ANTICOAGULATION MANAGEMENT, PEDIATRIC, INPATIENT

Updated: June 21, 2023

Clinical Pathway Summary

CLINICAL PATHWAY NAME: Anticoagulation Management, Pediatric, Inpatient

PATIENT POPULATION AND DIAGNOSIS: Pediatrics

APPLICABLE TO: Helen DeVos Children's Hospital

BRIEF DESCRIPTION: Pediatric/Neonatal inpatient anticoagulation treatment guideline for HDVCH

IMPLEMENTATION DATE: 5/30/23

LAST REVISED: 6/2023

Clinical Pathways Clinical Approach

HDVCH INPATIENT ANTICOAGULATION TREATMENT AND MANAGEMENT:

I. INTRODUCTION AND DISCLAIMER

The following information is intended to be used as a tool to assist the multidisciplinary care team with anticoagulation use and reversal if necessary. Due to various interpatient risk factors for bleeding and thrombotic complications and ongoing research, flexibility and clinical judgement should be exercised when using this tool. The editors do not assume any liability with the use of any specific information provided herein.

II. DRUG SPECIFIC DOSING AND MONITORING GUIDELINES

A. Unfractionated Heparin (UFH) Anticoagulation

1. UFH Continuous Infusion (non-ECMO)

a. Dosing

i. Prophylaxis dosing

1. Any dose ≤ 10 units/kg/hr

2. Suggested baseline labs: aPTT, PT/INR, and CBC, Factor VIII activity, Fibrinogen

3. No monitoring required unless signs or symptoms of bleeding.

4. Pediatric VTE Prophylaxis, Inpatient, Guideline

ii. Treatment dosing (any dose > 10 units/kg/hr)

1. Utilize age specific UFH titration nomogram for dosing and monitoring using Anti-Xa (Table 1, Table 2)

Table 1. Bolus and Initial Infusion Rates for Continuous Infusion UFH Treatment Dosing

Age	Bolus Dose (units/kg)	Maximum Bolus (units)	Initial Infusion (units/kg/hr)
Birth to 12 months	75	1,500	28
Children > 1 year	75	5,000	20
Children > 12 years	80	10,000	18

***Bolus prior to infusion is at the discretion of the provider**

b. Monitoring: Utilize age-specific UFH titration nomogram for dosing and monitoring using Anti-Xa (see above hyper-link)

i. Baseline aPTT, PT/INR, CBC prior to initiation of UFH.

ii. Check Anti-Xa (UFH) 4 hours after initiation.

iii. When two consecutive Anti-Xa (UFH) are in therapeutic range, repeat every 24 hours.

iv. Check CBC daily until it is clear that the levels are stable, and the patient is not having occult bleeding. Then check CBC at least once a week.

v. Consider heparin-induced thrombocytopenia if platelet count decreases to < 100K or decreases > 50% from baseline after the initiation of heparin or LMWH therapy.

Table 2. Recommendations for Dose Adjustments Using Unfractionated Heparin Level Anti-Xa Assay[3]				
Unfractionated Heparin Level Anti-Xa Assay (units/mL)	**Bolus Dose (Units/kg)***	**Hold Infusion (minutes)**	**Infusion Rate Change (units/kg/hr)**	**Repeat Level (hours after dose adjustment)**
< 0.1	50	0	Increase by 4	4
< 0.1-0.19	0	0	Increase by 3	4
0.2–0.29	0	0	Increase by 2	4
0.3–0.7	0	0	No change	In 4 h, then daily
0.71–0.8	0	0	Decrease by 1	4
0.81–0.9	0	30	Decrease by 2	4
0.91-1	0	60	Decrease by 3	4
≥ 1	If a single UFH level of 1 units/mL or greater, please discuss each of the following scenarios with the provider for applicability: 1) UFH greater than 1 units/mL and concerns for contamination or improperly timed sample and less than 4 hours since last bolus or rate change - Continue current infusion and check next UFH level at next scheduled time 2) UFH greater than 1 units/mL and concerns for contamination or improperly timed sample and greater than or equal to 4 hours since last bolus or rate change - Change current infusion: Hold infusion, contact provider, repeat STAT peripheral UFH level. If repeat UFH less than or equal to 1 units/mL, resume infusion according to nomogram based on UFH level range. 3) UFH greater than 1 units/mL and concerns for contamination or improperly timed sample and greater than or equal to 4 hours since last bolus or rate change - Change current infusion: Hold infusion, contact provider, repeat STAT peripheral UFH level. If repeat UFH greater than 1 units/mL, recheck STAT hourly UFH level until less than or equal to 0.7 units/mL then restart infusion at 4 units/kg/hr below current dose. 4) UFH greater than 1 units/mL and NO concerns for contamination or improperly timed sample - Change current infusion: Hold infusion, contact provider, recheck STAT hourly UFH level until less than or equal to 0.7 units/mL then restart infusion at 4 units/kg/hr below current dose.			

*Bolus option can be deselected using the "Pediatric Heparin Nomogram – UFH (NO BOLUS)" orderable. Please discuss with supervising attending if they would not want to bolus at <0.1 (ie. no bolus nomogran) or order bolus at <0.1 (bolus nomogram).

Note: Extreme care should be taken if sample for UFH monitoring is being drawn from a line that is running or being flushed with heparin. Heparin can contaminate the sample and results will not truly reveal systemic anticoagulation.

2. **UFH Continuous Infusion (ECMO)**
    a. Pediatric Extracorporeal Membrane Oxygenation (ECMO) Heparin Titration Nomogram
3. **UFH Reversal**
    a. To calculate protamine sulfate IV dose (provides 100% reversal):
        i. Total up number of units of all heparin received in last 2 hours = "Units of Heparin Administered"
        ii. Determine the time since last heparin dose administered = "minutes".
        iii. Use table below to determine dose of protamine.

Table 3. Protamine Dose for UFH Reversal	
Time Since Last Heparin Dose (minutes)	**Protamine Sulfate Dose (mg) for Each 100 "Units of Heparin Administered"**
< 30	1
30-60	0.5-0.75
60-120	0.375-0.5
> 120	0.25-0.375
Max Dose	50 mg

B. Low Molecular Weight Heparin (LMWH) Anticoagulation

1. Enoxaparin Dosing

a. Dosing (based on normal renal function)

Table 4. Enoxaparin Dosing				
Age	**Prophylactic Dosing (mg/kg/dose)**	**Treatment Dosing (mg/kg/dose)**	**Route**	**Dosing Interval**
< 2 months	0.75	1.5	Subcutaneous	every 12 hours
≥ 2 months	0.5	1	Subcutaneous	every 12 hours

b. Monitoring (optional for prophylactic dosing)

i. Baseline aPTT, PT/INR, CBC, and serum creatinine.

ii. Monitor serum creatinine weekly if inpatient and at increased risk of renal dysfunction.

1. May increase monitoring to every two weeks if patient is on a stable dose

iii. Monitor CBC weekly if there is increased risk for bleeding

iv. Low Molecular Weight Heparin (LMWH) Blood Level (obtain first level 4 hours after 3rd – 5th dose)

1. Goal for prophylactic dosing < 0.5 units/mL.

2. Regular monitoring for prophylaxis dosing is optional. Obtain if there is new bleeding, change in liver or renal function, or in critically ill patients.

v. For patients on enoxaparin prior to admission, check LMWH blood level 4 hours after the first or second hospital dose.

Table 5. Guidelines for Treatment Dose Titration Using LMWH Blood Level		
LMWH Blood level (units/mL)	**Dose Titration**	**Time to Repeat LMWH Blood Level**
< 0.35	**Increase** dose by 25%	4 hours after next dose
0.35-0.49	**Increase** dose by 10%	4 hours after next dose
0.5-1	Keep **same** dose	Next day, then 1 week later, then monthly (4 hours after dose)
1.1-1.5	**Decrease** dose by 20%	Before next dose**
1.6-2	**Hold** dose for 3 hours and decrease dose by 30%	Before next dose and then 4 hours after next dose**
> 2	**Hold** all doses until level is ≤ 0.5 units/mL, then decrease dose by 40%	Before next dose and every 12 hours until LMWH blood level ≤0.5 units/mL**

**Check serum creatinine if not recently checked, consult hematology for anticoagulation recommendations

2. Enoxaparin Reversal

- **a.** Protamine IV may provide partial reversal (approximately 60%).
- **b.** Check aPTT 2-4 hours after first dose of protamine. If this aPTT is prolonged or if the patient continues to bleed, administer a second dose of protamine (see Table 6).
- **c.** For neonates, smaller aliquots (10mg) of the total protamine dose administered every 2-3 hours until the anti-factor Xa level is < 2 units/ml may avoid potential toxicity from a large single protamine dose.
- **d.** LMWH blood level is never completely neutralized. Excessive protamine doses may worsen bleeding potential.

Table 6. Protamine Dose for Enoxaparin Reversal

Time Since Last Enoxaparin Dose	Protamine Sulfate Dose (mg) for Each 1 mg of Enoxaparin Administered
≤ 8 hours	1
> 8 hours	0.5
If second dose of protamine is needed	0.5
Max Dose	50 mg

C. Antithrombin III (ATIII) Monitoring and Supplementation in Non-ECMO Patients

- **a**. ATIII is an endogenous anticoagulant that inhibits coagulation enzymes, namely factor IIa and factor Xa.
- **b.** Heparin and low molecular weight heparin (LMWH) binds to ATIII, potentiating ATIII's inhibitory activity.
- **c.** Inadequate activity level of ATIII (congenital/inherited deficiency, protein-losing conditions such as enteropathy, nephrotic syndrome, or chylous output, DIC, liver disease, acute thrombosis, ECMO, hemodialysis, asparaginase therapy) can render a patient to be heparin-resistant (requiring high doses of heparin/LMWH to achieve or unable to achieve the desired anticoagulation monitoring goal).
- **d.** Routine monitoring of ATIII in a non-ECMO patient achieving adequate anticoagulation (i.e., the patient is not heparin-resistant) is not required.
- **e.** If a patient is deemed heparin-resistant, consider:
  - i. Obtaining plasma Antithrombin III (ATIII) Activity.
  - ii. Looking for acquired causes of low ATIII activity (i.e nephrotic syndrome).
  - iii. Consulting Pediatric Hematology/Oncology.
- **f.** Consider replacing with ATIII if the patient is considered heparin-resistant AND the ATIII activity is depressed.
  - i. ATIII activity goal is based on physician discretion; a goal of 50-75% is typically used. Of note, adult data uses an ATIII activity goal of 120% while HDVCH Pediatric and Neonatal ECMO guide uses a goal of 100%.
  - ii. Thrombate®: units per vial vary based on lot # but are approximately 500 or 1000 units per vial. When possible, round to nearest vial size to reduce waste.
  - iii. Dose (units) = $\frac{(\text{goal ATIII level} - \text{plasma ATIII level}) \times \text{actual weight (kg)}}{1.4}$
  - iv. After Thrombate replacement, monitor:
    - **1.** heparin/ LMWH doses and therapeutic goals frequently.
    - **2.** for bleeding.
    - **3.** peak ATIII activity levels (20 minutes after infusion) and trough (30 minutes prior to next scheduled dose, approximately 24 hours).
  - v. Subsequent doses, administered every 24 hours, may need to be recalculated depending on peak and trough levels obtained.

vi. The dose and duration of ATIII replacement are individualized and based on the indication for replacement, the clinical condition, the bleeding risk, response to therapy, and measured plasma ATIII activity levels.

g. For ECMO patients

D. Warfarin Anticoagulation

1. Contraindications

a. Warfarin is a teratogen, and therefore contraindicated with, some exceptions, during pregnancy. Birth control considerations should be made in patients of reproductive age.

2. Warfarin Dosing and Monitoring Guidelines

a. Special considerations:

i. Warfarin is available only in tablet form.

ii. The average warfarin dose required to achieve a therapeutic INR is:

1. Infants: average warfarin dose ~ 0.33 mg/kg/day (rarely recommended for infants < 2months of age)

2. Children 1 to 13 years: average warfarin dose ~ 0.14 mg/kg/day

3. Teenagers 13 to 18 years: average warfarin dose ~ 0.09 mg/kg/day

4. Adult: average warfarin dose ~ 0.04 to 0.08 mg/kg/day

iii. Several genetic polymorphisms have been associated with warfarin sensitivity.

iv. For most indications, the therapeutic target INR is 2.5 (range: 2-3). There are some patients who may require higher target INRs (mechanical/prosthetic mitral vales, recurrent thrombotic events). These patients' target INRs and guidelines should be set by their treating physician and followed accordingly.

v. For prophylaxis, the target INR is typically 1.7 (range: 1.5 to 1.9)

b. Overlap therapy:

i. Warfarin achieves pro-coagulant effects prior to achieving anticoagulant effects, making a period of overlap necessary between therapeutic UFH/LMWH and warfarin prior to stopping UFH/LMWH. This period of overlap is generally 4 to 5 days, at minimum, and at least 2 therapeutic INRs at approximately 24 hours apart.

ii. Warfarin loading period is approximately 4-7 days for most patients before a stable maintenance phase is achieved. Anticoagulation may be seen within 24 hours due to inhibition of factor VII synthesis, but peak anticoagulation activity is not achieved for 72-96 hours due to inhibition of factor II synthesis (2-3 days after 1st therapeutic INR).

iii. Patients with acute thrombosis and known Protein C or Protein S deficiency should be therapeutically anticoagulated with UFH or LMWH prior to starting warfarin due to the risk of skin necrosis (purpura).

c. DAY 1 loading dose / initiation of therapy recommendations:

Table 7. DAY 1 Loading Dose of Warfarin For Goal INR of 2-3 and 2.5-4

Baseline INR	Initial dose of warfarin (PO)
INR ≤ 1.3	0.2 mg/kg/dose (maximum 10 mg)
INR > 1.3	0.1 mg/kg/dose (maximum 5 mg)
Fontan or liver dysfunction	0.1 mg/kg/dose (maximum 5 mg)
Typically a dose of 5 mg is sufficient (maximum dose 10 mg)	

d. Dose adjustments recommendations:

Table 8. Warfarin Titration for GOAL INR of 2-3		
	INR	**Dosing Action for INR goal of 2-3**
DAY 2-4	**1.1 - 1.3**	Repeat initial loading dose
	1.4 - 3.0	Give 50% of initial loading dose
	3.1 - 3.5	Give 25% of initial loading dose
	> 3.5	HOLD warfarin until INR < 3.5, then restart at 50% of previous dose
DAYS ≥ 5	**< 1.5**	Increase dose by 20% of the previous dose
	1.5 - 1.9	Increase dose by 10% of the previous dose
	2 - 3	No change
	3.1 - 3.5	Decrease dose by 10% of the previous dose
	> 3.5	HOLD warfarin and check daily INR. When INR is < 3.5, then restart at 20% less than the previous dose

Table 9 Warfarin Titration for GOAL INR of 2.5-4		
	INR	**Dosing Action for INR goal of 2.5-4**
DAY 2-4	**< 1.8**	Repeat initial loading dose
	1.8 - 3.3	Give 50% of initial loading dose
	3.4 - 4	Give 25% of initial loading dose
	> 4	HOLD warfarin until INR < 4, then restart at 50% of previous dose
DAYS ≥ 5	**< 2**	Increase dose by 20% of the previous dose
	2 - 2.4	Increase dose by 10% of the previous dose
	2.5 - 4	No change
	4.1 - 4.5	Decrease dose by 10% of the previous dose
	> 4.6 - 5	Give one dose at 50% of prior dose, then decrease by 20%
	> 5	HOLD warfarin and check daily INR. When INR is < 3.5, then restart at 20% less than the previous dose

e. Monitoring

i. Baseline aPTT, PT/INR, CBC, urine pregnancy test in menstruating females prior to initiation of warfarin.
ii. At the initiation of warfarin, obtain daily INRs.
iii. After loading period (4-7days) and desired INR range is reached for 2 consecutive levels, then every 3rd day (if continued stable levels).
iv. Obtain INR/PT within 3 days of discharge from the hospital.
v. For patients on warfarin prior to admission, check INR within 24 hours of admission.
vi. Consult Nutrition to review the importance of dietary consistency.
vii. INR should be checked with any change to the patient's medications, dietary vitamin K intake (e.g, NPO to TPN, breastfeeding to infant formula), changes to GI absorption, prolonged antibiotic use, addition or removal of complementary/ alternative medications, systemic steroids, or change in hepatic function.
    1. If new medications are initiated while inpatient, review drug interactions with pharmacist.
    2. TPN contains 40mcg of vitamin K per ml of total multivitamin volume in < 40kg patient. When a pediatric patient weighs > 40 kg, the TPN contains 15mcg of vitamin K per ml of multivitamin.

3. Warfarin Reversal

a. The decision to reverse the effect of warfarin, how rapidly to reverse, and which reversal agent to use and the doses depend on the degree of elevation of the INR, the presence or absence of bleeding and the severity, and the risk of thrombosis if patient is not anticoagulated.
b. Repeat PT/INR to confirm elevated INR prior to reversal. If bleeding is present, a CBC, PTT should be obtained as well.
c. Patients with PT/INR that are unreliable (positive antiphospholipid antibodies or liver disease)
    i. The decision to reverse anticoagulation for these patients on chronic warfarin who presents with elevated INR above their therapeutic goal must be approached with extreme caution and consultation with Pediatric Hematology/ Oncology. For patients with antiphospholipid antibodies, factor II activity may be the only way to monitor their anticoagulation.
d. Effectiveness of vitamin K (phytonadione) can be monitored by INR
    i. Vitamin K IV: effect can be seen as soon as 4 to 6 hours, given for rapid reversal.
    ii. Vitamin K PO: effect can be seen 12-24 hours after enteral administration. NOTE: PO vitamin K is much more expensive than IV or SQ. If IV access is an issue, consider SQ administration.
e. Note that high doses of vitamin K can lead to warfarin resistance for 1 week
    i. Consider giving lower doses of vitamin K if the patient will require further oral anticoagulation, higher doses of vitamin K if the patient will no longer require further oral anticoagulation.
    ii. Consider bridging with uFH or LMWH in the short-term.
f. Patients on warfarin due to congenital heart disease are generally managed by Cardiology.
g. PT >90 secs and INR > 8 are reported as such
    i. Pediatric Hematology/ Oncology or Cardiology can contact Coagulation Dept to request testing on the BCX XP instrument for expanded reported.
        1. Report can be expanded to but not higher than PT >120.0 and INR >12.0.
        2. Report will be visible only as "comments".
        3. This process is only available to the pediatric population at HDVCH.

Table 10. Recommendations for Supratherapeutic INR in a Patient with Bleeding		
Severity of Bleeding	**Action**	**Additional Considerations**
Any INR With Major Bleeding (Defined by The International Society of Hemostasis and Thrombosis: fatal bleeding, overt bleeding with hemoglobin drop of > 2g/dL in 24 hours, bleeding into a critical organ (brain, lung, retroperitoneal), or bleeding requiring surgical intervention)	-Hold warfarin -Give Vitamin K 5 mg IV -Administer 4 Factor PCC* (Kcentra 25-50units/kg, round to nearest vial) -If PCC* is unavailable, give FFP (15ml/kg) -INR check every 6-12 hours	-May repeat Vitamin K IV at 12 hours -May repeat PCC* after 6 hours
Any INR With Minor Bleeding (Defined by The International Society of Hemostasis and Thrombosis: overt of macroscopic bleeding that does not meet criteria for major bleeding	**If high likelihood of progressing to major bleeding** -Hold warfarin -Give Vitamin K 2-5 mg IV -Consider 4 Factor PCC* (Kcentra 25-50units/kg, round to nearest vial) -If PCC* is unavailable, consider FFP (15ml/kg) -INR check every 12-24 hours	**If low likelihood of progressing to major bleeding** -Hold warfarin -Give Vitamin K 0.5-2mg IV -INR check every 12-24 hours

*PCC = KCentra (Prothrombin complex concentrates; 4-factor PCC) contains concentrated vitamin K-dependent coagulation factors II, VII, IX, X, Protein C, Protein S, and antithrombin.

Table 11. Recommendations for a Supratherapeutic INR in a Patient Without Bleeding		
INR	**Action**	**Additional Considerations**
> 8	Hold warfarin Give Vitamin K 2-5mg IV INR check every 12-24 hours	-May repeat Vitamin K IV at 24-48 hours -Resume therapy at lower dose when INR reaches therapeutic level
5 - 8	Hold warfarin INR check every 24 hours Consider Vitamin K 0.5-2mg IV	-Resume therapy at lower dose when INR reaches therapeutic level
> Goal, but < 5	Lower or omit next warfarin dose INR check every 24 hours	-Resume therapy at lower dose when INR reaches therapeutic level

Table 12. Alternative Weight and Age Based Vitamin K Dosing	
Weight and Age	**Dose (Slow Infusion over 15 to 30 minutes)**
Patients < 13 years old AND < 50 kg:	0.02 mg/kg/dose IV (max 1 to 2 mg) 0.03 mg/kg/dose IV (if surgery within < 24hr)
Patients $\geq$ 13 years AND $\geq$ 50 kg:	2.5 to 5 mg flat dose (if significant bleeding)

E. Bivalirudin Anticoagulation (ECMO)

1. Bivalirudin Anticoagulation Option for HDVCH ECMO

F. FXa Inhibitor Anticoagulation

1. Fondaparinux Dosing

a. Dosing (based on normal renal function)

Initial Dose	0.1 mg/kg/dose once daily (subcutaneous)

b. Monitoring

i. Baseline aPTT, PT/INR, CBC, and serum creatinine.
ii. Monitor serum creatinine weekly if inpatient and at increased risk of renal dysfunction.
iii. May increase monitoring to every two weeks if patient is on a stable dose
iv. Monitor CBC weekly if there is increased risk for bleeding
v. Anti-Xa blood level (measured 3-4 hours after subcutaneous administration)
    i. although fondaparinux is available on formulary, monitoring is done via a send out test using anti-Xa calibrated specifically for fondaparinux
vi. Goal for treatment dosing 0.5-1 mg/L.
vii. For patients on fondaparinux prior to admission, check fondaparinux anti-Xa blood level (send out lab) 4 hours after the first or second hospital dose.

c. Dose Titration

Fondaparinux Antifactor Xa Level	**Dose Titration**
<0.3 mg/L	Increase dose by 0.03 mg/kg
0.3 to 0.49 mg/L	Increase dose by 0.01 mg/kg
0.5 to 1 mg/L	Keep same dosage
1.1 to 1.2 mg/L	Decrease dose by 0.01 mg/kg
>1.2 mg/L	Decrease dose by 0.03 mg/kg

G. Other Anticoagulation Agents

Argatroban (direct thrombin inhibitor), Bivalirudin (non-ECMO) (direct thrombin inhibitor), are available and on formulary. Consider Pediatric Hematology/Oncology consult for use of these agents.

III. Suspected BT Shunt Thrombosis

Heparin and epinephrine should be given concurrently on all patients with a BT shunt while admitted. Order panel can be found within the pediatric cardiac surgery postoperative order-set.

Table 13. Anticoagulation for Suspected BT Shunt Thrombosis	
Drug (concentration)	**Dose**
Heparin (100 units/mL)	100 units/kg/dose
Epinephrine (0.1 mg/mL)	0.01 mg/kg/dose

IV. NEURAXIAL PUNCTURE OR CATHETER REMOVAL AND ANTICOAGULATION

Treatment doses of anticoagulation are contraindicated while an epidural catheter is in place. Prophylactic doses may be acceptable. Please discuss with Anesthesiology, Pharmacy, and primary care team regarding risks and benefits of any anticoagulation while an epidural catheter is in place.

Neurological exam (frequency agreed upon by primary team – consider at least q4-6 hours due to risk of hematoma formation) should be continued for 24 hours post catheter removal.

If patient has been receiving heparin or LMWH for > 4 days, check platelet count prior to catheter removal.

Table 14: Neuraxial Puncture or Catheter Removal/Manipulation Anticoagulation Guidelines[21]			
Drug	**Time Before Puncture/Catheter Manipulation or Removal** (Minimum time between LAST dose of anticoagulant and neuraxial procedure)	**While Catheter is in Place**	**Time after Puncture/Catheter Manipulation or Removal** (Minimum time after neuraxial procedure and NEXT dose of anticoagulant)
Unfractionated heparin (prophylaxis)	4 - 6 hours (IV) 12 hours (SQ)	Discuss risks/benefits with anesthesiology and decide whether to give or withhold	1 hour (both IV and SQ)
Unfractionated heparin (treatment)	4 - 6 hours (IV) 24 hours (SQ)	Discuss risks/benefits with anesthesiology and decide whether to give or withhold	1 hour (both IV and SQ)
LMWH ONCE daily dosing (prophylaxis) LMWH TWICE daily dosing (prophylaxis)	12 hours 12 hours	Discuss risks/benefits with anesthesiology and decide whether to give or withhold **Contraindicated**	12 hours after catheter placement or 4 hours after catheter removal whichever is greater
LMWH (treatment)	24 hours Consider checking residual anti-Xa levels esp in patients with renal insufficiency	**Contraindicated**	24 hours after catheter placement or 4 hours after catheter removal whichever is greater
Rivaroxaban	72 hours	Discuss risks/benefits with anesthesiology and decide whether to give or withhold	6 hours
Apixaban	72 hours	Discuss risks/benefits with anesthesiology and decide whether to give or withhold	6 hours
Dabigatran	CrCl: 30-49 mL/min: 120 hr 50-79 mL/min: 96 hr ≥80 mL/min: 72 hr	Discuss risks/benefits with anesthesiology and decide whether to give or withhold	6 hours
Coumadin	5 days and normal INR	Only with low-dose warfarin; Monitor daily INR	Remove catheter when INR is < 1.5 and within 12-24 hours of first dose of warfarin. Warfarin can be immediately initiated after catheter removal.
Direct Thrombin Inhibitors such as Argatroban or Bivalirudin	Contraindicated	Contraindicated	Contraindicated
Aspirin	None	None	None

Clopidogrel	5 - 7 days	Can be maintained for 1 - 2 days, provided no loading dose was administered	After catheter removal
Ticlopidine	10 days	Can be maintained for 1 - 2 days, provided no loading dose was administered	After catheter removal

V. PERIOPERATIVE BRIDGING FOR PLANNED PROCEDURES FOR PATIENTS RECEIVING WARFARIN THERAPY

Bridging Therapy Definition: The use of an anticoagulant agent provided at VTE treatment doses during interruption of warfarin therapy.

- **a.** Notify the primary team if a procedure is planned and anticoagulant has not been assessed/or held, if appropriate.
- **b.** Temporary interruption of anticoagulation is generally recommended for most procedures (discontinue warfarin approximately 5 days before surgery).
- **c.** Assess the perioperative thromboembolic risk and the need for bridging (Table 15).
    - **i.** A patient may have multiple low or moderate risk factors that together, may place them at higher risk for perioperative thromboembolism.
- **d.** Assess the perioperative bleeding risk and the dosing strategy of bridging therapy (therapeutic vs prophylaxis).
    - **i.** There is no evidence-based schema that can stratify the type of surgeries and the risk for bleeding with perioperative bridging therapy.
- **e.** The benefits of bridging therapy, dosing strategy (therapeutic vs prophylaxis), and type of anticoagulation used (IV UFH vs LMWH) should be discussed with the provider performing the procedure/ surgery.
- **f.** If bridging therapy is necessary, consider consulting Pediatric Hematology/Oncology or Cardiology.
- **g.** Discontinuation/re-initiation of bridging therapy prior/post to surgery
    - **i.** Therapeutic/ Prophylactic dosing
        1. IV UFH:
            - **a.** stop UFH 4 to 6 hours prior to the procedure/ surgery.
        2. LMWH
            - **a.** Administer the last preoperative dose of LMWH approximately 24 hours prior to the procedure/ surgery.
        3. Resumption of bridging therapy can be as early as 24 hours postoperatively.
            - **a.** Discuss with the provider performing the procedure/ surgery regarding the risk of postoperative bleeding with anticoagulation.
            - **b.** Assess for postoperative bleeding.
            - **c.** If > 72 hours without bridging anticoagulation secondary to postoperative bleeding and there is a high risk of thromboembolic disease, consider prophylactic dosing therapy.
            - **d.** When resuming warfarin after the bridging therapy, follow the same recommendations for initiation of warfarin (D.2).

Table 15. Bridging for Warfarin: Risk Stratification of Perioperative Thromboembolism		
Factors Associated with High Risk of Thromboembolic Disease **Recommend to bridge**	**Factors Associated with Moderate Risk of Thromboembolic Disease** **Consider bridging**	**Factor Associated with Low Risk of Thromboembolic Disease** **Bridging not required**
VTE within the last 3 months	VTE within the last 3 – 12months	VTE occurred > 12 months ago and no other risk factors
History of VTE and severe thrombophilia (Protein C, S, or ATIII deficiency, APL antibodies, homozygous FVL, or multiple abnormalities	History of VTE and other inherited thrombophilia (heterozygous FVL or heterozygous Prothrombin Gene G20210A mutation)	
History of prior stroke	Recurrent VTE	
History of thromboembolism during anticoagulation interruption	Active cancer	

APL: Antiphospholipid, FVL: Factor V Leiden

VI. SWITCHING ANTICOAGULATION

Table 16.	**Switch To →**				
Switch From ↓	Warfarin	UFH	Bivalirudin	Enoxaparin& Fondaparinux	Direct Xa inhibitor (Rivaroxaban, Edoxaban, Apixaban)[11]
Warfarin		Stop warfarin. Start UFH when INR < goal.	Stop warfarin. Start Bivalirudin when INR < goal.	Stop warfarin. Start enoxaparin when INR < goal.	Stop warfarin. Check INR 2 days later. Start DOAC once INR is <2 or lower INR limit of target range. If INR >2.5, repeat INR every 24-48 hrs until <2.
UFH	Start warfarin. Stop UFH after 5 days of overlap AND INR > 2 for two consecutive days		Stop UFH and initiate Bivalirudin	Stop UFH and start enoxaparin at the same time.	Start DOAC at hr 0 -2 after stopping UFH.
Bivalirudin	Start warfarin. Stop Bivalirudin after 5 days of overlap AND INR > 2 for two consecutive days	Stop Bivalirudin and initiate UFH		Stop Bivalirudin and start enoxaparin at the same time.	Start DOAC at hr 0 -2 after stopping Bivalirudin.
Enoxaparin& Fondaparinux	Start warfarin. Stop enoxaparin after both 5 days of overlap AND INR > 2 for two consecutive days	Stop enoxaparin. Start UFH 4 hours before next enoxaparin dose would have been due. If there is a high risk of bleeding, consider omitting initial bolus of UFH.	Stop enoxaparin. Start Bivalirudin 4 hours before next enoxaparin dose would have been due.		Stop enoxaparin and start DOAC at the time enoxaparin would have been due.
Direct Xa inhibitor (Rivaroxaban, Edoxaban, Apixaban)[11]	Start warfarin and continue DOAC. For edoxaban, decrease dose by half when starting warfarin. Check INR 3-5 days from initiation. If INR ≤ 2, recheck INR every 24-48 hrs. IF INR > 2, stop DOAC and recheck INR in 24-48 hrs. Obtain INR before DOAC dose as DOACs may falsely elevate INR.	Stop DOAC and start UFH at the time DOAC would have been due.	Stop DOAC and start Bivalirudin at the time DOAC would have been due.	Stop DOAC and start enoxaparin at the time DOAC would have been due.	

DOAC: direct oral anticoagulation

Pathway Information

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