Valsalva maneuver (during image acquisition).[29] This modified CTPA protocol for pregnancy improves image quality by enhancing pulmonary arterial opacification and reducing contrast bolus interruptions from unopacified blood in the inferior vena cava. For CTPA, technical adjustments should be made based on the size of pregnant individuals and dose-limiting techniques such as tube current modulation (adjusts the intensity of the X-ray beam) and dynamic collimation (limits the size of the X-ray beam to focus on only the area of interest).[30] To ensure optimal imaging, CTPA protocols should account for physiological changes in pregnancy, such as increased cardiac output, by using automated bolus triggering, high iodine concentration, and clear breathing instructions.

Both imaging modalities therefore have comparable accuracy. The choice of test should be based on equipment availability, considerations of CXR results, and suspicion of an alternative diagnosis. However, CTPA is more frequently used than $\dot{V}/\dot{Q}$ scanning, even in the presence of a normal CXR.[22] This can be partially explained by the higher availability of CTPA, clinicians' perceptions and preferences, and guidelines not favoring 1 modality over another.

Leg Ultrasonography Prior to Chest Imaging

CUS can be considered prior to chest imaging in patients with suspected PE and symptoms suggestive of DVT.[30] However, CUS to detect DVT in asymptomatic patients has a low diagnostic yield and may lead to preventable diagnostic delays according to a 2023 systematic review and meta-analysis of individual patient data.[31] Furthermore, focusing solely on leg imaging may not detect important findings in the chest or in the iliac veins, where CUS is less reliable to detect DVT during pregnancy and chest imaging should not be withheld following a negative CUS.[31,32] In fact, if the pretest probability is high, chest imaging should be prioritized; empirical anticoagulation may also be considered.[30,31]

Maternal and Fetal Safety Considerations

Exposure to Ionizing Radiation: Both CTPA and $\dot{V}/\dot{Q}$ scanning expose the pregnant patient and the fetus to ionizing radiation.[19,33] The absorbed radiation dose, expressed in milligrays, refers to the quantity of radiation deposited per unit mass of tissue.[34] Because different organs react differently to radiation because of varying radiosensitivity, the absorbed dose in milligrays is an estimate of the radiation dose received. The effective radiation dose incorporating organ-specific variation is expressed in millisieverts. It encompasses the overall dose received in its equivalent radiation effect, and it is the predominant measure used to compare ionizing radiation doses across imaging modalities. CTPA and $\dot{V}/\dot{Q}$ scans are both regarded as safe in pregnancy (Table 2).[19,22,26,27]

Fetal Safety: Radiation doses < 50 mGy are considered to indicate a negligible risk to the fetus.[36] The natural incidence of childhood cancer and leukemia between birth and 15 years of age, without exposure to radiation beyond natural background levels, is approximately 2 to 3 cases per 1,000 children.[37] Estimates suggest that the absolute risk of developing cancer during this age range

TABLE 3] Guidelines Recommendation for Ruling Out PE in Pregnancy[28,30,53,60-65]

Variable	ATS-STR	SOGC	ACOG	ASH
Comparison of recommendations for diagnosis of PE in pregnancy				
Year of publication	2011	2014	2018	2018
Country	United States	Canada	United States	United States
Clinical prediction rules	Not recommended (No grade of evidence provided)	Should not be used alone (Expert opinion)	NA	Needs to be further evaluated (No grade of evidence provided)
D-dimer testing	Not recommended (Expert opinion)	Should not be used alone (Expert opinion)	Not recommended (No grade of evidence provided)	Needs to be further evaluated (No grade of evidence provided)
Diagnostic evaluation				
Bilateral CUS	Should be performed in women suspected of having PE with symptoms and signs of DVT (Expert opinion)	Should reasonably begin with it (No grade of evidence provided)	When signs or symptoms suggest new-onset DVT, recommended initial diagnostic test (No grade of evidence provided)	Suggested if suspected DVT (Low certainty in evidence)
V̇/Q̇ scan	If negative chest radiograph (Expert opinion)	Preferred imaging modality (Expert opinion)	Can be used (No grade of evidence provided)	Preferred imaging modality (Low certainty in evidence)
CTPA	If positive chest radiograph (Expert opinion)	Can be used (Evidence-Based Recommendation)	Can be used (No grade of evidence provided)	Can be used (No grade of evidence provided)
Follow-up following indeterminate primary advanced imaging	Diagnostic testing specified for all patients per algorithm	Diagnostic testing specified for all patients per algorithm	NA	NA
Empirical treatment prior to diagnosis	Empirical treatment (No grade of evidence provided)	Not recommended (No grade of evidence provided)	Empirical treatment (No grade of evidence provided)	NA

(Continued)

following in utero exposure to radiation is around 600 cases per 10,000 individuals for every 1,000 mGy of radiation exposure.[37] This corresponds to a 0.06% increase in absolute risk for every 10 mGy of exposure.

A 2019 meta-analysis reported fetal doses for CTPA and V̇/Q̇ scans (Table 2).[26] It was limited by the use of varying CT scanners and protocols, precluding a direct comparison of V̇/Q̇ scan and CTPA radiation values.[19,26] Nevertheless, reported exposure levels were all well below a 10 mGy threshold.[26] More recently, a 2023 cohort study and the 2024 OPTICA study reported similar mean uterine/fetal doses.[22,27] As such, the imaging modalities used to diagnose suspected PE are below thresholds currently considered to be associated with any fetal risks.

Maternal Safety: The 2019 meta-analysis, a more recent cohort study of 473 pregnant and postpartum individuals, and the OPTICA study reported varying maternal effective breast-absorbed doses for CTPA and V̇/Q̇ scans, as summarized in Table 2.[22,26,27]

Although CTPAs have been linked to a higher exposure of radiation to breast tissue than V̇/Q̇ scanning, a population-based cohort study found no increased risk of early-onset breast cancer among women who were exposed to CTPA or V̇/Q̇ scanning during pregnancy or postpartum compared with the general population, regardless of exposure timing.[38] However, the study's

TABLE 3] *(Continued)*

EANM	ESC[a]	RCOG	GTH	SOMANZ[a]
2009	2019	2015	2016	2021
Europe	Europe	United Kingdom	International	Australia and New Zealand
NA	Should be considered to rule out PE (Evidence-based recommendation)	No evidence to support its use (Evidence-based recommendation)	Not recommended (No grade of evidence provided)	Limited utility (Evidence-based recommendation)
Not recommended (No grade of evidence provided)	Should be considered to rule out PE (Evidence-based recommendation)	Not recommended (Expert opinion)	Recommended (No grade of evidence provided)	Not recommended (will reduce incidence at the cost of missing 40% of PE cases) (Evidence-based recommendation)
Not recommended (No grade of evidence provided)	Should be considered in patients suspected of having PE particularly if presence of symptoms of DVT (Evidence-based recommendation)	Should be performed in women suspected of having PE with symptoms and signs of DVT (Evidence-based recommendation)	Always (No grade of evidence provided)	If there are symptoms or signs of DVT (Evidence-based recommendation)
Preferred imaging modality (Evidence-based recommendation or expert opinion)	If negative chest radiograph (Expert opinion)	If negative chest radiograph (Expert opinion)	If negative chest radiograph (No grade of evidence provided)	Preferred in hemodynamically stable women and if negative chest radiograph (Consensus- based Recommendation)
NA	Preferred if positive chest radiograph (Expert opinion)	If positive chest radiograph (Expert opinion)	If positive chest radiograph (No grade of evidence provided)	Preferred in hemodynamically unstable women or other pulmonary pathology suspected (Consensus-based recommendation)
Diagnostic testing specified for all patients per algorithm (No grade of evidence provided)	Expert imaging review (No grade of evidence provided)	Diagnostic testing recommended only for patients at high risk but testing modality not specified (No grade of evidence provided)	Diagnostic testing specified for all patients per algorithm (No grade of evidence provided)	Either treat or consider alternate/repeat imaging following consultation with appropriate expert (Evidence-based recommendation)
Not recommended (No grade of evidence provided)	Empirical treatment should be considered (Expert opinion)	Empirical treatment (Evidence-based recommendation)	Empirical treatment	Only in unstable women or if pulmonary imaging is not immediately available (Consensus-based recommendations)

ACOG = American College of Obstetricians and Gynecologists; ASH = American Society of Hematology; ASTH-SOMANZ = Australasian Society of Thrombosis and Haemostasis and the Society of Obstetric Medicine of Australia and New Zealand; ATS-STR = American Thoracic Society and Society of Thoracic Radiology; CTPA = CT pulmonary angiography; CUS = compressive ultrasound; DVT = deep vein thrombosis; EANM = European Association of Nuclear Medicine; ESC = European Society of Cardiology; GTH = Working Group in Women's Health of the Society of Thrombosis and Haemostasis; NA = not applicable; PE = pulmonary embolism; RCOG = Royal College of Obstetricians and Gynaecologists; SOGC = Society of Obstetricians and Gynaecologists of Canada; VQ = ventilation/perfusion.
[a]Published following the Pregnancy-Adapted YEARS Algorithm for the Diagnosis of Suspected Pulmonary Embolism study.

shorter follow-up duration, compared with the 13-year median for breast cancer diagnosis in patients treated with radiation for Hodgkin lymphoma, may limit long-term risk assessment.

Recent advances in technology have notably decreased CTPA radiation doses by 30%.[20] As such, contemporary CT scanners offer lower radiation doses than older models yet still expose breast tissue to higher radiation than $\dot{V}/\dot{Q}$ scans, with doses remaining within established safety limits.[5,22,24]

Optimizing Radiation Exposure: Ionizing radiation exposure can be further reduced for both CTPA and $\dot{V}/\dot{Q}$ scans. Low-dose CTPA protocols with reduced voltage and scanning area (aortic arch to diaphragm) can lower the maternal dose by 1 mSv and breast exposure by 2 mGy.[26,39,40] Optimizing the individual

scan length has been proven to be safe and effective, resulting in a decrease of fetal dose by 76% to 83%.[41] A 2021 systematic review found reduced scan coverage feasible for PE detection in nonpregnant populations without reducing diagnostic accuracy, but it highlighted risk of bias, limited image quality data, and the need for larger, high-quality studies.[42] The OPTICA study described a safe low-dose CTPA for suspected PE in pregnancy, using an 80 kV topogram, a 90 mA reference tube current, a defined scan range, and 60 mL of iodinated IV contrast followed by a saline bolus.[27]

With the use of $\dot{V}/\dot{Q}$ scanning for the diagnosis of PE, a 2-step protocol is usually suggested.[26] Performing perfusion scans only can reduce maternal breast radiation and fetal exposure.[19,26,43,44] Ventilation imaging can be reserved for cases in which perfusion images are abnormal.[19,26,44] Half-dose perfusion scintigraphy without a ventilation study is also common practice, and it is associated with acceptable diagnostic accuracy.[40,43] Omitting ventilation scintigraphy may be reasonable, as perfusion scintigraphy rarely yields inconclusive results, with about 75% of tests showing normal findings.[44] Perfusion scans use technetium-99m macroaggregated albumin, and its dose can be reduced by increasing the scanning time.[30] Replacing ventilation scans with Xenon-133 is encouraged to reduce the effective dose to the pregnant individual. As such, it is important to take advantage of the different optimizing techniques to obtain the best imaging results with the least radiation exposure.

Shielding is no longer a recommended practice because it can negatively influence the effectiveness of examinations and therefore lead to repeated imaging procedures.[45,46] A 2024 phantom study suggested that using shields can lead to an increased fetal radiation exposure, in particularly when older scanners are used.[47]

Fetal Exposure to Iodinated Contrast: Fetal exposure to iodinated contrast from CTPA has previously raised concern for secondary neonatal hypothyroidism due to free iodine entering fetal circulation and the amniotic fluid following IV administration. In a clinical trial of 151 newborns exposed to CTPA during pregnancy, no cases of neonatal hypothyroidism (defined as thyroid-stimulating hormone level $>$ 15 U/mL) were identified (95% CI, 0.0-2.5).[48] These findings provide reassuring data regarding the use of CTPA in pregnant individuals with suspected PE. An earlier study of 343 newborns exposed to high-dose iodinated contrast during CTPA found only one case of transiently elevated thyroid-stimulating hormone levels that had normalized by day 6, with no abnormal T4 levels or hypothyroidism.[49] As such, fetal exposure to iodinated contrast is no longer a concern for secondary neonatal thyroid disorders.

Treating PE Without Diagnosis

Misdiagnosing PE can result in serious consequences, including potentially life-threatening bleeding when anticoagulated, and significant long-term effects, such as the need for antithrombotic prophylaxis during future pregnancies and limitations on the use of hormonal contraceptives or replacement therapy.[50] Furthermore, although empirical use of therapeutic anticoagulation may be indicated in certain circumstances while awaiting diagnostic imaging, full-dose anticoagulation may limit access to neuraxial analgesia.[51] Accordingly, diagnostic imaging with a $\dot{V}/\dot{Q}$ scan or CTPA testing should not be withheld or unnecessarily postponed when PE is suspected.

Counseling Pregnant Patients Undergoing Diagnostic Imaging

Pregnant individuals may experience significant stress regarding the health of their fetus when undergoing diagnostic testing.[52] Counseling at the time of imaging is essential to optimize informed choices and to improve the quality and experience of care. Therefore, clinicians must be well informed and comfortable discussing the risks associated with imaging-associated radiation exposure to prevent delays in urgent testing.[53] A qualitative study revealed that patients value clear, detailed information on imaging risks, including impacts on miscarriage, preterm delivery, and breastfeeding.[52] Suggestions were made to compare the radiation with known safety thresholds and everyday radiation exposure to put risks into perspective, and to present the information in an accessible way.

In a recent retrospective cohort study, one in five pregnant patients with suspected PE refused diagnostic imaging, highlighting the importance of effective counseling.[54] Refusals were more frequent in nonobstetric settings such as in emergency departments.[54] As such, a communication support tool may be beneficial to support providers and patients during these counseling sessions and enable high-quality counseling across a wide range of health care contexts.[52,53] Efforts to that effect are currently underway,[55] combining a hybrid co-design method,[56] with principles of inclusive design,[57] information

design,[58] and guided by best practices for designing effective communication tools for patients.[59]

Current Best Practice Guidance

Nine organizations have issued best practice guidance and recommendations for the diagnosis and treatment of thromboembolic events during pregnancy (Table 3).[28,30,53,60-65]

Although most guidelines advise against using D-dimer testing alone or as part of a clinical risk prediction rule due to concerns about accuracy and reliability during pregnancy, these predate the ARTEMIS study. Following publication of the ARTEMIS study, the European Society of Cardiology now recommends D-dimer use as part of a clinical risk assessment strategy, whereas the Society of Obstetric Medicine of Australia and New Zealand has not changed position.[28,35] A 2023 systematic review and meta-analysis of noninvasive diagnostic work-up for suspected PE during pregnancy supports the new European Society of Cardiology guideline.[31]

All professional organizations mention that $\dot{V}/\dot{Q}$ scan and CTPA are considered safe in pregnancy. Although some favor $\dot{V}/\dot{Q}$ scanning, most recommend using CXR results to guide imaging choice.[18,53,66] Guidelines prioritize local availability and expertise to prevent diagnostic delays.[18,66] Advances made in CT technology reducing radiation and nondiagnostic rates may not yet be reflected in all recommendations.[19,22]

Sequential diagnostic algorithms following indeterminate first-line imaging and anticoagulation prior to confirmed diagnosis are suggested by some Societies. The Society of Obstetric Medicine of Australia and New Zealand reserves anticoagulation for unstable patients or when diagnostic testing is not immediately available.[53,66]

Future Directions

Further research is needed to explore barriers and facilitators to the implementation of risk assessment tools for PE during pregnancy. Moreover, additional documentation of real-world safety and effectiveness following the adoption of clinical decision rules is required. Resources to support effective communication between health care professionals and pregnant patients could improve the quality and experience of care during the investigation process for PE. In turn, such tools could help reduce diagnostic delays and the associated maternal morbidity from PE.

Summary

Clinical decision rules can avoid imaging in up to 40% of cases; however, CTPA and $\dot{V}/\dot{Q}$ scanning may remain necessary to rule out PE. Both imaging modalities are considered safe and valid options in pregnancy. Diagnostic testing should take into consideration equipment availability, CXR results, and suspicion of an alternative diagnosis. Testing for PE in pregnancy can be a stressful process for patients, and counseling is an important step. Although risk stratification tools to rule out PE in pregnancy are not universally recommended, upcoming guidelines are likely to reflect advances in the field and lead to further knowledge translation.

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