Diagnosis of deep vein thrombosis and pulmonary embolism in pregnancy: a systematic review
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CRD summary
This review assessed the ability of various tests to rule out deep vein thrombosis and pulmonary embolism during pregnancy. Three small studies were included and no formal quality assessment was undertaken. The authors' conclusions that impedance plethysmography and serial compression ultrasonography can be used to exclude deep vein thrombosis, and that negative or non-diagnostic ventilation perfusion scans can be used to exclude pulmonary embolism, should be interpreted with caution given the limited evidence.

Authors' objectives
To determine the accuracy of diagnostics tests performed for a clinical suspicion of pulmonary embolism (PE) or deep vein thrombosis (DVT) during pregnancy.

Searching
PubMed (1966 to November 2004), EMBASE (1980 to November 2004), the Cochrane Library (Issue 1, 2005) and Web of Science were searched; the keywords were reported. The reference lists of retrieved articles were reviewed for additional studies. No language restrictions were applied. The authors stated that they attempted to identify published clinical studies.

Study selection
Study designs of evaluations included in the review
Studies that enrolled consecutive patients were eligible for inclusion in the review. The duration of follow-up, where reported, ranged from 6 weeks to 20 months.

Specific interventions included in the review
The studies had to use validated tests to diagnose DVT and PE. These were compression ultrasonography (CUS), impedance plethysmography (IPG) or venography for a suspicion of DVT, or magnetic resonance imaging for a suspicion of iliac vein thrombosis, and pulmonary angiography, helical computed tomography or ventilation perfusion (VQ) lung scanning for PE. One included study evaluated CUS plus a SimpliRed D-dimer (SRDD) test.

Reference standard test against which the new test was compared
This was not a review of the accuracy of standard tests and the included studies did not use a reference standard.

Participants included in the review
Studies of pregnant women with a clinical suspicion of DVT or PE were eligible for inclusion. One of the included studies also included postpartum women with suspected DVT.

Outcomes assessed in the review
The primary outcome appeared to be the incidence of venous thromboembolic events during follow-up. The studies had to use validated diagnostic testing in patients with suspected venous thromboembolism (VTE) in follow-up, describe a pre-specified duration of follow-up of patients with negative tests, and withhold anticoagulant treatment in patients with negative tests. The included studies followed up patients using serial IPG or serial CUS.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed studies for inclusion. Any disagreements were resolved through referral to a third reviewer.
Assessment of study quality
The authors did not state that they assessed validity. However, stringent inclusion criteria, which included some methodological features, were applied.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. For each study, the number of patients with normal results on serial IPG or CUS, the number with VTE, and the percentage and 95% confidence interval (CI) of women with VTE, were reported.

Methods of synthesis
How were the studies combined?
The authors did not combine the results of the studies. Instead they summarised each individual study.

How were differences between studies investigated?
Differences between the studies were not formally assessed.

Results of the review
Four studies (n=282) were included. Three studies evaluated patients with suspected DVT and one retrospective study evaluated patients with suspected PE (n=121).

Diagnosis of DVT (3 studies).
Two studies evaluated the validity of negative results by serial IPG. In one study, 139 out of 152 patients had a normal result on serial IPG and none had a VTE 3 months postpartum (0%, 95% CI: 0, 2.1). In the second study, 45 out of 77 obstetric women (47 pregnant, 30 postpartum) with suspected DVT had normal serial IPG and none had VTE during 6 months' follow-up (0%, 95% CI: 0, 6.4).

The third study evaluated CUS combined with an SRDD test. None of the 31 women with a normal scan on both CUS and SRDD was diagnosed with DVT during follow-up (0%, 95% CI: 0, 9.2). Four of 18 women with normal CUS but abnormal SRDD were diagnosed with DVT on serial CUS; none of the remaining 14 women developed DVT on follow-up (0%, 95% CI: 0, 19.3).

Diagnosis of PE (1 study).
Of 121 pregnant women, 8 were receiving treatment for VTE prior to VQ scanning. In the remaining 113 women, 83 scans were interpreted as normal, 28 as non-diagnostic and two as high probability. Of these, 104 women did not receive anticoagulation treatment (80 with normal and 24 with non-diagnostic scans). None of these women experienced a thromboembolic event during a mean follow-up period of over 20 months (0%, 95% CI: 0, 1).

Authors' conclusions
Two studies supported withholding anticoagulant therapy in pregnant women with a clinical suspicion of DVT and normal results on serial IPG. However, this technique is no longer used. One study showed that a normal CUS at presentation combined with a normal D-dimer test, or an abnormal D-dimer test combined with a normal serial CUS, appeared promising for safely excluding DVT in pregnant women. One study concluded that anticoagulant therapy may be safely withheld in pregnant women with a normal or non-diagnostic VQ scan, but this needs confirmation in larger studies.

CRD commentary
This review addressed focused questions supported by clearly defined inclusion criteria. However, these criteria were fairly stringent and it might have been preferable to have included a broader range of studies (e.g. by not restricting to
consecutive patients) and to include a thorough quality assessment, which was not undertaken in this review. The
literature search was reasonable but did not include attempts to locate unpublished studies, thus the review may be
subject to publication bias. Some details of the review process were reported, such as appropriate steps to minimise
bias.

Limited details of the included studies were reported in the text, but it would have been helpful to have had a table of
study details to summarise further relevant information. In particular, features that raised the clinical suspicion of DVT
or PE were not reported, which makes it difficult to determine which population these results may apply to. The
narrative synthesis was appropriate given the small number of studies and the differences between these studies.
However, the authors only considered the consequences of negative findings on the tests evaluated and did not discuss
the consequences of positive findings. It is unclear whether this was because they chose to focus on the negative
findings for this review, or because this was all that was evaluated in the primary studies. A more informative analysis
would have considered test accuracy measures such as sensitivity and specificity, if possible from the information
provided in the primary studies. The authors' conclusions are supported by the results presented, but should be
interpreted with some degree of caution given the small number of studies with relatively small sizes and the fact that
no formal quality assessment was undertaken.

Implications of the review for practice and research
Practice: The authors made a number of recommendations for practice, but these were not based solely on the
conclusions of their report; they also considered biological plausibility and other data, including that from non-pregnant
women not evaluated in the review. The authors acknowledged that the recommendations were partly based on their
own personal opinions. They stated that CUS should be performed as a first test in pregnant women with a clinical
suspicion of DVT. Patients with an abnormal CUS can be diagnosed with DVT and should be treated appropriately.
Patients with a normal CUS should undergo serial CUS testing. If CUS becomes abnormal, DVT can be diagnosed. If
doubt about the presence of DVT persists, limited venography with abdominal shielding should be considered. The
authors also stated that when confronted with a clinical suspicion of PE in a pregnant woman, one should start with VQ
scan, helical computed tomography or bilateral CUS, depending on local availability and expertise. Management
algorithms were presented.

Research: The authors stated that there is a need for large prospective studies evaluating currently available and new
tests for the diagnosis of DVT in pregnant women. The use of CUS with or without D-dimer testing merits further
evaluation. Large prospective studies are needed to evaluate diagnostic strategies for pregnant women with suspected
PE.

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