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CLINICAL RESEARCH STUDY

Cost-effectiveness of prophylactic low molecular weight heparin in pregnant women with a prior history of venous thromboembolism

Joseph A. Johnston, MD, MSc,[a,b] Patrick Brill-Edwards, MD,[c] Jeffrey S. Ginsberg, MD,[c] Stephen G. Pauker, MD,[d] Mark H. Eckman, MD, MS[b]

[a]*The Health Services Research and Development Service, Veterans Affairs Medical Center, Cincinnati, Ohio;*
[b]*Department of Internal Medicine and Center for Clinical Effectiveness, Institute for Health Policy and Health Services Research, University of Cincinnati Medical Center, Cincinnati, Ohio;*
[c]*Department of Medicine, McMaster University, Hamilton, Ontario, Canada; and*
[d]*Department of Medicine, New England Medical Center, Boston, Massachusetts.*

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ABSTRACT

PURPOSE: Women with a history of prior venous thromboembolism have an increased risk for recurrence during pregnancy. Although thromboprophylaxis reduces this risk, recent evidence suggests that, in many cases, prophylaxis can be safely withheld because the estimated recurrence risk is very low. The balance of risks and benefits in women with different recurrence risks has not been examined.

METHODS: We developed a Markov state transition decision analytic model to compare prophylactic low molecular weight heparin to expectant management for pregnant women with a single prior venous thromboembolism. A lifetime time horizon and societal perspective were assumed. Input data were obtained by literature review. Outcomes were expressed as U.S. dollars per quality-adjusted life-year (QALY).

RESULTS: For "low-risk" women with a prior venous thromboembolism associated with a transient risk factor and no known thrombophilic condition (recurrence risk 0.5%), expectant management was both more effective and less costly than prophylaxis. For "high-risk" women with prior idiopathic venous thromboembolism or known thrombophilic condition (recurrence risk 5.9%), prophylaxis was associated with a reasonable cost-effectiveness ratio ($38,700 per QALY) given a risk of bleeding complications $<1.0\%$ (base case 0.5%).

CONCLUSION: For low-risk women with prior venous thromboembolism, expectant management during pregnancy leads to better outcomes than administration of prophylactic low molecular weight heparin. For high-risk women, antepartum thromboprophylaxis is a cost-effective use of resources.

Venous thromboembolism, including deep venous thrombosis and pulmonary embolism, is an important cause of morbidity and mortality in pregnancy.[1-4] Women with a prior history of venous thromboembolism are at a particularly high risk; the true incidence is unknown, but estimates are from zero to 13%.[5-9]

This study was conducted while Dr. Johnston was a research fellow at the University of Cincinnati Medical Center.

Requests for reprints should be addressed to Joseph A. Johnston, MD, MSc, Lilly Corporate Center, Indianapolis, Indiana 46285.

E-mail address: johnstonja@lilly.com.

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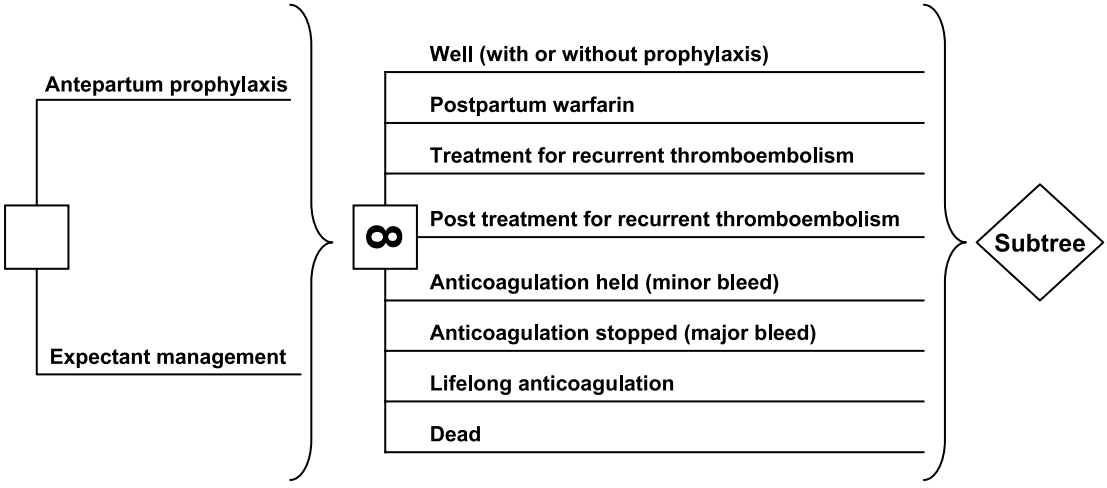

Figure 1 Markov State Transition Model. This diagram depicts the Markov state transition decision model used in the analysis. The solid square on the left represents a "decision" node, from which 2 branches, representing alternative management strategies, emanate. Each strategy leads to the same Markov node, represented by the solid square with the "∞" symbol inside. The branches leading from the Markov node represent the various potential health states patients pass through during the model simulation. Although the potential states for each strategy are the same, the initial distribution of patients among states and the probabilities associated with transitions between states will differ between strategies.

In other high-risk populations, anticoagulant therapy is both efficacious and cost-effective for the prevention of venous thromboembolism.[10-13] However, prophylactic anticoagulation during pregnancy is problematic for several reasons. Vitamin K antagonists (eg, warfarin) are teratogenic, particularly when given during the first trimester.[4,14] Although safe for the fetus, both unfractionated heparin and low molecular weight heparin are inconvenient and uncomfortable to use because they must be given parenterally. Unfractionated heparin and to a lesser extent low molecular weight heparin can cause thrombocytopenia as well as osteoporosis (which may be reversible) and symptomatic fracture when given for longer than 1 month, and low molecular weight heparin is expensive.[14-26] Furthermore, anticoagulation increases the risk of bleeding, particularly at the time of delivery.[27-29]

Thus, the optimal strategy for pregnant patients with prior venous thromboembolism remains unclear. For some women, for example, those with prior venous thromboembolism associated with a transient risk factor (eg, acute trauma, prolonged immobilization, or oral contraceptive use) and no known thrombophilic condition, the risk of recurrence is very low and antepartum surveillance without thromboprophylaxis, followed by postpartum anticoagulants, has been recommended.[27] For other subgroups of women, recommendations regarding the use of antepartum thromboprophylaxis are unclear; unfractionated heparin and low molecular weight heparin prophylaxis throughout pregnancy or clinical surveillance without thromboprophylaxis have been recommended.[27] Mitigating against a heparin compound is a recent study in which prophylaxis was withheld from 125 pregnant women with prior venous thromboembolism; the risk of recurrence was low (2.4%).[9] Those favoring prophylaxis point to trials demonstrating that unfractionated heparin and low molecular weight heparin are effective in preventing venous thromboembolism in other high-risk patients and that even a low risk of recurrence is too high.[6,30-33]

Limited evidence is available from clinical trials of pregnant patients with a history of venous thromboembolism, and randomized studies to date have been powered only to examine safety[6] or have included only high-risk women.[33] In addition, the cost-effectiveness of prophylactic therapy has not been properly examined. In the absence of such studies, we developed a decision analytic model to compare the effectiveness and cost-effectiveness of prophylactic low molecular weight heparin with clinical vigilance and investigation of symptomatic women during the antepartum period.

Methods

Decision analytic model

We constructed a Markov state transition decision model examining two strategies: antepartum prophylaxis with low molecular weight heparin; and expectant management during the antepartum period without prophylaxis (Figure 1). We assumed a societal perspective and used a 6-week time interval in modeling both antepartum events and future lifetime events. Model parameters were based on a review of the existing English-language literature. In view of the limited evidence available from clinical trials, we based many model assumptions regarding patient characteristics upon the recent study by Brill-Edwards and colleagues.[9] In this study, 125 women with prior venous thromboembolism