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Insight & Commentary

No Calibrated Anti-Xa Assay? No Problem! Utility of Heparin Based Assays for Factor Xa Inhibitor Assessment

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Emergent decision-making in anticoagulated patients demands pragmatism, not perfection. For patients who are on vitamin-K antagonists, like warfarin, monitoring is well established with the international normalized ratio (INR). Most clinicians feel comfortable in interpreting a patient's INR, reversal candidacy, and those that can proceed with emergent therapies or procedures. However, there remains some ambiguity and hesitation in how to interpret the degree of coagulopathy for patients on factor Xa inhibitors like apixaban or rivaroxaban.[1] In many instances time of last ingestion is the deciding factor for reversal, surgical, or other therapeutic candidacy. This subjective assessment is certainly fraught with inaccuracies as patients are often non-compliant or histories can be misleading. Additionally, traditional coagulation tests like the INR are only elevated at supratherapeutic levels and may not be accurate at normal serum concentrations that still provide clinically relevant coagulopathy.[2]

For decades, clinicians have relied on readily available, rapidly resulted heparin based anti–factor Xa (anti-Xa) assays to guide therapy in patients on unfractionated or low-molecular-weight heparins.[3] Many institutions defer using heparin based anti-Xa based assays and either opt for subjective assessment or chromogenic factor Xa when it comes to assessment of rivaroxaban or apixaban associated coagulopathy. Chromogenic and agent specific anti-Xa assays often are not available and lack expedited turnaround times.[4] In emergency settings, a heparin-calibrated anti-Xa result has demonstrated an ability to guide reversal, procedural safety, or thrombolytic eligibility decisions.[5-10] In emergent scenarios, the difference between a 30-minute and 3-hour turnaround can determine whether a patient receives thrombolysis, reversal, or surgery.

Multiple independent studies have shown a strong correlation between heparin-calibrated anti-Xa activity and factor Xa inhibitor plasma concentrations. Billoir et al. demonstrated a near-linear relationship between LMWH anti-Xa activity and both rivaroxaban and apixaban concentrations (R^2 = 0.947 and 0.959, respectively).[5] A LMWH anti-Xa <0.5 IU/mL reliably excluded plasma concentrations >30 ng/mL, levels considered safe for urgent procedures. Von Horn et al. similarly found that LMWH-calibrated assays closely mirrored drug-specific calibrations when compared to LC–MS/MS gold standard values for both apixaban and rivaroxaban.[6] Riahi et al. validated heparin-calibrated anti-Xa thresholds prospectively, establishing cutoffs of 0.3 IU/mL for invasive procedures and 0.51 IU/mL for thrombolysis, achieving sensitivities >97% and negative predictive values approaching 100%.[10] Shin et al. showed that a UFH-calibrated anti-Xa <1.4 IU/mL predicted plasma rivaroxaban levels <100 ng/mL with 100% sensitivity, again supporting safe clinical thresholds.[9]

Across these investigations, the message is consistent: a reduced heparin anti-Xa result effectively rules out clinically significant DOAC levels, allowing clinicians to proceed safely with thrombolysis or urgent interventions when delay could be catastrophic.

Few would consider reversing warfarin without first checking an INR. Yet, many institutions withhold heparin-based anti-Xa assays for factor Xa inhibitor users on the premise that the test is not "specific" enough. Like INR, an anti-Xa value offers context, not perfection. The question in an emergency is not "exactly how many nanograms per milliliter?" but rather "is there enough residual anticoagulant effect that necessitates therapy or can be proceeded with safely?" A heparin-calibrated anti-Xa assay answers that question rapidly and accurately enough to inform action.

Delaying therapy based solely on last-known ingestion time, or conversely, administering expensive reversal agents empirically, carries measurable risk. Overestimating factor Xa inhibitor exposure may withhold lifesaving thrombolytics; underestimating exposure risks intracranial hemorrhage or surgical bleeding. Now with andexanet no longer available on the markert agents like prothrombin complex concentrates (PCCs) are utilized in the management of factor Xa associated bleeds, but are not benign therapies and erroneous resuscitation could lead to disastrous prothrombic effects.[11] Furthermore, with the cost of these agents being relatively expensive, objective testing before administration is not only clinically rational but fiscally essential.[12]

Turnaround time is arguably the most compelling argument for the heparin-based approach. At most institutions, results are available within 20–30 minutes. That timeline aligns with the urgency of stroke thrombolysis, neurosurgical evacuation, or trauma resuscitation. The assays are already validated within hospital quality systems for therapeutic heparin monitoring; extending their interpretation to factor Xa inhibitors simply leverages existing infrastructure. Given andexanets removal from the markert, it's plausible that with heparin-based anti-Xa assays and PCCs reg-

Table 1. Heparin Anti-Xa Assay Value and Suggestive Interpretation

Value	Interpretation
<0.3 IU/mL	Safe to proceed with most invasive or thrombolytics interventions
0.3 - <0.5 IU/mL	Cautious consideration for therapeutic decision
≥0.5 IU/mL	Therapeutic serum concentration or higher for factor Xa inhibitor

ularly stocked in automated dispensing cabinets that time to administration of these agents will be drastically reduced.[13] The cumulative data support a simple, implementable algorithm for emergency practice (Table 1).

The pursuit of chromogenic precision should not come at the expense of timely, evidence-based decisions. Heparin-calibrated anti-Xa assays are not a compromise but are a pragmatic, validated tool that bridges the gap between pharmacologic science and bedside urgency. When seconds matter, good enough is exactly what patients need.

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