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Anaesthetic Management of Thromboembolic Disorders in Obstetric Patients

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Abstract
Background: Thromboembolic Disorders, especially venous (VTE), pose a serious risk to obstetric patients, especially during pregnancy and the postpartum period, because to variables such as the ageing of the mother population, the prevalence of obesity, and the growing frequency of caesarean sections. Mortality rates remain at around 1.5 per 100,000 births in the UK, despite the fact that the total risk of VTE during pregnancy is minimal (0.2%). These results highlight the crucial nature of this problem in obstetric care and the immediate need for improved prevention, diagnostic, and treatment techniques. **Objective:** This This systematic study intended to provide an actionable approach for identifying, diagnosing, and treating obstetric patients with thromboembolic diseases in anesthesiology. **Conclusions:** Effective Obstetric patients with thromboembolic diseases need a multimodal strategy to therapy, including close monitoring of coagulation status and the prompt use of anticoagulation for either prophylaxis or treatment. Neuraxial blockade should be conducted with caution, and understanding of the possible dangers connected with the insertion and removal of catheters is crucial. In addition, the proper length of medication and prompt postpartum care are key factors in lowering the incidence of VTE.

Keywords: Thromboembolic Conditions, Giving Birth, Anesthesia, Neuraxial Blockade, Thromboembolic Diseases.

1. Introduction

Venous About 1.2 out of every 1000 pregnancies are affected by venous (VTE). In high-income nations, thrombosis and are the primary causes of maternal morbidity (1). The most common cause of direct maternal mortality in the United Kingdom and Ireland between the third trimester of pregnancy and six weeks after delivery is venous (VTE), which comprises deep vein thrombosis (DVT) and pulmonary embolism (PE). Those lucky enough to make it through may suffer from post-thrombotic syndrome (PTS) or chronic thromboembolic pulmonary hypertension (CTEPH) later in life (2).

It has been observed that a woman's chance of developing a venous (VTE) increases by a factor of four to six during pregnancy and by a factor of up to sixty in the weeks after delivery. This higher risk of VTE during pregnancy is thought to be due to the hypercoagulable condition of pregnancy, which developed to protect from severe bleeding during labour and miscarriage (3).

Keep in mind "Virchow's trinity," which consists of venous stasis, endothelial injury, and hypercoagulability, to understand the aetiology of this prothrombotic condition. It is estimated that a 50% drop in venous flow may be noticed between weeks 25 and 29 of pregnancy, and that this reduction in venous flow may last until weeks 6 postpartum due to a hormonally driven decrease in vascular tone and blockage of venous flow by the growing uterus. Damage to the endothelium of the veins in the pelvis may occur during labour and delivery or as a result of venous hypertension (4).

Non-specific signs and symptoms of deep vein thrombosis (DVT) include lower leg oedema and discomfort, which are also common pregnancy symptoms. DVTs are more likely in the left leg of pregnant who are experiencing symptoms. The increased risk of iliofemoral DVT in the third trimester is thought to be caused by the gravid uterus pressing on the left iliac vein where it crosses the right iliac artery. The vast majority of thrombi may be seen in the proximal iliac or femoral veins. Thrombi most often occur in the calf arteries of non-pregnant individuals. Diagnosing a pulmonary embolism (PE) during pregnancy might be challenging. It may not be readily clear which patient has benign pathology and which has a significant, life-threatening diagnosis since the physiological changes of pregnancy sometimes resemble those of PE. Heart palpitations, nervousness, chest discomfort, cyanosis, profuse perspiration, and a cough might all point to pulmonary embolism (5).

The Wells and Geneva criteria, which are often used in nonpregnant patients, have not been validated for use in pregnant . Because of this, identifying VTE during pregnancy might be difficult. presenting with symptoms and indications of an acute PE should first have basic examinations such an electrocardiogram (ECG) and a chest X-ray, as recommended by

the Royal College of Obstetricians and Gynecologists (RCOG). These recommendations do not advise routine D-dimer testing for pregnant who have suspected acute VTE. This is because levels of the protein D-dimer rise as pregnancy progresses. If a woman appears with symptoms of DVT and suspicion of PE, a compression duplex ultrasound should be done. Once a DVT diagnosis has been made, therapy for the condition should continue and additional diagnostic testing is not required. who have symptoms and risk factors for PE but no evidence of DVT should undergo additional testing, such as a ventilation/perfusion (V =Q_) lung scan or CT pulmonary angiography (CTPA) (6).

In pregnant with hemodynamic stability, low-molecular-weight heparin is the therapy of choice for venous (). The molecular weight of the heparins in is around 5000 kDa. They evolved from unfractionated heparin (UFH) and quickly replaced it as the gold standard in clinical settings that had recommended UFH. Its several advantages include the following: decreased platelet binding, resulting in almost no heparin-induced thrombocytopenia; increased bioavailability (92-100%); and a longer half-life, resulting in the requirement for fewer dose intervals, all of which translate to less bleeding for the same antithrombotic action. Heparins are safe for pregnant to use since they do not enter the foetal circulation. who are hemodynamically unstable due to a major pulmonary embolism, who are in labour or have a significant risk of bleeding, who are allergic to heparin, and who have severe renal impairment are all examples of situations in which routine therapy is insufficient. It is recommended that the obstetrician, haematologist, and anaesthetist all work together to care for these (7).

Several anaesthesia professional organisations have produced guidelines on the use of neuraxial anaesthesia for anticoagulated patients. Despite differences in pharmacokinetics of anticoagulants, competing risks of general anaesthesia, and foetus development, pregnant and nonpregnant are treated similarly in anaesthesia recommendations such as the American Society for Regional Anesthesia (ASRA) guidelines, which were first published in 1998 and are based on expert consensus opinion, pharmacokinetic principles (such as elimination half-lives), and vigilant tracking of spinal epidural hematoma (SEH) cases. The only recommendations that take into account the kind of neuraxial technique used (single injection spinal vs. epidural) and its effect on maternal morbidity and mortality are those of the Scandinavian Society of Anesthesiology and Intensive Care Medicine. Professional organisations and the US Food and Drug Administration (FDA) agree that a neuraxial procedure or the withdrawal of an epidural catheter must wait 12 hours after "prophylactic" doses of (e.g., enoxaparin 40 mg subcutaneous [SQ] once daily or 30 mg SQ twice daily) and 24 hours after "therapeutic" doses of (e.g., enoxaparin 1 mg/kg SQ twice daily (8).

The purpose of this study was to provide a workable outline for the prevention, diagnosis, and management of thromboembolic diseases in obstetric patients undergoing anaesthetic procedures.

2. in the veins (VTE)

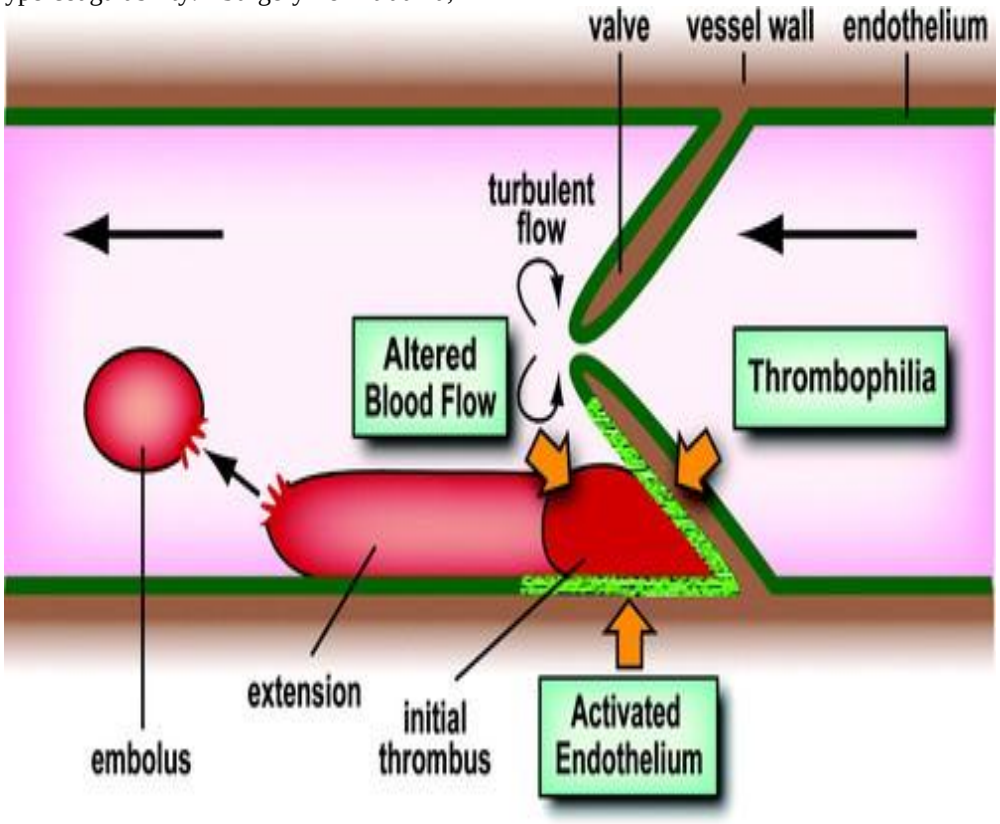
A blood clot in a vein is medically referred to as venous (VTE). VTE include both pulmonary embolism and deep vein thrombosis (DVT) (PE). A deep vein thrombosis (DVT) develops when a blood clot forms in the lower leg, thigh, or pelvis. DVTs may also develop in the arms, and this is particularly true if a big intravenous central line is already implanted in the vein. When a blood clot breaks away and travels through the circulatory system to the lungs, it is called a pulmonary embolism. Instances of VTE are prevalent. Annual VTE incidence in the US is estimated at 600,000. (9).

Serious surgery, major injury, and periods of infection and inflammation all increase the chance of having VTE. This is because vein damage from surgery or injury increases the risk of blood clot formation. The risk of blood clots increases with inactivity, such as after surgery or during lengthy car rides. The risk of blood clots is further increased by inflammation and severe illness. Symptoms of deep vein thrombosis include inflammation, redness, and discomfort. The symptoms of a pulmonary embolism include acute chest discomfort and difficulty breathing (10).

Anticoagulation is the cornerstone of treatment for DVT, with the objective of avoiding progression to PE and recurrence of thrombosis. The 30-day death rate surpasses 3 percent in patients with DVT who are not anticoagulated, and this mortality risk rises 10-fold in individuals who develop PE. DVT therapy has changed significantly with the introduction of direct oral anticoagulants (DOACs), prompting a comparison of these novel medicines to the tried-and-true vitamin K-antagonists (VKAs) (11).Pathogenesis

First established in 1856, Virchow's Triad suggests that venous stasis, vascular damage, and hypercoagulability all have a role in the

development of thrombosis. Venous stasis is the most critical of the three elements, yet stasis alone seems to be inadequate to trigger thrombus development. However, the risk of clot formation is considerably amplified when venous stasis is present with vascular damage or hypercoagulability. Surgery or trauma, malignancy, extended immobility, pregnancy, congestive heart failure, varicose veins, obesity, advanced age, and a history of DVT (12) are the clinical factors most closely linked with DVT and are essentially connected to the aspects of Virchow's Triad (Figure 1).



A thrombus forms in a deep vein, as seen in Figure 1. In the diagram, thrombophilia, active endothelium, and changes in blood flow are all shown as potential contributors to thrombus development in a big vein. Veins with valves have less smooth blood flow and less oxygen to the endothelium lining the valves (light green), both of which may stimulate the endothelium and promote thrombus formation. The thrombus, once established, may travel the length of the vessel and embolize. Femoral veins have been examined for valve pocket thrombi (13).

The Causes of VTE and How to Prevent Them

Multiple risk factors for VTE exist in the majority of people who have it. Demographic variables (such as age and sex), inherent blood features (such as factor V Leiden, non-O blood type, and sickle cell disease), lifestyle choices (such as smoking and obesity), and acquired risk factors all contribute to an increased likelihood of an adverse outcome (e.g., malignancy, hormonal therapies, acute infection). The chance of developing a venous (VTE) increases with age, with the largest risk being related with female sex among those less than 65 years old (14).

Assessment of the pretest probability, followed by D-dimer testing and imaging, is necessary for diagnosis since the incidence of DVT in patients with suspected DVT and no previous history of VTE is less than 20%.36 (Figure 2).

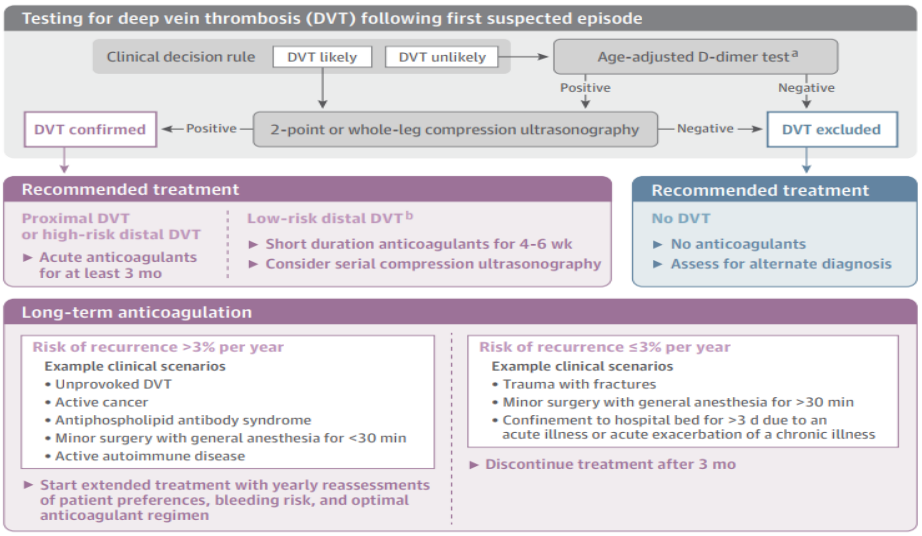


Fig. (2) A Suggested Algorithm for Diagnosing and Treating Patients Suspected of Having Deep Vein Thrombosis (14)

3. Pregnancy-related venous

During pregnancy, a woman's chance of developing a venous or arterial increases. Pregnant have a 3- to 4-fold higher risk of arterial (strokes and heart attacks) and a 4- to 5-fold higher risk of venous (VTE). The danger increases after giving birth (20-fold). About 2 in every 1000 births are affected by a thromboembolic episode during pregnancy. Only around 20% of these occurrences are arterial, whereas the remaining 80% occur in the veins.

Approximately 80 percent of venous thromboembolic occurrences during pregnancy are deep vein thrombosis (DVT) and 20 percent are pulmonary emboli.

4

About a third of all cases of DVT and half of all pulmonary embolisms in pregnant occur after the baby is born.

Pregnancy is associated with a higher risk of proximal, large, and left lower extremity DVT (4).

Although proximal thromboses under the effect of oestrogen are more likely to develop on the left, distal thromboses might happen on either side. It is hypothesised that a relative stenosis of the left common iliac vein between the lumbar vertebral body and the right common iliac artery is to blame for this left-sided predominance, although this theory lacks sufficient evidence. Less than 1% of all occurrences of DVT are caused by a thrombosis in the pelvic veins; however, around 10% of DVT occurs in the pelvis during pregnancy and the postpartum period (16).

Reduced venous capacitance and venous outflow, presumably due to mechanical blockage by the uterus, and maybe due to diminished mobility all contribute to an increased risk of VTE in pregnant .

Even though these risk factors and vascular damage are most significant after delivery, the risk of VTE is similar in the first and third trimesters. Since the risk of VTE rises before many of the physical changes of pregnancy occur, this suggests that hypercoagulability is the primary cause of the increased risk of VTE during pregnancy (17).

4. Guidelines for the Diagnosis, Management, and Prevention of Venous in Pregnancy

Until a diagnosis of VTE is ruled out, anticoagulation should be started in any woman who exhibits symptoms consistent with VTE and addressed with an experienced doctor. Except in cases where there is a clinical suspicion that labour or delivery may occur within the next 24 h or when the patient is critically sick, is the therapy of choice in acute VTE. Because its effects may be reversed with protamine more quickly, unfractionated heparin (UFH) infusions may be preferable in certain situations. The patient's booking weight is utilised to determine the appropriate dose (18).

FBC, coagulation screen, renal function tests, and liver function tests are all necessary before beginning anticoagulation. Because of the thrombosis and hemostatic changes that occur during pregnancy, a thrombophilia test is not suggested in the acute context. Pregnancy-related alterations, such as decreased protein S, increased FVIII, and acquired resistance to activated protein C, might further complicate matters (19).

Pregnancy and postpartum anticoagulant medication selection

Clinicians face a number of difficulties when patients take anticoagulants while pregnant.

The need to treat the sudden beginning of labour and the possibility of neuraxial blockage must be weighed against the risk of teratogenic consequences and the complexities of the various anticoagulants (20).

Fetal anticoagulation is not caused by heparins since they do not reach the placenta. The minimal maintenance, consistent anticoagulation response, and user friendliness of s make them the drug of choice. Heparin-induced thrombocytopenia is less likely to occur in this population as well (HIT). Since UFH's activity may be quickly reversed, it may be preferred when delivery is near. Since clearance is virtually entirely renal, this alternative may be utilised in individuals with severe renal impairment (21).Warfarin is typically avoided during pregnancy. Early exposure may cause embryopathy, whereas late exposure can cause foetal bleeding, including cerebral haemorrhage. After careful assessment of maternal and foetal hazards, warfarin may be given later in pregnancy for at extremely high risk of (such as those with a mechanical heart valve) (22).

Due to a lack of data on the effectiveness and foetal safety of direct oral anticoagulants, such as the thrombin inhibitor dabigatran and the factor Xa inhibitors rivaroxaban and apixaban, they are not used during pregnancy. Unless there is a contraindication to heparin (such HIT) or injections, non-heparin anticoagulants are not typically utilised during pregnancy. Danaparoid is a derivative of that is not placenta-permeable (23).

Anticoagulants should be used with caution in certain situations. Active bleeding or high risk of bleeding (such as placenta praevia), allergy, bleeding diathesis or acquired coagulopathy, thrombocytopenia (platelets75109), HIT, acute stroke in the previous 4 weeks, severe liver disease (with a prolonged PT), and uncontrolled hypertension (BP>200 mmHg systolic or >120 mmHg diastolic) are all examples (24).

of during pregnancy varies from that used for patients who are not expecting a child and is instead depending on the patient's booking weight. It is important to examine local regulations since international recommendations may differ. The Royal College of Obstetricians and Gynecologists (RCOG) in the United Kingdom established thromboprophylaxis and treatment regimens depending on patient weight (Table 1). According to them, "lower dosages of should be administered if the creatinine clearance is less than 30 ml min1" (for enoxaparin and) or "less than 20 ml min1" (for tinzaparin) (25).

The RCOG-recommended prophylactic and therapeutic doses of are listed in Table 1. (26). Dosage splitting is allowed.

Table 2, Table 3, and Figure 1 display pharmacological (non-invasive) therapies, invasive VTE therapy options, and supporting measures.

Drug-Based Therapies (Non-Surgical Options)

Options for treating invasive VTE and available supportive care, table 3

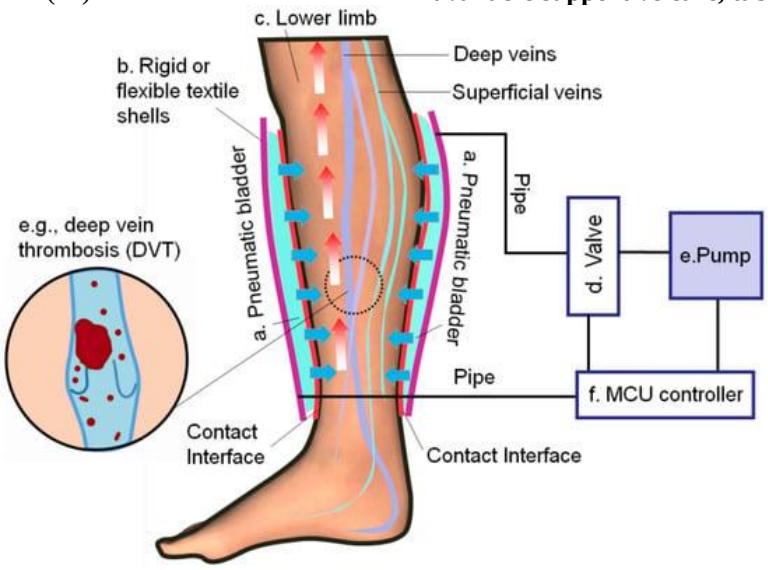


Fig. (3) is a depiction of a common device used in lower limb compression treatment, intermittent pneumatic compression (IPC) (27).

Pregnancy-related VTE treatment recommendations and potential adverse effects of anticoagulant therapy (Table 3):

Treatment for Venous During Pregnancy (28).

5. Obstetric Anesthesia and Venous

Due to the desire for neuraxial anaesthesia in obstetrics, it is essential to limit contraindications to neuraxial operations, which obstetric anesthesiologists must do often

in urgent or emergency circumstances. One-third of all deliveries in the United States are C-sections, and there are several conditions that call for immediate or emergency delivery. The risk of venous (VTE) among patients, some of whom may need urgent anaesthetic, has increased as a result of the current trend toward more widespread prenatal venous (VTE) prevention. The dangers of general anaesthesia, which may be amplified in obstetric patients, must be weighed while making this decision (29). Neuraxial anaesthesia has benefits such as decreased chance of surgical infection, enhanced bonding between mother and newborn, reduced need for opioids, and the possibility of father participation. Neonatal advantages include decreased respiratory depression risk, minimising in-utero exposure to inhalational drugs, and earlier breastfeeding beginning. In obstetric patients receiving VTE prophylaxis, the main danger of neuraxial anaesthesia is an increased risk of epidural hematoma and neurological damage (30).

Spinal hematoma: prevalence, risk factors, and neurological outcome

Bleeding within the vertebral canal, or spinal/epidural hematoma (SEH), is an extremely uncommon but possibly fatal consequence of neuraxial anaesthesia.

It is more common for SEH to arise on its own than as a side effect of neuraxial anaesthesia. While idiopathic reasons account for the most majority of spontaneous hematomas, anticoagulant treatment and vascular abnormalities are also important factors (31).

Several writers have characterised the risk factors for SEH, and they are summarised here (Table 5). An increased risk of SHE is associated with the use of anticoagulants with neuraxial anaesthesia. The risk of developing SEH after surgery varies by procedure, patient age, and gender. The frequency is predicted to be 1:200,000 in pregnant patients undergoing neuraxial anaesthesia and 1:3,600 in elderly undergoing knee arthroplasty. Reasons for this trend include anticoagulant buildup owing to undetected decline in renal excretion, double antiaggregant/anticoagulant medication, and the increased prevalence of spinal deformities associated with osteoporosis among people of this age (31).

Table 5: Factors linked to SEH incidence (32).

❖ **Coagulation's cellular mechanism**

Platelets, blood coagulation proteins, natural anticoagulants, the fibrinolysis system, and other components of the hemostatic system are all part of the intricate cellular mechanism of coagulation. Injuries to the vascular endothelium, collagen exposure, and platelet adhesion are the triggers that set off this complex system. As a result of membrane glycoprotein-mediated platelet-collagen adhesion, intracellular signalling, calcium elevation, and platelet activation occur. When platelets become active, they produce granules containing a variety of chemicals, including thromboxane-A2 (TxA2), which plays a role in further activating the platelets. Glycoproteins and fibrinogen molecules help platelets clump together, and factors like prostacyclin (PGI-2) and phosphodiesterase enzyme may control how much they clump together (PDE). A wide variety of antiplatelet medicines are available to affect coagulation, including nonsteroidal anti-inflammatory drugs (NSAIDs), thienopyridines, direct and indirect ADP inhibitors, phosphodiesterase (PDE) inhibitors, and glycoprotein IIb/IIIa inhibitors (33-35).

Antiplatelet medication when under a spinal or epidural anaesthetic (36):

The following table provides a concise overview of the various drug classes commonly used in clinical practise, including nonsteroidal anti-inflammatory drugs, thienopyridines, direct inhibitors of ADP receptors, glycoprotein IIb/IIIa inhibitors, and phosphodiesterase inhibitors, as well as their mechanisms of action, potential risks when used in conjunction with neuraxial anaesthesia, and suggested best practises. These guidelines are helpful for ensuring patients' safety during neuraxial treatments because they include recommendations for when different classes of drugs should be stopped and restarted depending on their pharmacological qualities and clinical context (Table 6).

Table 6: Safety and Timing Recommendations for Drugs Affecting Coagulation in Neuraxial Anesthesia

6. Conclusions

Effective Obstetric patients with thromboembolic diseases need a multimodal strategy to therapy, including close monitoring of coagulation status and the prompt use of anticoagulation for either prophylaxis or treatment. When administering a neuroaxial block, it's crucial to be aware of the possible dangers related with catheter insertion and removal. In addition, the proper length of medication and prompt postpartum care are key factors in lowering the incidence of VTE.

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