No. 308, June 2014 (Replaces No. 95, September 2000)

Venous Thromboembolism and Antithrombotic Therapy in Pregnancy

This clinical practice guideline has been prepared by the VTE in Pregnancy Guideline Working Group, reviewed by Maternal Fetal Medicine and Family Physician Advisory committees, and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

PRINCIPAL AUTHORS

Wee-Shian Chan, MD, Vancouver BC

Evelyne Rey, MD, Montreal QC

Nancy E. Kent, MD, Vancouver BC

VTE IN PREGNANCY GUIDELINE WORKING GROUP

Wee-Shian Chan, MD (Co-Chair), Vancouver BC

Nancy E. Kent, MD (Co-Chair), Vancouver BC

Evelyne Rey, MD (Co-Chair), Montreal QC

Thomas Corbett, MD, Edmonton AB

Michèle David, MD, Montreal QC

M. Joanne Douglas, MD, Vancouver BC

Paul S. Gibson, MD, Calgary AB

Laura Magee, MD, Vancouver BC

Marc Rodger, MD, Ottawa ON

Reginald E. Smith, Pharm D, Victoria BC

Disclosure statements have been received from all contributors.

Abstract

Objective: To present an approach, based on current evidence, for the diagnosis, treatment, and thromboprophylaxis of venous thromboembolism in pregnancy and postpartum.

Evidence: Published literature was retrieved through searches of PubMed, Medline, CINAHL, and The Cochrane Library from November 2011 to July 2013 using appropriate controlled vocabulary (e.g. pregnancy, venous thromboembolism, deep vein thrombosis, pulmonary embolism, pulmonary thrombosis) and key words (e.g., maternal morbidity, pregnancy complications, thromboprophylaxis, antithrombotic therapy). Results were restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies published in English or French. There were no date restrictions. Grey (unpublished) literature was identified through searching the websites of clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Values: The quality of evidence in this document was rated using the criteria described in the Report of the Canadian Task Force on Preventative Health Care (Table 1).

Key Words: Venous thromboembolism, deep vein thrombosis, pulmonary embolism, thromboprophylaxis, assisted reproductive technology, heparin, neuraxial analgesia, adverse pregnancy outcomes, pregnancy or puerperal complications

Recommendations

1. Objective testing is required following clinical suspicion of deep vein thrombosis or pulmonary embolism. (II-2A)
2. For the diagnosis of deep vein thrombosis, ultrasonography is recommended, and should be repeated at least once over 7 days if the initial study is negative. For each examination, the entire length of the venous system from the external iliac to the popliteal vein must be visualized and compression manoeuvres performed from the femoral to the popliteal vein. (II-2B)
3. For the diagnosis of pulmonary embolism, either ventilation-perfusion scan or computed tomographic angiography can be used. (II-2A) In pregnant women, a ventilation-perfusion scan is the preferred test. (III-B)
4. Neither D-dimer alone nor clinical prediction rules should be used to rule out venous thromboembolism in pregnant women without objective testing. (III-D)
5. Pregnant women diagnosed with acute venous thromboembolism should be hospitalized or followed closely as outpatients for the first 2 weeks after the initial diagnosis. (III-C)
6. Low molecular weight heparin is the preferred pharmacologic agent over unfractionated heparin for the treatment of venous thromboembolism in pregnancy. (II-2A)
7. Heparin-induced thrombocytopenia in pregnant women is extremely rare. Consultation with a hematologist or thrombosis specialist is recommended to consider the use of heparanoids for treatment of venous thromboembolism if it occurs. (II-3B)

J Obstet Gynaecol Can 2014;36(6):527–553

Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

Quality of evidence assessment*	Classification of recommendations†
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2: Evidence from well-designed cohort (prospective or retrospective) or case–control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category	D. There is fair evidence to recommend against the clinical preventive action
	E. There is good evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.[187]

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.[187]

8. Vitamin K antagonists should only be considered in exceptional circumstances for the treatment of venous thromboembolism in pregnancy. (II-2A)
9. We recommend against the use of oral Xa inhibitors and oral direct thrombin inhibitors for the treatment of venous thromboembolism in pregnancy. (III-D)
10. For the treatment of acute venous thromboembolism in pregnancy we recommend adhering to the manufacturer's recommended dosing for individual low molecular weight heparins based on the woman's current weight. (II-1A) Low molecular weight heparin can be administered once or twice a day depending on the agent selected. (III-C)
11. For pregnant women initiated on therapeutic low molecular weight heparin, baseline platelet counts should be done and repeated a week later to screen for heparin-induced thrombocytopenia. (III-C)
12. For pregnant women with an acute venous thromboembolism we recommend therapeutic anticoagulation for a minimum of 3 months. (I-A)
13. Following initial treatment, anticoagulation intensity can be decreased to intermediate or prophylactic dose for the remainder of the pregnancy and for at least 6 weeks postpartum. (III-C)
14. In pregnant women with acute proximal leg deep vein thrombosis, the use of graded compression stockings can be considered for relief of symptoms. (III-C)
15. Thrombolytic therapy in pregnancy should only be considered in limb-threatening deep vein thrombosis or massive pulmonary embolism. (III-C)
16. Vena cava filters should only be used in pregnant women with acute pulmonary embolism or deep vein thrombosis and contraindications to anticoagulation. (III-C)
17. Computed tomographic venography and/or magnetic resonance imaging should be performed to rule out cerebral venous thrombosis if suspected. (I-C)
18. Therapeutic dose anticoagulation should be initiated for confirmed cerebral venous thrombosis. (II-2A)
19. Thromboprophylaxis should be considered in future pregnancies following a cerebral venous thrombosis. (II-1C)
20. For superficial thrombophlebitis, compression ultrasound should be performed to exclude deep vein thrombosis (II-2A), and it should be repeated if proximal extension is suspected based on worsening phlebitis. (III-C)
21. Prophylactic or intermediate dose low molecular weight heparin for 1 to 6 weeks is recommended for women with bilateral superficial thrombophlebitis, for very symptomatic women, and for superficial thrombophlebitis located ≤ 5 cm from the deep venous system (saphenofemoral and saphenopopliteal junctions) or affecting ≥ 5 cm of vein. (I-A)
22. Observation alone is recommended in women with superficial thrombophlebitis at low risk of deep vein thrombosis and for those who do not require symptom control. Clinical follow-up of these women should occur within 7 to 10 days, with a repeat compression ultrasound within one week. (I-A)
23. Computed tomography and/or magnetic resonance imaging (with or without angiography) are the definitive imaging modalities to rule out ovarian vein thrombosis. (II-2A)
24. For confirmed ovarian vein thrombosis, we recommend parenteral broad-spectrum antibiotics, continued for at least 48 hours after defervescence and clinical improvement. (II-2A) Longer antibiotic therapy is necessary for septicemia or complicated infections. (III-C)
25. For confirmed ovarian vein thrombosis, therapeutic dose anticoagulation could be considered for 1 to 3 months. (III-C)
26. Routine screening for all inherited thrombophilias in all women with a first episode of venous thromboembolism diagnosed in pregnancy is not indicated. (III-C)
27. Testing for protein S, protein C, and antithrombin deficiencies is indicated following a venous thromboembolism in pregnancy if there is a family history of these particular thrombophilias, or if thrombosis occurs in an unusual site. (III-C)