Venous Thromboembolism in Pregnancy and Postpartum

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Highlights

- CT Pulmonary Angiography is the gold standard for diagnosis of pulmonary embolism
- Low molecular weight heparin (LMWH, Lovenox) is the first line anticoagulant during pregnancy for prophylactic and therapeutic dosing for most conditions.
- Anticoagulation to prevent venous thromboembolism (VTE) during pregnancy and postpartum should be based on medical history including prior VTE, and presence of thrombophilia.
- Recommend scheduling delivery at or after 39w0d (or sooner as clinically indicated) and discontinuing LMWH anticoagulation 24 hours prior to admission for those who are on adjusted-dose (full anticoagulation) and 12 hours for those on prophylactic dosing of LMWH.[4-6]
- **Patients who were receiving antepartum anticoagulation should continue anticoagulation postpartum for at least 6 weeks**. This dose should always be equal to or greater in dose than antepartum anticoagulation for any given patient.

Diagnosis

The diagnosis of Deep Vein Thrombosis (DVT) and/or Pulmonary Embolism (PE) requires thorough history, physical exam, and imaging. See Figure 1 for diagnostic work up for DVT and see Figure 2 for diagnostic work up for PE.

Figure 1. Evaluation of a patient with findings concerning for DVT

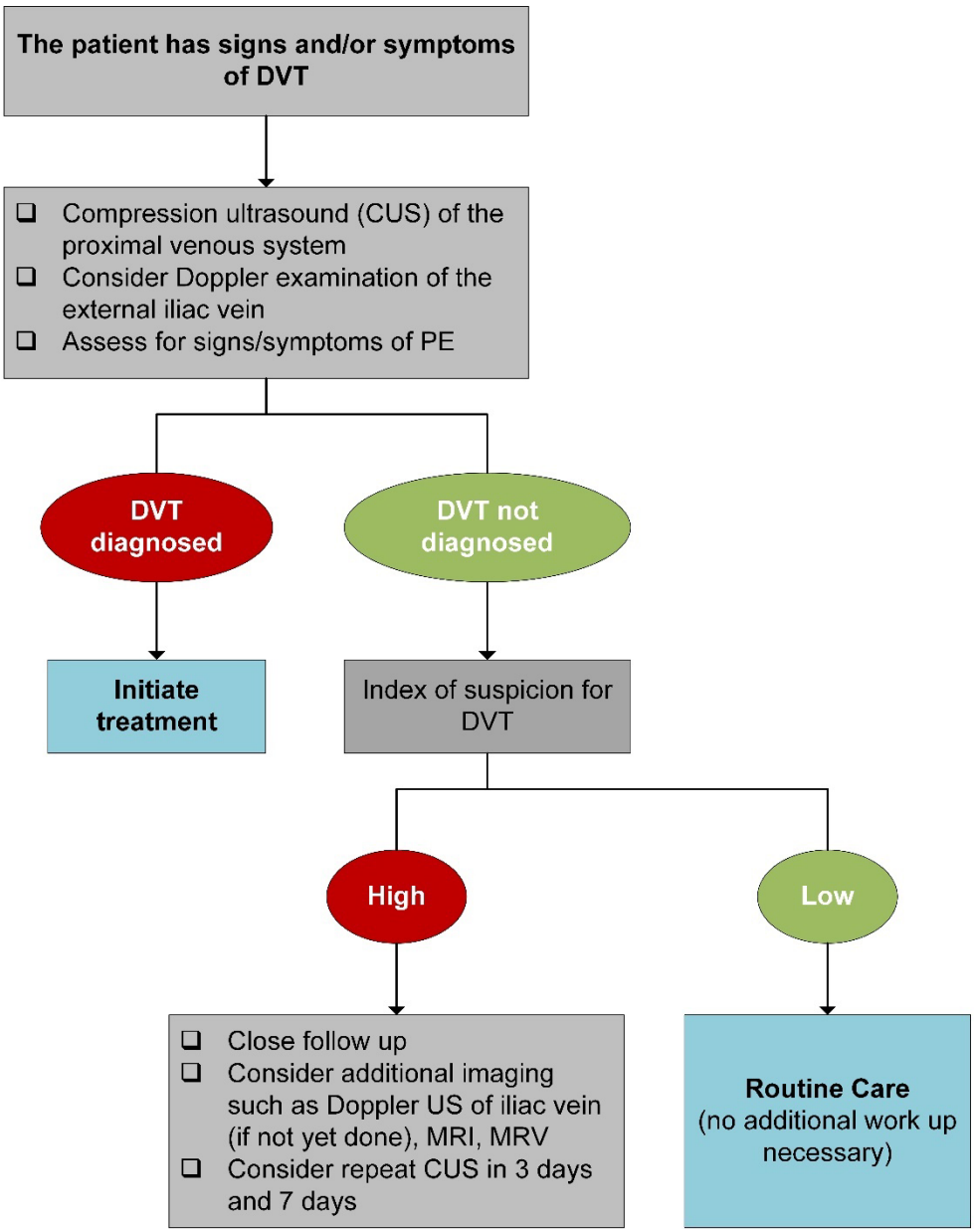
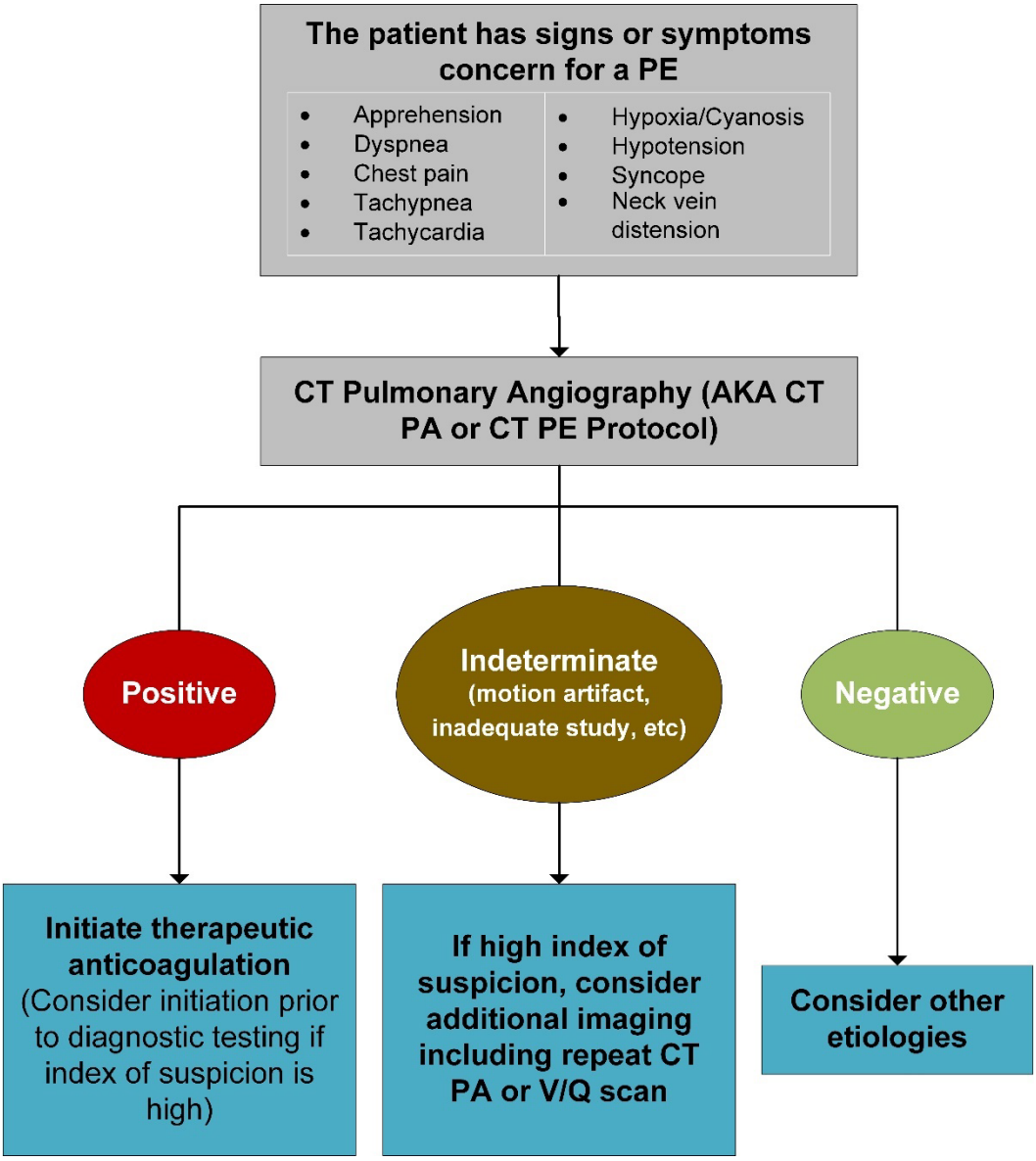


Figure 2. Evaluation of a patient with findings concerning for PE



Antepartum thromboprophylaxis

Need for outpatient VTE prophylaxis during pregnancy depends on risk factors including prior history of VTE, family history, and presence of inherited thrombophilia (Table 1).

Table 1. Anticoagulation during pregnancy based on risk (outpatient)

Clinical Scenario		Antepartum Recommendations	Postpartum Recommendations[a]
No history of DVT, No Thrombophilia		Anticoagulation therapy not indicated	Individualize
VTE diagnosed during pregnancy		Adjusted	Adjusted for a minimum of 6 weeks
History of SINGLE prior <u>provoked</u> VTE • Identified precipitating event (i.e. trauma, surgery, immobility) • Unrelated to estrogen/pregnancy		Anticoagulation therapy not indicated	Surveillance without anticoagulation therapy if **no** additional risk factors[b] Prophylactic if additional risks factors[b]
History of SINGLE prior VTE (<u>unprovoked</u> OR estrogen/pregnancy-related)		Prophylactic	Prophylactic if **no** additional risk factors[b] Intermediate or Adjusted if additional risks factors present[b]
Low risk thrombophilia • Heterozygous Factor V Leiden (FVL) • Heterozygous Prothrombin Gene Mutation (PGM) • Protein C or S deficiency • Antiphospholipid Antibody Positive (without APLS)	**No personal or 1st degree relative with VTE**	Anticoagulation therapy not indicated	Surveillance without anticoagulation therapy if no additional risk factors[b] Prophylactic if additional risks factors[b]
	First degree relative with a history of VTE	Anticoagulation therapy not indicated	Prophylactic
	Personal history of single VTE, not requiring lifelong AC	Prophylactic	Prophylactic if **no** additional risk factors[b] Intermediate if additional risks factors present[b]
High risk thrombophilia • APLS • Antithrombin III deficiency (ATIII) • Homozygous FVL or PGM • Combined Heterozygous FVL and PGM	**No personal or 1st degree relative with VTE**	Prophylactic	Prophylactic if **no** additional risk factors[b] Intermediate if additional risks factors present[b]
	First degree relative with a history of VTE	Prophylactic	Prophylactic if **no** additional risk factors[b] Intermediate if additional risks factors present[b]
	Personal history of single VTE, not requiring lifelong AC	Prophylactic, intermediate, or adjusted dose	Prophylactic if **no** additional risk factors[b] Intermediate if additional risks factors present[b]
Two or more prior VTE (regardless of thrombophilia)	**Not on long term AC**	Intermediate	Intermediate if **no** additional risk factors[b] Adjusted if additional risks factors present[b]
	On Long term AC	Adjusted	Adjusted

Adapted from ACOG Practice bulletin No 196 Obstetrics and Gynecology Vol 132 (1) Pg e7. July 2018[4]

[a]The use of Rivaroxaban (Xarelto), a Direct Oral Anticoagulant, can be considered postpartum even in breastfeeding patients as there are studies supporting its safety. This should be done with Hematology consultation.

[b]Risk factors include Cesarean delivery, postpartum hemorrhage, blood transfusion, preeclampsia, heart disease, systemic lupus erythematosus, immobility for at least 1 week antepartum, BMI > 40, smoking, multiple gestation.

Hospitalized Patients

- All hospitalized antepartum patients should wear SCD's while in bed.
- For hospitalized antepartum patients already receiving anticoagulation or who meet criteria per Table 1, continue anticoagulation during hospital stay
- For patients NOT already on subcutaneous anticoagulation who do not meet the indications in Table 1, antepartum admission is not a sole indication to start anticoagulation.

Anticoagulation Recommendations

First line agent

Low molecular weight heparins (LMWH), such as enoxaparin, are the preferred agents for VTE prophylaxis and treatment during pregnancy.[5]

Dosing recommendations are based on ACOG and SMFM guidelines. Where ACOG allows for options in dosing, **BCM OB/Gyn Perinatal Guidelines Committee recommends the lowest dose regimen (i.e., prophylactic over intermediate, intermediate over adjusted) to minimize risk of bleeding complications at delivery and increase the likelihood of neuraxial anesthesia/analgesia**. Management can be individualized, as clinically indicated.

BCM OB/Gyn Perinatal Guidelines Committee recommends continuation of LMWH therapy until delivery rather than conversion to unfractionated heparin.

Dosing

Adjusted (therapeutic) dosing should be used to treat an acute DVT and/or PE.
See Table 2 for information on all dosing considerations.

***Table 2**. Anticoagulation Dosing*[4,6-9]

Anticoagulation	Drug	Dosing	Monitoring
Prophylactic	Heparin	Trimester Dependent: 1st trimester: 5000 units subcutaneous q12H 2nd trimester: 7500 units subcutaneous q12H 3rd trimester: 10000 units subcutaneous q12H	Consider platelet count periodically for HIT (heparin induced thrombocytopenia)
	LMWH	40mg subcutaneous daily	None
Intermediate	LMWH	40mg q12H	None
Adjusted dose (therapeutic)	Heparin SC	333 units/kg subcutaneous followed by 250 units/kg subcutaneous q12H	Titrated to target of 1.5-2.5x baseline aPTT 6 hours after injection (if acute VTE goal minimum of 2x baseline)
	Heparin IV	80 units/kg (or 5000 units) IV bolus followed by infusion 18 units/kg/hr	Maintain aPTT at least 2x baseline OR heparin Anti Xa level 0.3-0.7 units/mL 6 hours after dose adjustment
	LMWH	1mg/kg subcutaneous q12H (round to nearest 10mg)	Anti Xa level 4-6 hours after dosing. Goals: 0.8-1.2 units/mL for mechanical heart valves 0.6-1.2 units/mL for all other indications *Consider Anti-Xa level monitoring for renal dysfunction, obesity, or other high-risk conditions (ex: increased risk of bleeding)*
** **CrCl < 30mL/min: contact clinical pharmacist**			

Duration of treatment

Optimal duration of anticoagulation for treatment of VTE is unknown but is most commonly 3 months in duration at minimum. If VTE treatment course ends before or during the post-partum period, anticoagulation should continue for at least 6 weeks postpartum.[4-6]

Peripartum Anticoagulation Recommendations

See Figure 3 for timing of discontinuation of anticoagulation prior to delivery.
See Figure 4 for timing of resumption of anticoagulation following delivery.

Figure 3. Anticoagulation Management During Delivery

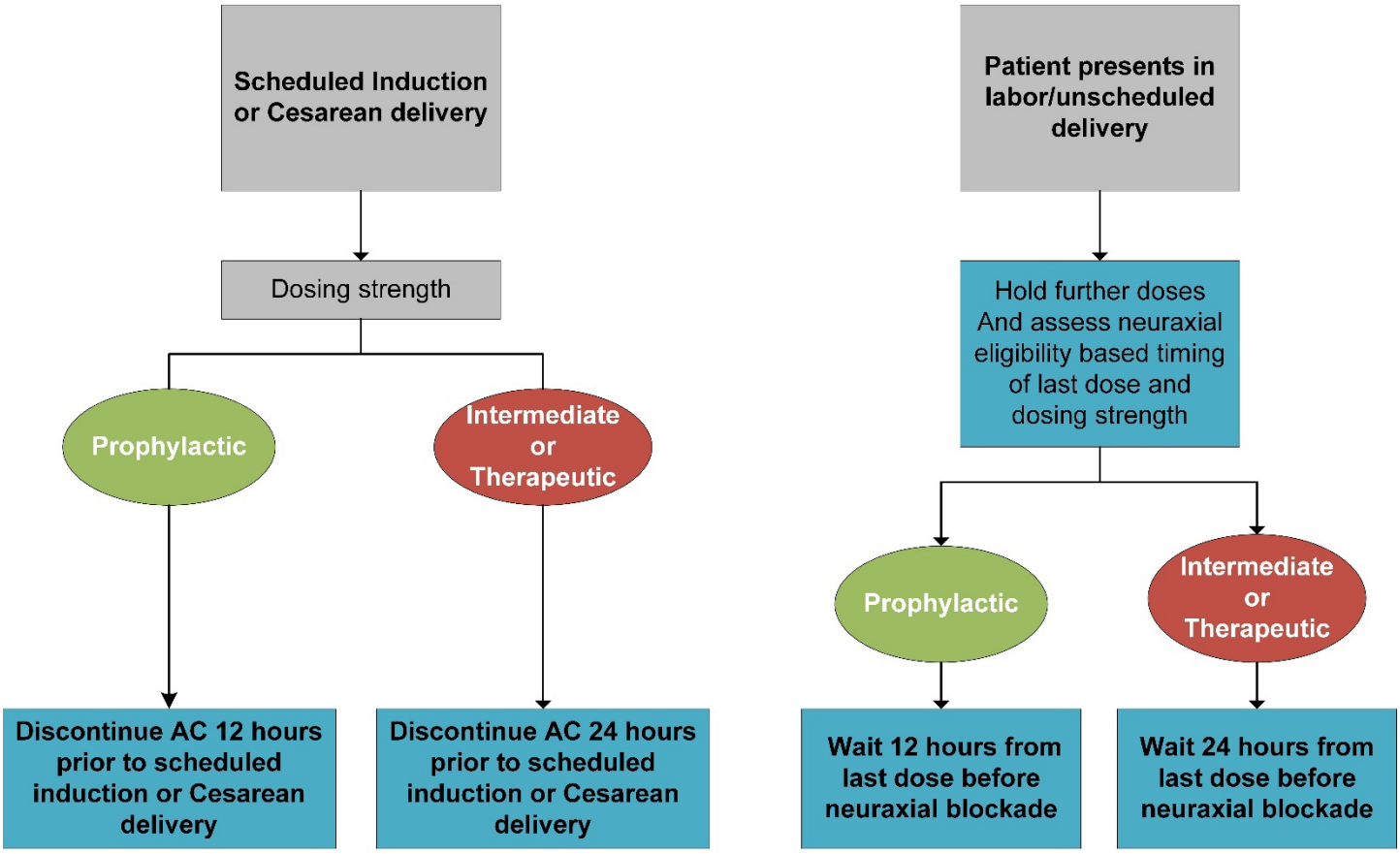
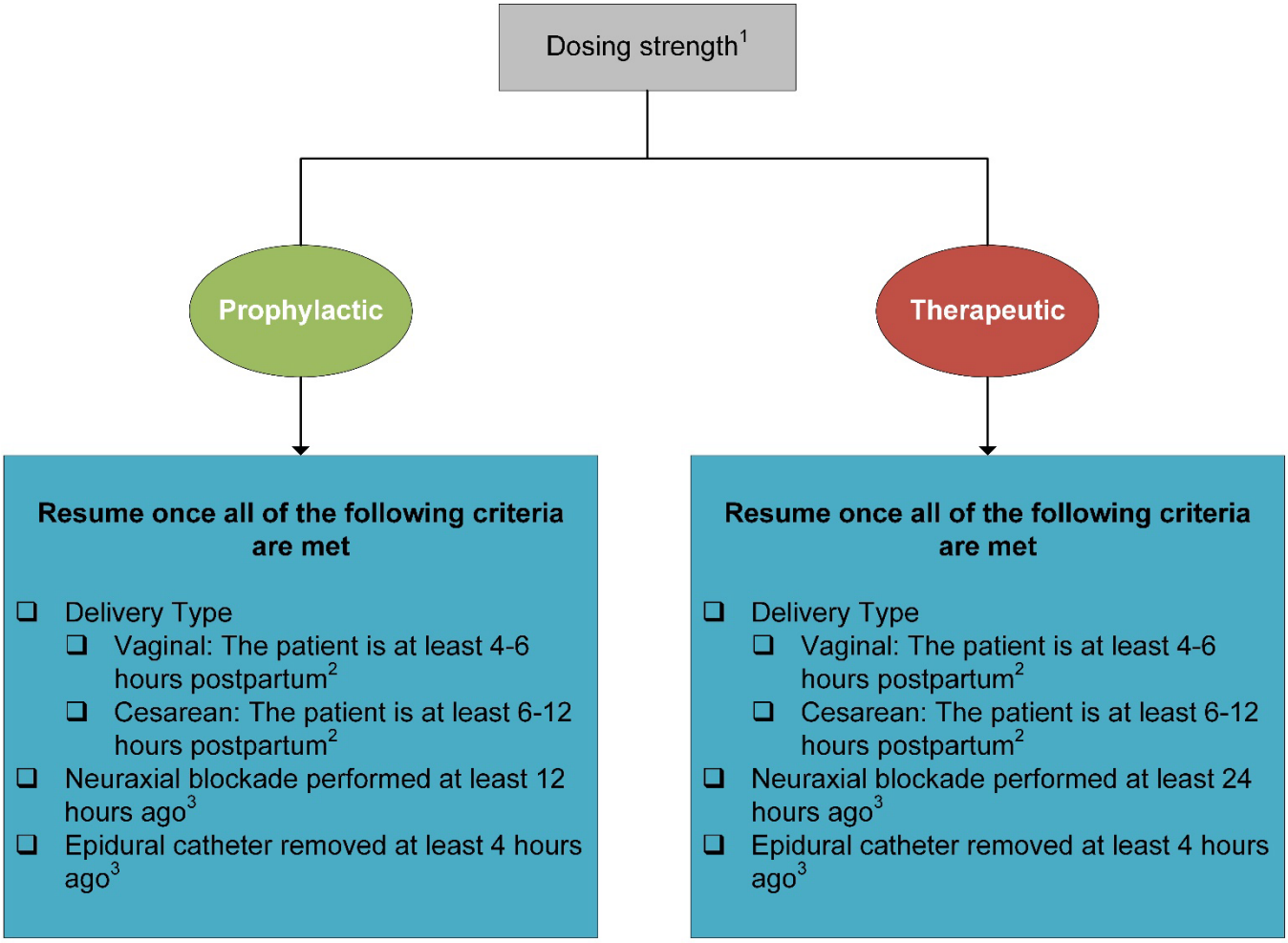


Figure 4. Timing of anticoagulation resumption postpartum is based on LMWH dosing strength, delivery type, and timing of neuraxial anesthesia



[1]The postpartum dose should always be equal to or greater than antepartum anticoagulation dose for any given patient.
[2]Consider delay if the patient experienced a postpartum hemorrhage or there is an ongoing concern for bleeding
[3]Can resume IV unfractionated heparin 1 hour after blockade and removal if there is a high risk for VTE

Postpartum Anticoagulation[2,4-6]

- The risk of VTE is particularly elevated during the postpartum period, and especially after Cesarean delivery or for patients who have an underlying condition that can cause increased risk for clotting (ex. Sickle Cell Anemia, high risk thrombophilia, prior history of a VTE or PE).
- **Patients who were receiving antepartum anticoagulation should continue anticoagulation postpartum for at least 6 weeks.** The postpartum dose should always be equal to or greater than antepartum anticoagulation dose for any given patient.
- Table 1 provides postpartum recommendations for patients at increased risk of VTE based on medical history. The checklist in Figure 5 can also be used to help select the appropriate method for post-Cesarean anticoagulation.
- Figure 4 provides an algorithm for resumption of anticoagulation postpartum. As use of UFH antepartum is increasingly uncommon, this figure focuses on LMWH timing.

Figure 5. Thromboembolism Prophylaxis after Cesarean Delivery[2,3]

BOX

Thromboembolism prophylaxis after cesarean delivery checklist

Thromboembolism Prophylaxis After Cesarean Delivery
Checklist following the Guidelines of SMFM Consult Series #51
This checklist is a SAMPLE only and does not dictate an exclusive course of action for individual patients.

For all cesarean deliveries:
- ☐ Pneumatic sequential compression devices (SCDs) placed prior to surgery start
- ☐ SCDs continued until patient is fully ambulatory

For women with personal history of deep venous thrombosis or pulmonary embolism:
- ☐ SCDs as above
- ☐ Prophylactic low-molecular-weight heparin (eg, enoxaparin 40 mg SC daily); see section below for starting time; continue for 6 weeks postoperatively

For women with inherited or acquired thrombophilia[a] and no previous thrombosis:
- ☐ SCDs as above
- ☐ Prophylactic low-molecular-weight heparin (eg, enoxaparin 40 mg SC daily); see section below for starting time; continue for 6 weeks postoperatively

For women with body mass index (BMI) 40 kg/m^2 or greater (class 3 obesity) who have thrombophilia[a] or history of deep venous thrombosis or pulmonary embolism:
- ☐ SCDs as above
- ☐ Intermediate-dose low-molecular-weight heparin (eg, enoxaparin 40 mg SC every 12 hours); see section below for starting time; continue for 6 weeks postoperatively

For women with combinations of the above risk factors:
- ☐ SCDs as above
- ☐ Individualized management, such as intermediate-dose low-molecular-weight heparin (eg, enoxaparin 40 mg SC every 12 hours) or adjusted-dose (therapeutic) low-molecular-weight heparin (eg, enoxaparin 1 mg/kg SC every 12 hours); see section below for starting time; continue for 6 weeks post-operatively

Appendix

Example Smartphrase

@NAME@ is taking her Lovenox daily at X and Y. I counseled @NAME@ on anticoagulation around delivery and timing of delivery. I explained that she will remain on therapeutic/prophylactic anticoagulation until at least 6 wks postpartum due to her VTE during pregnancy. I explained that regional anesthesia cannot be placed within 12 hours of prophylactic Lovenox and 24 hours of intermediate or therapeutic Lovenox. For this reason, I explained that our general approach is to offer IOL at 39 weeks and plan to hold her last Lovenox dose the day prior to IOL to facilitate neuraxial. I explained that indicated/spontaneous delivery prior to her scheduled IOL may result in inability to receive regional analgesia/anesthesia during labor, resulting in the potential for increased bleeding complications and general anesthesia if CD becomes necessary. I also counseled her to present to the hospital for regular contractions and/or LOF and to hold her Lovenox dose prior to coming to hospital if around the time of scheduled administration.

Plan as follows:

1. Continue twice daily therapeutic Lovenox/Continue once daily prophylactic Lovenox
2. IOL at 39 weeks.
3. Hold Lovenox the day prior to scheduled IOL
4. Resume Lovenox after delivery: if prophylactic Lovenox, can resume 12 hours after neuraxial blockade and at least 4 hours after catheter removal; if intermediate or therapeutic Lovenox, wait at least 24 hours after neuraxial blockade and at least 4 hours after epidural catheter removal. Additionally, Lovenox should not be started sooner than 4-6 hours after uncomplicated vaginal delivery and 6-12 hours after uncomplicated CD.
5. Consider use of a Direct Oral Anticoagulant for postpartum thromboprophylaxis, but should be based on discussion with Hematology (Xarelto is compatible with breastfeeding).
6. Recommend continuation of LMWH therapy until delivery rather than conversion to unfractionated heparin since unfractionated heparin doses of 7,500 units subcutaneous twice a day or more also require discontinuation at least 12 hours before scheduled induction of labor or cesarean delivery and therapeutic levels can be difficult to achieve with Heparin.

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