Therapeutic Dosing of Unfractionated Heparin - Adult - Inpatient/Emergency Department

Consensus Care Guideline

Population/Problem:

This consensus care guideline is intended to provide physicians, advanced practice providers, nurses, and pharmacists with a process to standardize the initiation, maintenance, and monitoring of intravenous unfractionated heparin in the adult population. Practices considered include guidance on selection of dosing nomograms, initial and maintenance monitoring of heparin infusions, initial and maintenance heparin dose adjustments, and transitioning between dosing nomograms.

Definitions:

Gradual Anticoagulation Nomogram – Initiates unfractionated heparin at a lower initial infusion rate with the intent to achieve a therapeutic range within 24-36 hours. This nomogram is typically reserved for patients receiving concomitant thrombolytics, who have a new mechanical valve during current admission or when concerns for bleeding outweigh the need for quickly reaching a therapeutic goal.[1]

Rapid Anticoagulation Nomogram – Initiates unfractionated heparin with the intent to achieve a therapeutic range within 18-24 hours. This nomogram is typically reserved for venous or atrial thrombosis, acute coronary syndrome, history of mechanical valves or when therapeutic anticoagulation is needed quickly.[2,3]

Recommendations:

Heparin (UFH) infusions with the intent for titration to a therapeutic goal must be ordered via the Heparin Anticoagulation Supplemental Order Set. No modifications of these nomograms are allowed. While discouraged, if patient circumstances require heparin dosing that differs from established nomograms, specific orders must be written.

1. Baseline laboratory monitoring[4]
   a. Prior to starting the UFH infusion collect the following baseline labs if not already resulted in the previous 48 hours
      - PT/INR
      - CBC with platelet
      - Heparin anti-Xa level: only if on an oral Xa inhibitor (apixaban, rivaroxaban) prior to starting the UFH infusion
      - Drug specific anti-Xa level: only if on an oral Xa inhibitor (apixaban, rivaroxaban) in the previous 48 hours prior to starting the UFH infusion

2. Select the indication for UFH use

Table 1. Initial UFH Dosing Based on Indication[1-5] *(UW Health GRADE high quality evidence, strong recommendation)*

Indication	Anti-Xa Target Goal	Initial Bolus	Initial Infusion Rate
Anticoagulation for COVID (Rapid Nomogram unless high bleed risk)	0.3-0.7 IU/mL	80 units/kg (max 10,000 units)	18 units/kg/hr
Venous Thromboembolism/ Atrial Thrombosis (Rapid Nomogram unless high bleed risk)	0.3-0.7 IU/mL	80 units/kg (max 10,000 units)	18 units/kg/hr
Mechanical Heart Valve (historical) (Rapid Nomogram unless high bleed risk)	0.3-0.7 IU/mL	80 units/kg (max 10,000 units)	18 units/kg/hr
Mechanical Heart Valve (new during admission) (Gradual Nomogram)	0.3-0.7 IU/mL	None	12 units/kg/hr
Therapeutic anticoagulation with elevated bleeding risk (Gradual Nomogram)	0.3-0.7 IU/mL	None	12 units/kg/hr
Systemic thrombolytics used in previous 24 hours (Gradual Nomogram)	0.3-0.7 IU/mL	None	12 units/kg/hr
Acute Coronary Syndrome with GP IIb/IIIa inhibitor (e.g. eptifibatide) (Gradual Nomogram)	0.1-0.3 IU/mL	None	12 units/kg/hr (max 1,000 units/hr)
Acute Coronary Syndrome without GP IIb/IIIa inhibitor (Rapid Nomogram unless high bleed risk)	0.3- 0.7 IU/mL	60 units/kg (max 4,000 units)	12 units/kg/hr (max 1,000 units/hr)

Initial boluses and infusion rates are based on actual body weight

3. Titration of UFH infusion
   a. The nomogram for titration will be specified in the administration instructions of the heparin infusion order

Table 2. Gradual Anticoagulation Nomogram (e.g., Therapeutic anticoagulation with elevated bleeding risk, systemic thrombolytics used in past 24 hours, mechanical heart valve (new during admission), acute coronary syndrome with GP IIb/IIIa inhibitor) *(UW Health GRADE low quality evidence, conditional recommendation)*

Heparin Level by Anti-Xa (IU/mL)	Bolus/Hold	Infusion Rate Change
<0.1	Bolus 20 units/kg & inform MD (max 5,000 units)	increase by 2 units/kg/hr
0.1 – 0.29	None	increase by 1 units/kg/hr
0.3 – 0.7	None	NO CHANGE; Therapeutic Range
0.71 – 0.8	None	decrease by 1 units/kg/hr
0.81 – 1.7	Hold infusion 1 hr	decrease by 2 units/kg/hr
>1.7	Hold infusion 1½ hr & inform MD	decrease by 3 units/kg/hr

Table 3. Rapid Anticoagulation Nomogram (e.g., Anticoagulation for COVID, venous thromboembolism, atrial thrombus, mechanical heart valve (historical), acute coronary syndrome without GP IIb/IIIa inhibitor) *(UW Health GRADE low quality evidence, conditional recommendation)*

Heparin Level by Anti-Xa (IU/mL)	Bolus/Hold	Infusion Rate Change
<0.1	Bolus 40 units/kg & inform MD (max 10,000 units)	increase by 3 units/kg/hr
0.1 – 0.19	Bolus 20 units/kg & inform MD (max 5,000 units)	increase by 2 units/kg/hr
0.2 – 0.29	None	increase by 1 units/kg/hr
0.3 – 0.7	None	NO CHANGE; Therapeutic Range
0.71 – 0.8	None	decrease by 1 units/kg/hr
0.81 – 1.7	Hold infusion 1 hr	decrease by 2 units/kg/hr
>1.7	Hold infusion 1½ hr & inform MD	decrease by 3 units/kg/hr

Table 4. Nomogram for Treatment of Acute Coronary Syndrome with GP IIb/IIIa inhibitor *(UW Health GRADE low quality evidence, conditional recommendation)*

Heparin Level by Anti-Xa (IU/mL)	Bolus/Hold	Infusion Rate Change
< 0.1	Bolus 20 units/kg & inform MD (max 5,000 units)	increase by 3 units/kg/hr
0.1 – 0.3	None	NO CHANGE; Therapeutic Range
0.31 – 0.5	None	decrease by 1 units/kg/hr
0.51 – 0.8	None	decrease by 2 units/kg/hr
> 0.8	Hold infusion 1 hr & inform MD	decrease by 3 units/kg/hr

4. Heparin and Direct Xa Inhibitors[6-9] (apixaban, rivaroxaban) *(UW Health GRADE low quality evidence, conditional recommendation*
    a. In the presence of a direct Xa inhibitor the measured anti-Xa level may be relatively high in proportion to the antithrombin activity. This may result in over estimation of the heparin activity by the assay. To account for this, a higher anti-Xa goal may be used for patients with recent use of direct Xa inhibitors.
    b. Target a higher anti-Xa range (Table 5) in patients who received a direct Xa inhibitor in the previous 48 hours and if the baseline heparin anti-Xa level is elevated.
    c. A drug specific anti-Xa level should be drawn prior to starting the heparin infusion:
        i. If the drug specific anti-Xa level is within or elevated outside of the target range, then heparin infusion should not be started.
        ii. If unable to wait for the drug specific anti-Xa level to result, then patient risk/benefit for thrombotic and bleeding risks should be weighed prior to starting the heparin infusion.
    d. Return to the standard anti-Xa goal based on indication for unfractionated heparin 48 hours after the last dose of the direct Xa inhibitor (apixaban, rivaroxaban) was given (See Table 1).

Table 5. Nomogram for Direct Xa inhibitor in Previous 48 hours and Elevated Baseline Heparin Anti-Xa *(UW Health GRADE low quality evidence, conditional recommendation)*

Heparin Level by Anti-Xa (IU/mL)	Bolus/Hold	Infusion Rate Change
< 0.1	Bolus 40 units/kg & inform MD (max 10,000 units)	increase by 3 units/kg/hr
0.1 – 0.39	Bolus 20 units/kg & inform MD (max 5,000 units)	increase by 2 units/kg/hr
0.4 – 0.69	None	increase by 1 units/kg/hr
0.7 – 1	None	NO CHANGE; Therapeutic Range
1.01 – 1.4	None	decrease by 1 units/kg/hr
1.41 – 1.7	Hold infusion 1 hr	decrease by 2 units/kg/hr
> 1.7	Hold infusion 1½ hr & inform MD	decrease by 3 units/kg/hr

5. Titration Pearls:
    a. If the infusion is held for a procedure it is ok to resume the infusion at the previous rate prior to the hold. *(UW Health low quality evidence, conditional recommendation)*

    b. If goal is not reached within 24 hours for rapid nomogram or 36 hours for gradual nomogram, with correct titration, the patient may not be an appropriate candidate for adjustments based on these heparin nomograms. Recommend consultation with Pharmacy and/or Hematology for assistance with dosing.

6. Laboratory Monitoring

Table 6. Laboratory monitoring for UFH infusion[4]

Lab	Initiation/Titration	Maintenance
Heparin level by anti-Xa	6 hours after initiation or resumption of infusion following a hold 6 hours after any rate change	Once 3 consecutive levels are in target range, then check daily
Hemoglobin	24 hours after initiation	Every other day for up to 14 days
Platelets	24 hours after initiation	Every other day for up to 14 days

7. Transitioning between nomograms and anticoagulants[10-14]

Table 7. Transitioning between UFH and other anticoagulants

Gradual to Rapid Rapid to Gradual	Continue current infusion rate When next level results titrate with new nomogram
Heparin to Enoxaparin	Stop heparin Administer enoxaparin 2-4 hours later
Heparin to DOAC	Stop heparin Give oral anticoagulant at the same time
Heparin to Fondaparinux	Stop heparin Administer fondaparinux 2-4 hours later

Disclaimer

Consensus care models assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

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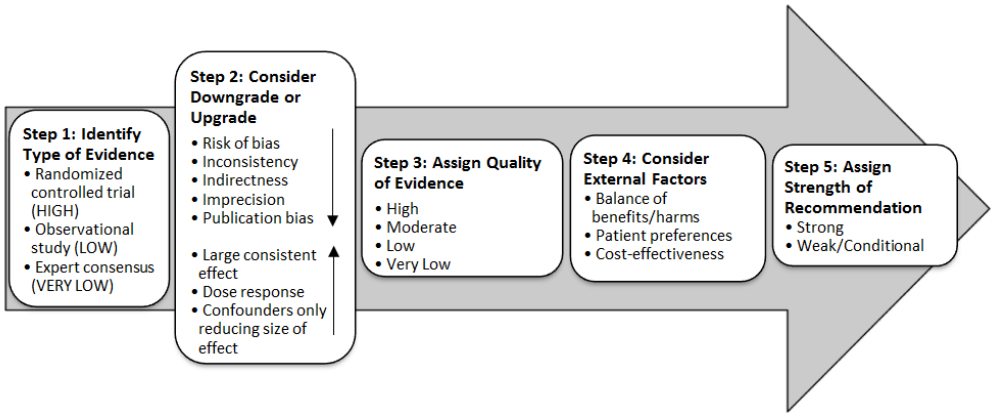

Table 1. GRADE Ranking of Evidence[15]

High	We are confident that the effect in the study reflects the actual effect.
Moderate	We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.
Low	The true effect may differ significantly from the estimate.
Very Low	The true effect is likely to be substantially different from the estimated effect.

Table 2. GRADE Ratings for Recommendations for or Against Practice

Strong (S)	Generally, should be performed (i.e., the net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.)
Conditional (C)	May be reasonable to perform (i.e., may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.)

Revise guideline as necessary, based on workgroup feedback and continued evidence

Collateral Tools & Resources

Metrics
- VTE Performance Measure – VTE 4 – UFH with dosage and platelet monitored by protocol
- Guideline adherence: anti-Xa level monitoring, infusion rate adjustments, nomogram selection
- Time to achieve a target Xa level, supra-therapeutic Xa levels, bleeding, and thrombotic events

Order Sets & Smart Sets
- IP/ED - Heparin Anticoagulation - Adult - Supplemental [4373]

Protocols
Heparin Infusion Titration – Adult – Inpatient [4]

Other Related Documents and Tools
- Extracorporeal Membrane Oxygenation (ECMO): Initiation and Management - Adult - Inpatient/Emergency Department Consensus Care Guideline
- UW Health Mechanical Circulatory Device (MCD) - Adult - Inpatient/Ambulatory/Emergency Department Clinical Practice Guideline
- IP - ECMO Heparin Anticoagulation - Adult - Supplemental [5894]
- IP - Total Artificial Heart Heparin Anticoagulation - Adult - Supplemental [5559]
- IP - Ventricular Assist Device Heparin Anticoagulation - Adult - Supplemental [4999]

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