

Factor XI Deficiency: A Retrospective Review

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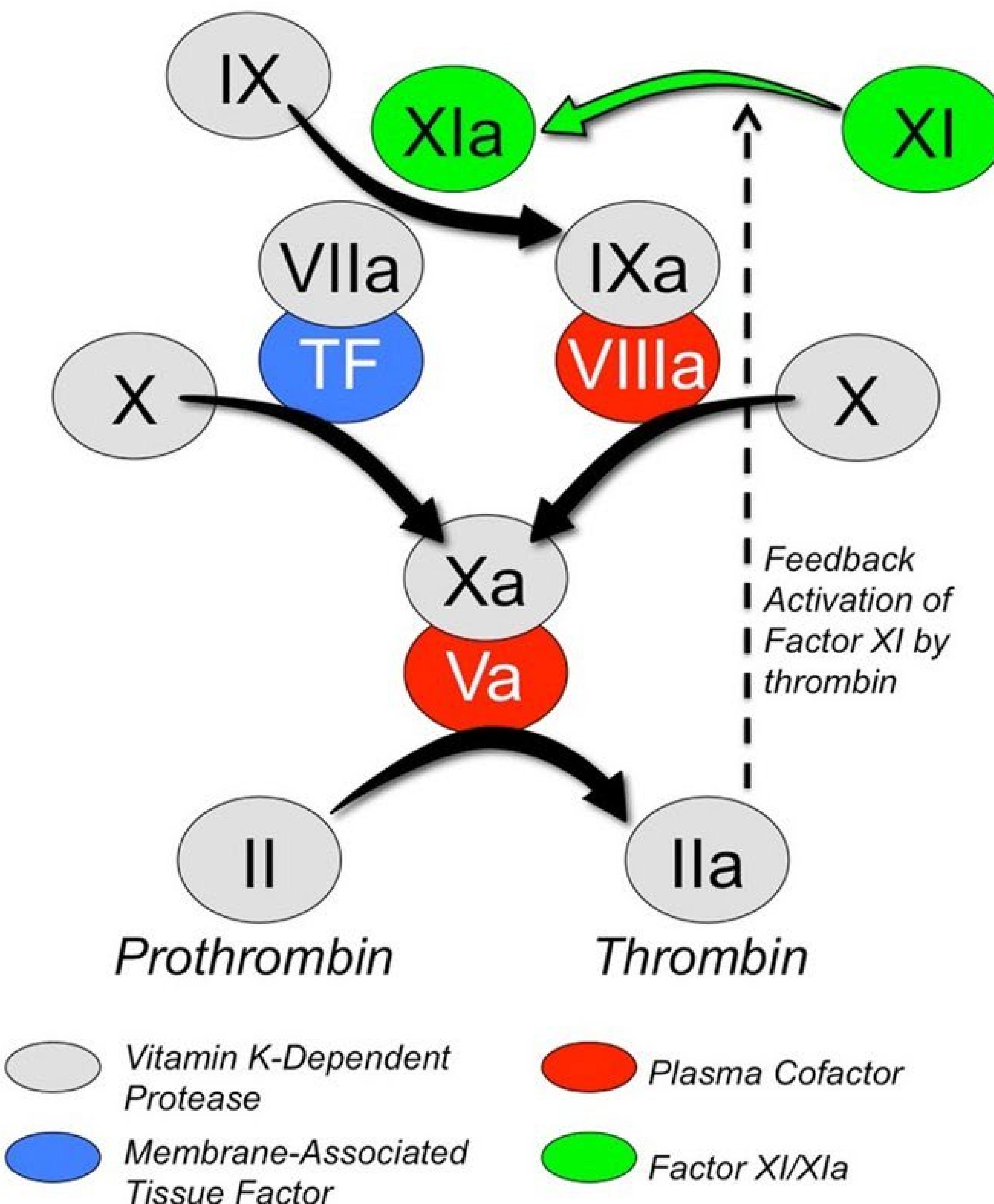
INTRODUCTION

- Factor XI (FXI) deficiency is a rare inherited coagulation disorder.
- The number of patients presenting to labor and delivery with FXI deficiency has significantly increased.
- There is poor correlation between factor levels and bleeding, which presents a clinical challenge, especially in the consideration of neuraxial anesthesia.
- There is a paucity of literature on FXI deficiency in obstetric anesthesia, and there is no clear consensus on the safe level of factor XI for neuraxial anesthesia placement.
- We present a retrospective review of the anesthetic management of 29 patients incidentally diagnosed with factor XI deficiency during routine antenatal genetic screening.

METHODS

- Data collected included factor XI levels, history of bleeding symptoms, hematologic management prior to pregnancy, type of delivery, type of anesthesia performed, prophylactic treatment received prior to delivery, lab abnormalities, total EBL during delivery, and any other complications that occurred during labor.
- Severe deficiency was defined as FXI levels <15%
- Moderate deficiency as FXI levels 15-45%
- Mild deficiency as FXI levels 46-75%

Plasma Thrombin Generation



Factor XI Deficiency

Potential Modifiers of Bleeding

Tissue Factor (TF) Activity

- TF concentration varies by tissue
- Factor VIIa level
- TFPI level/activity

Coagulation Protease Regulation

- Antithrombin activity
- ZPI or protein Z activity
- C1-Inhibitor activity (inhibits Factor XIa)

Factor Va & VIIIa Regulation

- Protein C or Protein S activity
- Factor V Leiden

Fibrinolytic activity

- PAI-1 activity
- α 2-antiplasmin activity

Platelet Activity

- Platelet count
- Platelet activity
- von Willebrand Factor level

Figure 1. The role of Factor XI in hemostasis

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RESULTS

- Of the total 29 patients, 23 (76.7%) received neuraxial anesthesia (FXI level median 46% IQR: 41 – 56%).
- 7 patients (23.3%) did not receive neuraxial anesthesia (FXI level median 35% (IQR: 4% - 47%).
- Of those 7 patients who did not receive neuraxial anesthesia, 1 delivered via c-section while the remaining 6 had vaginal deliveries.
- Only 2 patients total were found to have abnormal values of partial thromboplastin time.
- No relationship was found between EBL and factor XI level (as a whole) ($p=0.477$).
- No relationship was found between EBL and factor XI level when sub-grouped to compare vaginal (0.249) vs. Cesarean section delivery (0.252).

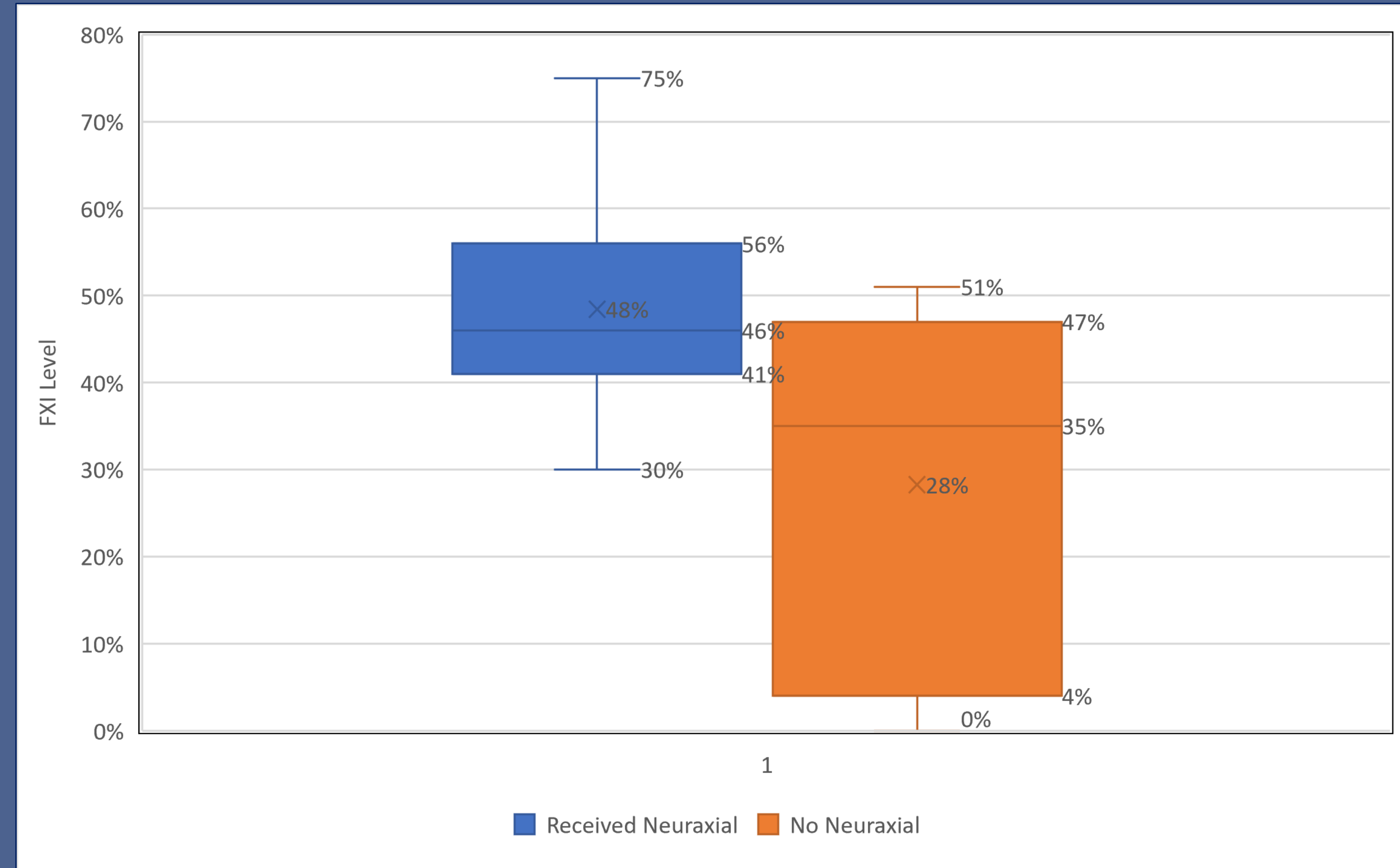


Figure 2. Factor XI levels in those receiving and not receiving neuraxial technique

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More Information on Patients with Factor XI Deficiency

To the Editor:—It has been called to our attention that our recent Clinical Concepts and Commentary article, “Current Concepts of Hemostasis: Implications for Therapy,” contains a statement that implies that postoperative bleeding in patients with factor XI deficiency is usually mild.¹ We wish to clarify this implication. Patients with factor XI deficiency over a lifetime are mild bleeders who do not usually

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CORRESPONDENCE

of the journal pointed out to one of us *via* e-mail that patients with factor XI deficiency undergoing cardiopulmonary bypass may bleed excessively. We agree with this statement, and at our institution, such patients would be treated, preoperatively and postoperatively, with recombinant factor VIIa or with plasma replacement therapy, which may require plasma exchange transfusions to increase factor XI to 50% or greater. Factor XI concentrates are available in Europe but not in the United States, and these concentrates have occasionally been associated with thrombotic side effects. In summary, we wish to emphasize that even though patients with factor XI deficiency usually have mild bleeding episodes over a lifetime, this does not mean that they may not experience extensive hemorrhage after severe trauma or surgery. Although some patients with factor XI deficiency do not bleed after operative procedures, a family history of bleeding after surgery is suggestive that relatives of such patients will also bleed during surgery.

It has been recommended that replacement therapy for factor XI deficiency also include the use of antifibrinolytic agents such as tranexamic acid because it seems that one function of factor XI is to boost

experience the chronic, crippling hemarthrosis or other severe bleeding episodes so typical of severe classic hemophilia or hemophilia B. Nonsurgical bleeding episodes in factor XI-deficient patients are usually mild over a lifetime. We wish to make it clear, however, that it is quite possible for patients with factor XI deficiency undergoing surgery to bleed severely unless they are pretreated. The replacement therapy for factor XI deficiency in the United States usually consists of plasma replacement therapy before an operation. More recently, recombinant factor VIIa has been used for factor XI deficiency, and it has been found to be effective, although it is not yet approved by the US Food and Drug Administration for this indication.² One of the readers

thrombin generation to the extent that the “thrombin activatable fibrinolytic inhibitor” (TAFI) can be activated.³ Adding tranexamic acid enhances the antifibrinolytic effect.

We are grateful to the reader who called this potential interpretation of factor XI deficiency to our attention.

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CONCLUSIONS

- Many providers are still hesitant to perform neuraxial anesthesia on patients who are heterozygous for the factor XI.
- Our results showed that there was no complications from neuraxial anesthesia for patients who were classified as having mild-moderate deficiencies.
- Although more studies are needed for a clear consensus on the proper anesthetic management of heterozygous carriers, we hope that our results can help guide other anesthesia providers when they are questioning performing a neuraxial technique for FXI patients.

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