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Obstetrical venous thromboembolism: Epidemiology and strategies for prophylaxis

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ABSTRACT

Venous thromboembolism (VTE) is a leading cause of severe maternal morbidity and mortality. While pregnancy alone is a risk factor for VTE, additional population-based risk factors such as obesity are becoming increasingly common, particularly in the developed world. Maternal death from VTE is amenable to prevention and VTE thromboprophylaxis is the most readily implementable means of systematically reducing the maternal death rate. In the United States, prophylaxis is recommended primarily for patients at extremely high risk for thromboembolism and women undergoing cesarean delivery, whereas in the United Kingdom a larger proportion of the population is targeted. Given the maternal burden of obstetric VTE and varying strategies for prevention, this article will provide a review of the following topics: (1) global epidemiology of obstetric VTE, (2) prophylaxis guidelines in the United States and the United Kingdom, and (3) maternal mortality from VTE in the United States and the United Kingdom in the setting of differing prophylaxis strategies.

Introduction

Obstetric venous thromboembolism (VTE) is a leading cause of maternal mortality in the developed world.[1–4] Maternal death from VTE is amenable to prevention and thromboprophylaxis is the most readily implementable means of systematically reducing the maternal death rate. In the United States, strategies to reduce venous thromboembolism (VTE) have focused primarily on perioperative cesarean prophylaxis and prenatal risk assessment of women at particularly high risk for events.[5–9] In the United Kingdom, national guidelines similarly recommend postpartum pharmacologic prophylaxis for women with prior venous thrombolic events and/or thrombophilias. Additionally, these guidelines recommend prophylaxis for other common risk factors including obesity, maternal age >35 years, smoking, preeclampsia, postpartum hemorrhage, and prolonged labor.[4,10] As a result, the United Kingdom recommendations support pharmacologic prophylaxis for a much larger proportion of the obstetric population.

Given these varying recommendations for prevention, and the maternal burden posed by obstetric VTE, this review will cover the following topics:

1. An overview of obstetric venous thromboembolism risk factors and incidence.
2. Guidelines for prevention of obstetric VTE from major societies in the United States and United Kingdom.

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3. Review of maternal mortality trends from VTE in the United Kingdom and the United States in the setting of differing guideline recommendations.

Global epidemiology

Venous thromboembolism accounts for a larger proportion of maternal deaths in developed as compared to developing countries.[11] In part, this is secondary to death from hemorrhage, sepsis, obstructed labor, hypertension, and other medical conditions occurring much more frequently in the developing world and thus accounting for a larger proportion of deaths. In the developed world death from hemorrhage and sepsis are relatively rare on a population basis and thromboembolism is responsible for a larger proportion of mortality.[12] Overall series suggest that approximately 2% of maternal deaths in the developing world may be due to thromboembolism. The Confidential Enquiry into Maternal Death in South Africa found that embolism was responsible for 2.0%, 1.9%, and 1.4% of deaths in 1999–2001, 2002–2004, and 2005–2007, respectively.[13] Other reports from Africa implicate embolism in a similar proportion of deaths.[14–16] In contrast, a systematic review of maternal deaths performed by the World Health Organization implicated embolism in 14.9% of maternal deaths in developed countries,[1] and the United Kingdom's Confidential Enquiries into Maternal Death found that from 2003 to 2005 thromboembolism caused 31.1% of deaths directly related to pregnancy.[4]

Increasing incidence of VTE events may represent a contributing factor to the relatively large proportion of maternal death secondary to this cause in the developed world. Callaghan et al.[2] analyzed data from the Nationwide Inpatient Sample (NIS) and found that thrombotic embolism increased 72% between 1998 and 2009 for women hospitalized for delivery. In particular for women who are hospitalized for vaginal delivery—and who rarely receive prophylaxis in the United States—risk may be increasing.[17] Increased risk for VTE may be related to more prevalent population-based risk factors including obesity, cesarean delivery, advanced maternal age, and medical comorbidities. The 2009–2010 National Health and Nutrition Examination Survey found that 31.9% of U.S. women aged 20–39 had a body mass index $>30\ kg/m^2$, with rates increasing perennially over 3 decades.[18] From 1990 through 2012 birth rates for women age 35–39 and 40–44 in the United States rose steadily in the setting of overall declining fertility.[19]

These increasingly prevalent risk factors are commonly implicated in obstetric VTE. Data from the Nationwide Inpatient Sample demonstrated that medical and obstetrical conditions including diabetes, heart disease, hypertension, obesity, blood transfusion, hemorrhage, pre-eclampsia and postnatal infection were each significantly more likely to be present during delivery hospitalizations during which VTE occurred in 2006–2009 compared to 1994–1997.[13] A population-based study from the United Kingdom of 376,154 pregnancies demonstrated that in an adjusted model (accounting for mode of delivery) obesity, multiparity, and hemorrhage were associated with increased risk for VTE with incidence risk ratios (IRR) of 3.45 (95% CI: 2.54–4.69), 1.92 (95% CI: 1.22–2.99), and 2.53 (95% CI: 1.34–4.79), respectively.[10] Increased risk for events has also been noted during and shortly after non-delivery hospitalizations.[20] Other reports from diverse data sets similarly support an association between obstetric, demographic and medical factors, and obstetric VTE risk.[10,21–26]

Major society guidelines for thromboembolism prophylaxis in the United States and the United Kingdom

This section reviews society obstetric thromboprophylaxis and risk assessment guidelines from:

(1) The American Congress of Obstetricians and Gynecologists (ACOG).
(2) The American College of Chest Physicians (ACCP).
(3) The Royal College of Obstetricians and Gynaecologists (RCOG).

While VTE risk assessment is a Joint Commission recommendation (core measure VTE 1), commonly used medical and surgical systems are not tailored to obstetric patients and universal risk-factor-based screening of obstetric patients on a hospital basis in the United States is rare.[27,28]

Recommendations from the American Congress of Obstetricians and Gynecologists

Risk-factor-based prophylaxis

ACOG recommends antenatal and post-partum pharmacologic prophylaxis with low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH) for a very small portion of obstetric patients at particularly high risk for thromboembolism (Table 1)—those women with prior events and/or thrombophilias.[6,29] Antenatal pharmacologic prophylaxis is recommended for all women who have had prior events, except those with a single provoked event caused by a transient risk factor that is no longer present and is not estrogen related (such as pregnancy or birth control). Postpartum criteria for prophylaxis are similar with the exception that pharmacologic prophylaxis is recommended for women with prior unprovoked events as well as for women with low-risk thrombophilias in the setting of other major risk factors.

Cesarean delivery thromboprophylaxis

For cesarean delivery, ACOG recommends universal perioperative use of pneumatic compression devices for all women not already receiving pharmacologic thromboprophylaxis.[6] Available data and expert opinion support the use of pneumatic compression device thromboprophylaxis for all women undergoing cesarean delivery.[30] ACOG recommendations are otherwise not prescriptive about post-cesarean prophylaxis; pharmacologic prophylaxis may be used for women with additional risk factors, however, criteria are not specified.