VTE, Thrombophilia, Antithrombotic Therapy, and Pregnancy

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Background

• The use of anticoagulant therapy during pregnancy is challenging because of the potential for both fetal and maternal complications.
For pregnant patients, we recommend LMWH for the prevention and treatment of VTE, instead of UFH (Grade 1B).
For women receiving anticoagulation for the treatment of VTE who become pregnant, we recommend LMWH over vitamin K antagonists during the first trimester (Grade 1A), in the second and third trimesters (Grade 1B), and during late pregnancy when delivery is imminent (Grade 1A).
For women requiring long-term VKAs who are attempting pregnancy and are candidates for LMWH substitution, we suggest performing frequent pregnancy tests and substituting LMWH for VKAs when pregnancy is achieved rather than switching to LMWH while attempting pregnancy (Grade 2C).

Remarks: Women who place little value on avoiding the risks, inconvenience, and costs of LMWH therapy of uncertain duration while awaiting pregnancy and a high value on minimizing the risks of early miscarriage associated with VKA therapy are likely to choose LMWH while attempting pregnancy.
For pregnant women, we suggest limiting the use of fondaparinux and parenteral direct thrombin inhibitors to those with severe allergic reactions to heparin (eg, HIT) who cannot receive danaparoid (Grade 2C).
For pregnant women, we recommend avoiding the use of oral direct thrombin (eg, dabigatran) and anti-Xa (eg, rivaroxaban, apixaban) inhibitors (Grade 1C).
For women undergoing assisted reproduction, we recommend against the use of routine thrombosis prophylaxis (Grade 1B).
For women undergoing assisted reproduction who develop severe ovarian hyperstimulation syndrome, we suggest thrombosis prophylaxis (prophylactic LMWH) for 3 months postresolution of clinical ovarian hyperstimulation syndrome rather than no prophylaxis (Grade 2C).

Remarks: Women who are averse to taking medication for very small benefit and those who consider self-injecting a considerable burden will be disinclined to use LMWH for extended thrombosis prophylaxis. Given that the absolute benefit decreases as time from the hyperstimulation event increases, such women will be very disinclined to continue prophylaxis throughout the entire resultant pregnancy.
For women undergoing cesarean section without additional thrombosis risk factors, we recommend against the use of thrombosis prophylaxis other than early mobilization (Grade 1B).
For women at increased risk of VTE after cesarean section because of the presence of one major or at least two minor risk factors (see next slide) we suggest pharmacologic thromboprophylaxis (prophylactic LMWH) or mechanical prophylaxis (elastic stockings or intermittent pneumatic compression) in those with contraindications to anticoagulants while in hospital following delivery rather than no prophylaxis (Grade 2B).

Remarks: The reduced bleeding risk with mechanical prophylaxis should be weighed against the inconvenience of elastic stockings and intermittent pneumatic compression.
### Risk Factors for VTE Postpartum

**Table 3** [6.2.1-6.2.4] Risk factors for VTE resulting in a baseline risk of postpartum VTE > 3%

#### Major Risk Factors (odds ratios > 6): Presence of at least 1 risk factor suggests a risk of postpartum VTE of >3%

- Immobility (strict bed rest for a week or more in the antepartum period)
- Postpartum hemorrhage ≥1000 ml with surgery
- Previous VTE
- Preeclampsia with fetal growth restriction
- Thrombophilia
  - Antithrombin deficiency*
  - Factor V Leiden (homozygous or heterozygous),
  - Prothrombin G20210A (homozygous or heterozygous)
- Medical conditions
  - SLE
  - Heart disease
  - Sickle cell disease
- Blood transfusion
- Postpartum infection

#### Minor Risk factors (odds ratios > 6 when combined): Presence of at least 2 risk factors or 1 risk factor in the setting of emergency cesarean section suggests a risk of postpartum VTE of >3%

- BMI>30kg/M²
- Multiple pregnancy
- Postpartum hemorrhage >1L
- Smoking >10 cigarettes per day
- Fetal growth restriction (Gestational age + sex adjusted birth weight <2.5th percentile)
- Thrombophilia
  - Protein C deficiency
  - Protein S deficiency
  - Preeclampsia
For women undergoing cesarean section who are considered to be at very high risk for VTE and who have multiple additional risk factors for thromboembolism that persist in the puerperium, we suggest that prophylactic LMWH be combined with elastic stockings and/or intermittent pneumatic compression over LMWH alone (Grade 2C).
For selected high-risk patients in whom significant risk factors persist following delivery, we suggest extended prophylaxis (up to 6 weeks after delivery) following discharge from the hospital (Grade 2C).
For pregnant women with acute VTE, we recommend therapy with adjusted-dose SC LMWH over adjusted-dose UFH (Grade 1B).
For pregnant women with acute VTE, we recommend LMWH over vitamin K antagonist treatment antenatally (Grade 1A).
For pregnant women with acute VTE, we suggest that anticoagulants should be continued for at least 6 weeks postpartum (for a minimum total duration of therapy of 3 months) in comparison with shorter durations of treatment (Grade 2C).
For pregnant women receiving adjusted-dose LMWH therapy and where delivery is planned, we recommend discontinuation of LMWH at least 24 h prior to induction of labor or cesarean section (or expected time of neuraxial anesthesia) rather than continuing LMWH up until the time of delivery (Grade 1B).
For all pregnant women with prior VTE, we suggest postpartum prophylaxis for 6 weeks with prophylactic- or intermediate-dose LMWH or VKAs targeted at INR 2.0 to 3.0 rather than no prophylaxis (Grade 2B).
For pregnant women at low risk of recurrent VTE (single episode of VTE associated with a transient risk factor not related to pregnancy or use of estrogen), we suggest clinical vigilance antepartum rather than antepartum prophylaxis (Grade 2C).
For pregnant women at moderate to high risk of recurrent VTE (single unprovoked VTE, pregnancy- or estrogen-related VTE, or multiple prior unprovoked VTE not receiving long-term anticoagulation), we suggest antepartum prophylaxis with prophylactic- or intermediate-dose LMWH rather than clinical vigilance or routine care (Grade 2C).
For pregnant women receiving long-term VKAs, we suggest adjusted-dose LMWH or 75% of a therapeutic dose of LMWH throughout pregnancy followed by resumption of long-term anticoagulants postpartum, rather than prophylactic-dose LMWH (Grade 2C).
For pregnant women with no prior history of VTE who are known to be homozygous for factor V Leiden or the prothrombin 20210A mutation and have a positive family history for VTE, we suggest antepartum prophylaxis with prophylactic- or intermediate-dose LMWH and postpartum prophylaxis for 6 weeks with prophylactic- or intermediate-dose LMWH or VKAs targeted at INR 2.0 to 3.0 rather than no prophylaxis (Grade 2B).
For pregnant women with all other thrombophilias and no prior VTE who do not have a positive family history for VTE, we suggest antepartum and postpartum clinical vigilance rather than pharmacologic prophylaxis (Grade 2C).
For women with recurrent early pregnancy loss (three or more miscarriages before 10 weeks of gestation), we recommend screening for antiphospholipid antibodies (APLAs) (Grade 1B).
For women with a history of pregnancy complications, we suggest not to screen for inherited thrombophilia (Grade 2C).
For women who fulfill the laboratory criteria for APLA syndrome and meet the clinical APLA criteria based on a history of three or more pregnancy losses, we recommend antepartum administration of prophylactic- or intermediate-dose UFH or prophylactic LMWH combined with low-dose aspirin, 75 to 100 mg/d, over no treatment (Grade 1B).

See the next slide for criteria for APLA syndrome.
For women considered at risk for preeclampsia, we recommend low-dose aspirin throughout pregnancy, starting from the second trimester, over no treatment (Grade 1B).
For women with two or more miscarriages but without APLA or thrombophilia, we recommend against antithrombotic prophylaxis (Grade 1B).
For pregnant women with prosthetic valves at high risk of thromboembolism, we suggest the addition of low-dose aspirin, 75 to 100 mg/d (Grade 2C).