Monitoring Unfractionated Heparin in Patients Transitioning from Factor Xa Inhibitors: A Quality Improvement Analysis Using Anti-Xa Levels

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Introduction

- Unfractionated Heparin (UFH) remains the cornerstone of inpatient anticoagulation, traditionally monitored by partial thromboplastin time (PTT).[1]
- Recently, anti-Xa levels have become the preferred monitoring method for UFH, offering better correlation with heparin activity.[1,2]
- Patients admitted on factor Xa inhibitors may have elevated baseline anti-Xa levels, complicating UFH interpretation and dosing. In such cases, reverting to PTT monitoring is indicated until anti-Xa levels are normalized.[3] At ARMC, anti-Xa monitoring for UFH was implemented in May 2025.
- Serial monitoring of anti-Xa levels (every 6 hours) in those starting UFH and an elevated baseline anti-Xa level along with PTT monitoring was utilized until the anti-Xa level reached a measurable threshold of ≤ 0.7 IU/mL.

Objective

The purpose of this study is to characterize the time to anti-Xa normalization in patients with recent factor Xa inhibitor exposure and to optimize monitoring recommendations within our pharmacy-managed UFH protocol.

Methods

- A retrospective review of patients initiated on a pharmacist-managed heparin protocol between May 2025 and June 2025 was conducted. Of the 217 protocols reviewed, 51 patients were included who had prior factor Xa inhibitor use with an elevated baseline anti-Xa level >0.7 IU/mL. (**Figure 1**)
- Those with a baseline anti-Xa level of ≤ 0.7 IU/mL were excluded.
- Data collection included: gender, age, indication, Xa inhibitor used, and the duration in hours of the elevated anti-Xa level identified as anti-Xa >0.7 IU/mL. Serial anti-Xa measurements were taken every 6 hours.
- Descriptive statistics were used for data analysis. Approval by the ARMC Institutional Review Board was obtained.

Results

Figure 1. Study Inclusion

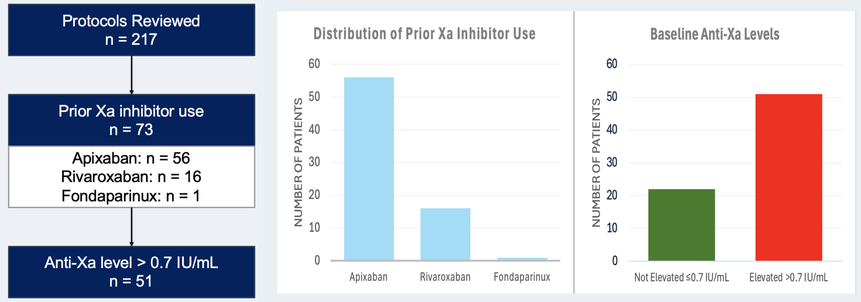

Table 1. Baseline Patient Characteristics (N = 51)

Characteristic	Mean ± SD or n (%)
Age (years)	69 ± 13.6
Male	39 (76.5)
Weight (kg)	89.5 ± 29.2
Anti-Xa Level >1.1 IU/mL	44 (86.3)
Heparin Protocol Indication	
Cardiac	38 (74.5)
Thrombus	12 (23.5)
Stroke	1 (2.0)

Table 2. Time to Anti-Xa Normalization Among Patients With Elevated Levels

Time in Hours (± SD)
Mean 23.06 (± 13.15)
Median 24
Range 6 to 60

Anti-Xa Levels: Therapeutic Range 0.3-0.7 IU/mL; Elevated >0.7 IU/mL

Discussion

- Our retrospective, observational analysis found that transition from a factor Xa inhibitor to UFH was associated with delayed anti-Xa normalization (mean 23 hours; median 24 hours). (**Table 2**)
- These findings suggest that 6-hour anti-Xa monitoring offers limited clinical value and may lead to unnecessary laboratory testing.
- As a result, our heparin protocol (**Figure 2**) was revised for patients with known factor Xa inhibitor use and an elevated baseline anti-Xa level. The updated approach recommends using PTT alone for initial heparin dose adjustment, monitoring anti-Xa levels every 24 hours until therapeutic, and then transitioning to anti-Xa monitoring only for subsequent adjustments.
- This change streamlines workflow, reduces blood draws and lab resource use, and enhances protocol clarity.

Conclusion

Adapting our pharmacy heparin protocol to account for prior factor Xa inhibitor use improved workflow efficiency without compromising patient safety. Future evaluation should assess clinical outcomes such as bleeding and thrombosis.

References

Figure 2. Institutional Heparin Dosing Nomogram

PTT Therapeutic (seconds)	Heparin Anti-Xa (IU/mL)	Dose Change	Assay
<40	< 0.1	Bolus* and increase rate by 3 units/kg/hr *Bolus dosing, unless NEVER BOLUS ordered • Cardiac 50 units/kg (Max: 4,000 units) • Thrombus 50 units/kg (Max: 10,000 units) • Neuro/Ischemic stroke– NEVER BOLUS	Repeat lab in 6 hours (timed study) AFTER making adjustment.
40 to 58.9	0.1 to 0.19	Increase rate by 2 units/kg/hr	
59 to 75.6	0.2 to .29	Increase rate by 1 unit/kg/hr	
75.7 to 104.1	0.3 to 0.7	**NO CHANGE** **Therapeutic Range**	Repeat lab in 6 hours (timed study). Once therapeutic for 2 consecutive assays, change to once-daily assay (routine study) *
104.2 to 120.9	0.71 to 0.8	Decrease rate by 1 unit/kg/hr	Repeat lab in 6 hours (timed study) AFTER making adjustment.
121 to 135.9	0.81 to 0.9	Hold infusion for 1 hr and then decrease rate by 2 units/kg/hr	
136 to 149.9	0.91 to 1	Hold infusion for 2 hr and then decrease rate by 3 units/kg/hr	
≥150	>1	**Ensure appropriate blood draw technique and review current rate for accuracy.** **Potentially contaminated sample:** • If < 6 hrs since most recent bolus or rate change: continue rate, and repeat assay at the appropriate time • If ≥ 6 hours since most recent bolus or rate change: ○ Turn OFF heparin infusion ○ Repeat STAT assay immediately using peripheral blood draw ▪ Anti-Xa ≤1 or PTT <150 → resume heparin according to algorithm ▪ Anti-Xa >1 or PTT ≥ 150 → follow steps below **Properly timed, non-contaminated sample:** • Turn OFF heparin infusion and notify provider • Hold heparin infusion for 2 hours and then repeat assay ○ Anti-Xa ≤1 or PTT < 150: decrease rate by 4 units/kg/hr	

Management of therapeutic heparin in the presence of recent Xa inhibitor use:

- Rivaroxaban, apixaban, edoxaban, low molecular weight heparin (LMWH), and fondaparinux can prolong anti-Xa assays.
  a. PTT is less sensitive to these agents and will be therapeutic monitoring parameter of choice when:
     i. The baseline anti-Xa level is supratherapeutic (> 0.7) **AND**
     ii. A patient has recently received one these of these agents
  b. The following monitoring procedure is recommended:
     i. Heparin to be monitored/dose adjusted per PTT therapeutic.
     ii. Re-check anti-Xa daily with morning labs UNTIL anti-Xa levels results in a therapeutic range (0.3 to 0.7 IU/mL)
     iii. Then revert to anti-Xa monitoring/adjustments *alone* (PTT for dose adjustments no longer required)

**It is still required to modify the start time of heparin to transition appropriately between anticoagulation therapies after consulting with the provider (consistent with Section A - Subsection C).*

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