Diagnosis of suspected pulmonary embolism in pregnancy

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CORRESPONDENCE

Diagnosis of Suspected Pulmonary Embolism in Pregnancy

TO THE EDITOR: In reporting the results of the Artemis study, van der Pol et al. (March 21 issue)[1] suggest that a pregnancy-modified YEARS algorithm can safely rule out pulmonary embolism without the use of computed tomographic (CT) pulmonary angiography. In the DiPEP (Diagnosis of PE in Pregnancy) study involving 219 prospectively recruited pregnant women, we tested this approach and a similar strategy (described by Righini et al.[2]) involving clinical probability scoring and D-dimer measurements to avoid diagnostic lung imaging.[3,4]

The strategy described by van der Pol et al. would have resulted in the discharge of 96 of 219 women (43.8%) without scanning, but this number would have included 5 of 12 women with pulmonary embolism. The sensitivity of this strategy was 58.3% (95% confidence interval [CI], 27.7 to 84.8) and the specificity was 44.0% (95% CI, 37.1 to 51.0). The strategy described by Righini et al. would have resulted in the discharge of 46 of 219 women (21.0%) without scanning, including 3 of 12 women with pulmonary embolism (sensitivity, 75.0%; 95% CI, 42.8 to 94.5%; and specificity, 20.8%; 95% CI, 15.5 to 26.9).

These findings suggest that neither strategy accurately rules out pulmonary embolism and that the absence of events shown in prospective management studies may reflect a limited power to detect the consequences of a missed pulmonary embolism. The upper limits of the 95% confidence interval for the event rates of 0 among women who did not undergo scanning were 1.9% in the study by van der Pol et al.[1] and 7.7% in the study by Righini and colleagues.[2] The potentially catastrophic consequences of a missed pulmonary embolism mean that these strategies cannot be considered safe.

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TO THE EDITOR: The study by van der Pol et al. showed reduced maternal and fetal exposures to radiation and iodinated contrast when an algorithm based on clinical findings, D-dimer levels, and assessment for lower-extremity deep-vein thrombosis was used to detect pulmonary embolism. This algorithm limited the use of CT pulmonary angiography or ventilation–perfusion scanning.

In addition to their interesting approach, an alternative, emerging, radiation-free tool to diagnose pulmonary embolism in pregnant women is magnetic resonance imaging (MRI).[1] Although the use of gadolinium-based contrast agents is contraindicated because of uncertainty about fetal effects,[2] noncontrast magnetic resonance angiography using bright blood, steady-state, free-precession sequences can detect a pulmonary embolism in the central, lobar, segmental pulmonary arteries with sufficient image quality.[3]

If a contrast agent is required, initial studies have shown promising positive results with ferumoxytol, an iron-based, paramagnetic agent that increases the blood signal on T_1-weighted images.[4] Ferumoxytol is used on an off-label basis for magnetic resonance angiography in the United States because the Food and Drug Administration has limited its approval to use as an intravenous iron supplement. Recently, these imaging techniques have been gaining attention at some academic centers for the assessment of suspected pulmonary embolism in pregnant women.

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Dr. Bikdeli reports receiving consulting fees for serving as a consulting expert (on behalf of the plaintiff) in litigation related to a specific type of inferior vena caval filters; and Dr. Prince, holding patent agreements with Bayer, Bracco Diagnostics, GE Healthcare, and Guerbet/Mallinckrodt. No other potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: Goodacre et al. retrospectively analyzed the pregnancy-adapted YEARS algorithm and suggested that it could not be used safely to rule out pulmonary embolism. We disagree with their opinion. The DiPEP study, which prospectively and retrospectively followed women during and after pregnancy, was descriptive and did not involve a fixed algorithm.[1] In contrast, our study, which involved only pregnant women, had a predefined algorithm and design for the management of suspected pulmonary embolism with 3 months of follow-up. The assumption of Goodacre et al. that pulmonary embolism was the most likely diagnosis was made retrospectively in a considerable number of patients. Since the D-dimer threshold critically depends on the presence of no YEARS criteria rather than one to three YEARS criteria, these retrospective assumptions are per se not valid. Moreover, in the DiPEP study, D-dimer levels were not available for all included patients, and the majority of patients (240 of 328) received anticoagulant treatment for an unknown period, which causes false normalization of D-dimer levels.[1] Finally, the diagnosis of pulmonary embolism was not always confirmed by imaging tests but rather was based on clinical evaluation. We conclude that their observational and partly retrospectively collected data are not valid to evaluate the algorithm used in our study. Our strategy led to a very low incidence of diagnostic failure, as evidenced by the incidence of venous thromboembolism at 3 months of 0.21% (95% CI, 0.04 to 1.20). In addition, CT pulmonary angiography was avoided in 65% of the patients who began the study in the first trimester and in 32% who began in the third trimester.

Mehdipoor et al. suggest the use of MRI without contrast agents to confirm or exclude the diagnosis of pulmonary embolism. We agree that in pregnant patients, magnetic resonance angiography is contraindicated because of uncertain long-term effects of gadolinium on the fetus,[2] and we are aware of the development of MRI techniques for thrombus detection without contrast.[3] MRI techniques cannot be used in routine clinical practice in the diagnostic workup of suspected pulmonary embolism in pregnant and nonpregnant women because outcome studies showing sufficient safety and feasibility are lacking. Moreover, published studies have mostly shown high rates of nondiagnostic imaging results. Although CT pulmonary angiography and ventilation–perfusion scanning are associated with radiation exposure, the risk–benefit ratio clearly favors the early detection of potentially fatal pulmonary embolism.[4] If CT pulmonary angiography or ventilation–perfusion scanning is not performed in pregnant patients with suspected pulmonary embolism and a D-dimer level above the YEARS threshold, a pulmonary

embolism may be missed, with associated morbidity and mortality.

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