

APIXABAN AND COAGULATION CORRELATION

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CASE:

73 years-old female Patient with past medical history of:

Stage 3a chronic kidney disease, AKI (acute kidney injury), Longstanding persistent atrial fibrillation, Primary hypertension, Diabetes mellitus and Primary hyperparathyroidism.

The patient was admitted to the emergency department due to anemia. Her chief complaint was abnormal labs (Had labs yesterday were told her Hemoglobin was 5.3- was advised to go to ED to recheck). She reports mild fatigue but otherwise she feels well. She denied melena, vaginal bleeding, hematemesis, hematochezia or any other bleeding symptoms. She denied any chest pain, shortness of breath, palpitations, side effects from medications. She reports she is not on dialysis. She does not smoke.

Medications: Carboxymethylcellulose sodium, Cholecalciferol 1000 IU, Cyclosporine 0.05%, Metformin XR 500 mg, Metformin 500 mg, Atorvastatin 20 mg, Clonidine 0.1 mg, Digoxin 125 mcg, Furosemide 40 mg, Hydralazine 25 mg, Potassium chloride 20 mEq, Losartan 100 mg, Magnesium oxide 400 mg, Metoprolol succinate 100 mg, Spironolactone 25 mg, Apixaban 5 mg.

She was on Eliquis.

Allergies: No Known Allergies

Past surgical history: Tubal ligation

Vitals in ER: Temp:97.8 97.6 °F, Heart rate: 89, Respiratory rate: 17 BP: 175/93,

SpO2: 100%, BMI: 25.06 kg/m²

Physical examination was normal.

LABS: Labs were considered to rule out hyperkalemia, hypokalemia, hyponatremia, hypernatremia, hypercalcemia, hypocalcemia, anemia, AKI.

XR CHEST 04/21/2026, results were normal.

US RENAL 04/21/2026, results were normal.

ELECTROCARDIOGRAM 04/21/26, Atrial fibrillation (same as before)

| Test | 04/21/2026 (ED) | 04/22/2026 (After transfusion) | Interpretation |
|------------------------|-----------------|--------------------------------|------------------------------|
| Sodium | 138 | 138 | Stable |
| Potassium | 4.3 | 4.3 | Stable |
| Chloride | 104 | 105 | Slight increase |
| CO2 | 22 ↓ | 22 ↓ | Low |
| BUN | 28 ↑ | 20 | Improved |
| Creatinine | 1.14 ↑ | 1.00 ↑ | Slight improvement |
| Glucose | 136 ↑ | 106 ↑ | Decreased |
| Calcium | 9.7 | 9.6 | Stable |
| WBC | 9.23 | 11.07 | Mild increase |
| RBC | 2.87 ↓ | 3.39 ↓ | Increased (post-transfusion) |
| Hemoglobin | 5.5 ↓↓↓ | 7.6 ↓ | Significant improvement |
| Hematocrit | 19.8 ↓ | 25.2 ↓ | Improved |
| Platelets | 610 ↑ | 504 ↑ | High but decreasing |
| PT | 34.4 ↑ | 15.4 ↑ | Improved |
| INR | 3.4 ↑ | 1.2 | Near normalization |
| PTT | 41.2 ↑ | — | Elevated initially |
| Iron | 20 ↓ | 58 | Improved |
| TIBC | 386 | 434 ↑ | Elevated |
| Transferrin Saturation | 5.2 ↓ | 13.4 ↓ | Still low |
| Ferritin | 20 | 21 | Low-normal |
| Vitamin B12 | 180 ↓ | — | Deficient |
| NT-proBNP | 1190 ↑ | — | Cardiac strain |
| Troponin | Normal | Normal | No acute MI |

PLAN:

The patient received 2 units of packed red blood cells, after which she reported feeling better, and her hemoglobin increased to 7.6 g/dL.

She needs colonoscopy. Will need to bridge with lovenox for colonoscopy.

COLONOSCOPY RESULT: Ascending colon carcinoma (She was bleeding from colon cancer.)

SCAN FOR DETAILED INFO AND RESOURCES



APIXABAN AND COAGULATION REVIEW:

Apixaban is a direct, selective factor Xa inhibitor (oral DOAC) whose mechanism prevents prothrombin→thrombin conversion[1]. It has a half-life ~12 h, ~27% renal clearance, and is metabolized by CYP3A4[1]. Unlike warfarin, it has a rapid onset/offset and predictable effect, so no routine PT/INR monitoring is required[2][3].

Coagulation tests: Apixaban can prolong PT, INR and aPTT (and, to a lesser extent, ROTEM/TEG clotting times), but **changes are small, highly variable, reagent-dependent, and unreliable for quantification**[2][4]. A normal PT/INR/aPTT does *not* exclude substantial drug effect[5][3]. Thrombin time is **unaffected** by apixaban (since it does not inhibit thrombin)[6]. Anti-factor Xa assays (with drug-specific calibration) correlate much better with apixaban levels ($r^2 \approx 0.88$) than PT/INR ($r^2 \approx 0.36$)[7], but no standardized “therapeutic range” exists.

- **PT/INR:** Apixaban can prolong the PT and INR in a dose-dependent manner, but the effect is *modest and inconsistent*. In practice, an **elevated INR can indicate apixaban effect, but the magnitude is unreliable**, and many patients have “normal” INR despite therapeutic apixaban (especially at trough)[5][4]. Notably, studies show *rivaroxaban* tends to increase INR more than apixaban, reflecting stronger PT sensitivity to rivaroxaban[16][4].
- **aPTT:** Apixaban also prolongs aPTT to a variable degree. In general, aPTT is **less sensitive** than anti-Xa assays and may even remain normal at therapeutic apixaban levels. Thus, aPTT is neither quantitative nor reliable for monitoring apixaban.
- **Anti-Xa assays:** Studies have demonstrated **strong correlation** between apixaban plasma level and anti-Xa activity ($R^2 \approx 0.88-0.89$)[7]. By contrast, PT/INR correlates poorly ($R^2 \approx 0.36$)[7].
- **Thrombin time (TT):** Apixaban has **no effect** on TT (also called TCT or fibrinogen clotting time).
- **Viscoelastic tests (ROTEM/TEG):** routine viscoelastic assays are **not reliably sensitive** to apixaban.

Reagent and dose/timing effects: All coagulation assays are sensitive to the apixaban dose and timing. Peak levels occur ~2–4 h post-dose ($C_{max} \approx 150-250$ ng/mL in typical dosing). PT/INR and aPTT will be longest at peak; after ~24 h (trough), these clotting times often revert near baseline even though the patient still has drug on board[5]. This means that *when* the sample is drawn critically affects interpretation. In summary, **test sensitivity is limited and not**

standardized: a mildly elevated PT/INR in one lab may mean little or a lot depending on the reagent[15][4].

Timing/Dose Effects: Peak anticoagulant effect occurs ~2–4 hours post-dose; PT/INR may transiently rise (INR ~1.5–2.5) at peak[8] Measuring tests **relative to dose timing** is critical: a high PT soon after a dose likely reflects apixaban, whereas a low PT at trough does *not* guarantee clearance. Factors slowing elimination (renal impairment, high dose, drug interactions) prolong the effect.

Guidelines and Drug Labels: NICE and specialty guidelines advise baseline and periodic checks of **renal function, liver enzymes and full blood count** (for bleeding risk)[10][11], but not coagulation tests. Expert panels (ACC/AHA/ASH/ISTH) recommend use of calibrated anti-Xa levels or specialized assays only in select situations (e.g. urgent surgery or bleeding)[5][12].

Clinical Interpretation: Because PT/INR response is unpredictable, **PT/INR is not useful for dosing or routine surveillance**. It may be used qualitatively in emergencies: an unexpectedly elevated INR suggests significant apixaban effect, while a normal INR (especially at trough) is not reassuring[5][2]. By contrast, a calibrated anti-Xa assay (with apixaban calibrator) or LC-MS/MS can quantify drug levels if needed, though these are not always available.

Practice Recommendations: In most situations (routine therapy) rely on clinical monitoring and checking renal/hepatic function (per SPS/NHS guidance[10][11]). Use PT/INR sparingly: e.g. in major bleeding or before urgent surgery to *flag* a coagulation effect (and even then interpret cautiously)[5][4]. Prefer specialized assays: if available, measure apixaban-specific anti-Xa activity (or “DOAC level” assay) at peak/trough based on the clinical question. Manage bleeding with standard protocols (supportive care, PCC/andexanet) irrespective of PT result. For perioperative management follow local protocols (generally stop 48h before high-risk surgery)[13]. Adjust dose only per label criteria (e.g. 2.5 mg BD if ≥ 2 of: age ≥ 80 , weight ≤ 60 kg, Cr ≥ 1.5)[14]. Watch for drug interactions (strong CYP3A4/P-gp inhibitors require dose reduction) and extreme body weight (consider specialist input or level-check if concerned).

Key Points: Normal PT/INR/aPTT do not exclude apixaban effect[5][3]. Use these tests only to provide a quick signal in emergencies, not to quantify. When in doubt, treat the patient’s bleeding risk clinically (hold drug, give reversal if major bleed) rather than relying on INR. Always correlate any test result with timing of last dose and renal function.