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Ruling out PE in pregnancy

Can clinical probability and a high-sensitivity D-dimer test reliably and safely rule out pulmonary embolism during pregnancy?

PRACTICE CHANGER

Use a clinical probability score to identify patients at low or intermediate risk for pulmonary embolism (PE) and combine that with a high-sensitivity D-dimer test to rule out PE in pregnant women.

STRENGTH OF RECOMMENDATION

B: Prospective diagnostic management outcome study.[1]

Righini M, Robert-Ebadi H, Elias A, et al. Diagnosis of pulmonary embolism during pregnancy: a multicenter prospective management outcome study. *Ann Intern Med.* 2018;169:766-773.[1]

ILLUSTRATIVE CASE

A 28-year-old G2P1001 at 28 weeks' gestation presents to your clinic with 1 day of dyspnea and palpitations. Her pregnancy has been otherwise uncomplicated. She reports worsening dyspnea with mild exertion but denies other symptoms, including leg swelling.

The current incidence of venous thromboembolism (VTE) in pregnant women is estimated to be a relatively low 5 to 12 events per 10,000 pregnancies, yet the condition is the leading cause of maternal mortality in developed countries.[2,3,4] Currently, there are conflicting recommendations among relevant organization guidelines regarding the use of D-dimer testing to aid in the diagnosis of pulmonary embolism (PE) during pregnancy. Both the Working Group in Women's Health of the Society of Thrombosis and Haemostasis (GTH) and the European Society of Cardiology (ESC) recommend using D-dimer testing to rule out PE in pregnant women (ESC Class IIa, level of evidence B based on small studies, retrospective studies, and observational studies; GTH provides no grade).[5,6]

Conversely, the Royal College of Obstetricians and Gynaecologists (RCOG), the Society of Obstetricians and Gynaecologists of Canada (SOGC), and the American Thoracic Society (ATS)/Society of Thoracic Radiology recommend against the use of D-dimer testing in pregnant women because pregnant women were excluded from D-dimer validation studies (RCOG and SOGC Grade D; ATS weak recommendation).[4,7,8] The American College of Obstetricians and Gynecologists does not have specific recommendations regarding the use of D-dimer testing during pregnancy, but has endorsed the ATS guidelines.[4,9]

In addition, SOGC recommends against the use of clinical prediction scores (Grade D), and RCOG states that there is no evidence to support their use (Grade C).[7,8] The remaining societies do not make a recommendation for or against the use of clinical prediction scores because of the absence of high-quality evidence regarding their use in the pregnant patient population.[4,5,6]

STUDY SUMMARY

Prospective validation of a strategy to diagnose PE in pregnant women

This multicenter, multinational, prospective diagnostic study involving 395 pregnant women evaluated the accuracy of PE diagnosis across 11 centers in France and Switzerland from August 2008 through July

2016.[1] Patients with clinically suspected PE were evaluated in emergency departments. Patients were tested according to a diagnostic algorithm that included pretest clinical probability using the revised Geneva Score for Pulmonary Embolism (www.mdcalc.com/geneva-score-revised-pulmonary-embolism), a clinical prediction tool that uses patient history, presenting symptoms, and clinical signs to classify patients as being at low (0-3/25), intermediate (4-10/25), or high (≥ 11/25) risk;[10] high-sensitivity D-dimer testing; bilateral lower limb compression ultrasonography (CUS); computed tomography pulmonary angiography (CTPA); and a ventilation-perfusion (V/Q) scan.

PE was excluded in patients who had a low or intermediate pretest clinical probability score and a negative D-dimer test result (< 500 mcg/L). Patients with a high pretest probability score or positive D-dimer test result underwent CUS, and, if negative, subsequent CTPA. A V/Q scan was performed if the CTPA was inconclusive. If the work-up was negative, PE was excluded.

Untreated pregnant women had clinical follow-up at 3 months. Any cases of suspected VTE were evaluated by a 3-member independent adjudication committee blinded to the initial diagnostic work-up. The primary outcome was the rate of adjudicated VTE events during the 3-month follow-up period. PE was diagnosed in 28 patients (7.1%) and excluded in 367 (clinical probability score and negative D-dimer test result [n = 46], negative CTPA result [n = 290], normal or low-probability V/Q scan [n = 17], and other reason [n = 14]). Twenty-two women received anticoagulation during the follow-up period for other reasons (mainly history of previous VTE disease). No symptomatic VTE events occurred in any of the women after the diagnostic work-up was negative, including among those patients who were ruled out with only the clinical prediction tool and a negative D-dimer test result (rate 0.0%; 95% confidence interval [CI], 0.0%-1%).

WHAT'S NEW

Clinical probability and D-dimer rule out PE in pregnant women

This study ruled out PE in patients with low/intermediate risk as determined by the revised Geneva score and a D-dimer test, enabling patients to avoid further diagnostic testing. This low-cost strategy can be applied easily to the pregnant population.

CAVEATS

Additional research is still needed

From the results of this study, 11.6% of patients (n = 46) had a PE ruled out utilizing the revised Geneva score in conjunction with a D-dimer test result, with avoidance of chest imaging. However, this study was powered for the entire treatment algorithm and was not specifically powered for patients with low- or intermediate-risk pretest probability scores. Since this is the first published prospective diagnostic study of VTE in pregnancy, further research is needed to confirm the findings that a clinical prediction tool and a negative D-dimer test result can safely rule out PE in pregnant women.

In addition, further research is needed to determine pregnancy-adapted D-dimer cut-off values, as the researchers of this study noted that < 500 mcg/L was useful in the first and second trimester, but that levels increased as gestational age increased.

CHALLENGES TO IMPLEMENTATION

None to speak of

Implementing a diagnostic algorithm that incorporates sequential assessment of pretest clinical probability based on the revised Geneva score and a D-dimer measurement should be relatively easy to implement, as both methods are readily available and relatively inexpensive. JFP

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