

# THROMBIN GENERATION OF PATIENTS WITH FACTOR XI DEFICIENCY

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- Factor XI (FXI) deficiency is an autosomal recessive rare bleeding disorder.
- Patients with severe FXI deficiency usually have a plasma FXI:C <15-20 %
- Bleeding phenotype is neither correlated with FXI activity<sup>1</sup> nor with genotype<sup>2,3</sup>.
- Routine laboratory assays do not help physicians to estimate the individual bleeding risk of these patients.
- Thrombin generation test (TGT) is a comprehensive and global function test of the clotting system.

## OBJECTIVE

We investigated whether or not the bleeding tendency of patients with FXI deficiency is correlated with features of the TGT.

## METHODS

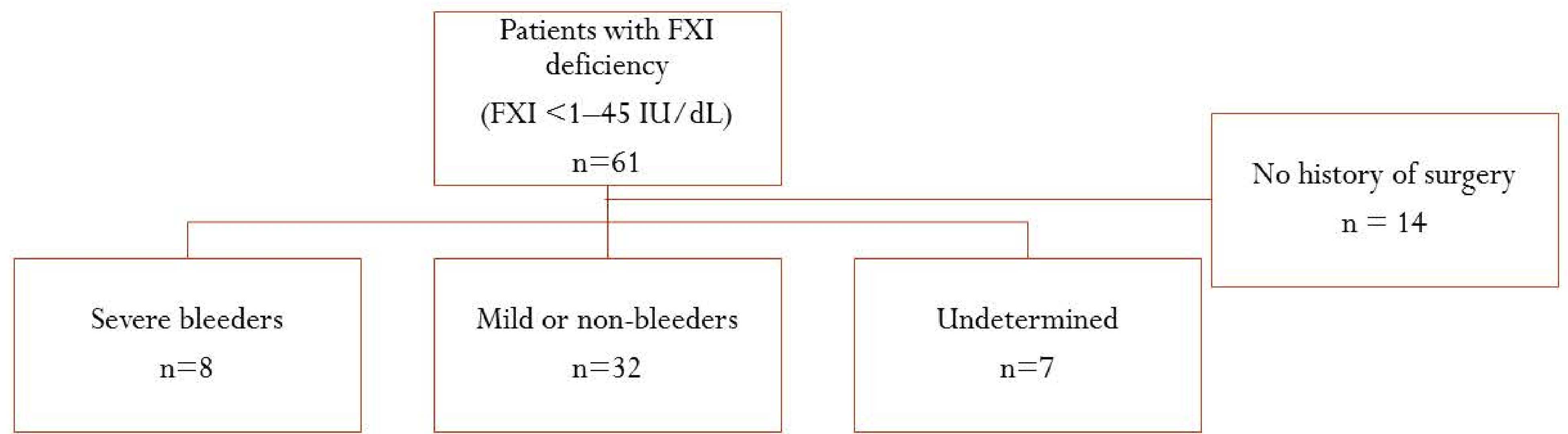


Figure 1 : patients with FXI deficiency were divided into 3 groups according to their bleeding phenotype. All severe bleeders had a personal history of surgery-related severe bleeding. All mild or non-bleeders had a personal history of surgery with no bleeding complication and in the absence of replacement therapy. Patients with undetermined bleeding phenotype have presented heterogeneous bleeding phenotype after different surgeries.

Thrombin generation was measured in platelet rich plasma (PRP) using a very low concentration of tissue factor at 0.5 pM  
Results obtained were compared to normal values established in 29 healthy controls.

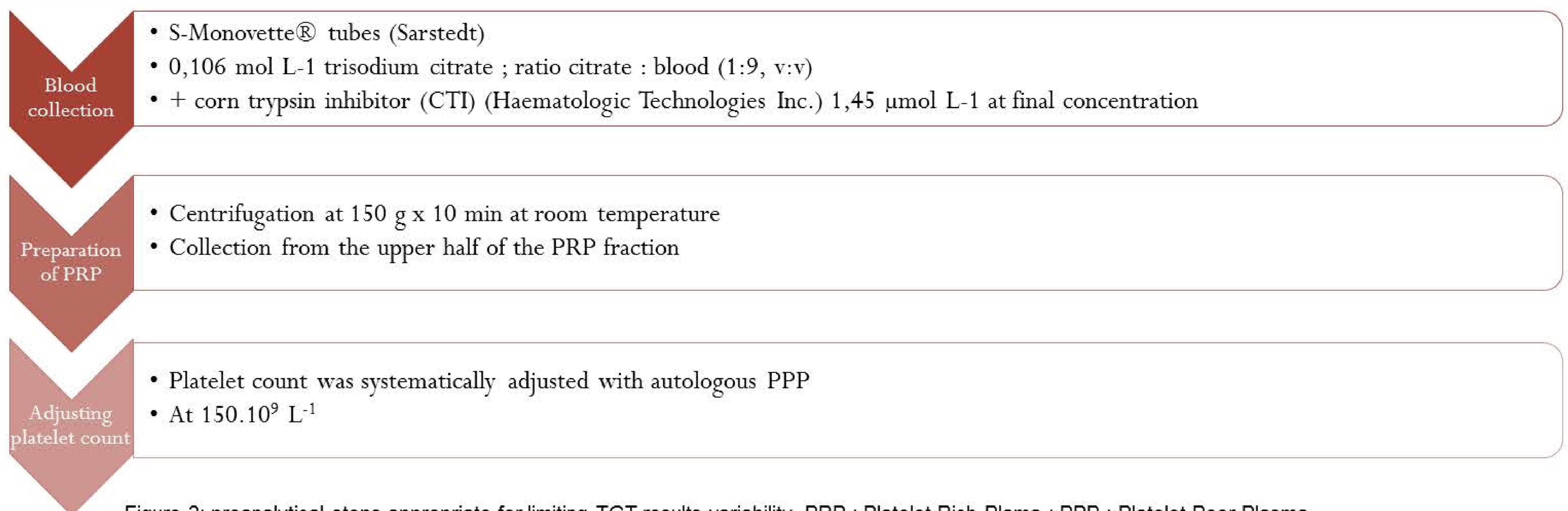


Figure 2: preanalytical steps appropriate for limiting TGT results variability. PRP : Platelet Rich Plasma ; PPP : Platelet Poor Plasma

## RESULTS

Patients	n	Ila peak (nM)	Ila Velocity (nM/min)
Controls	29	78 ± 22,5	5,7 ± 2,6
Non bleeders	32	76 ± 25	5,6 ± 3,4
Undetermined	7	54 ± 17	3,3 ± 1,3
Bleeders	8	41 ± 12,5	2,7 ± 2,2
Patients with FXI < 45%	47	66,6 ± 26,4	4,8 ± 3,3

Table 1. Results of Ila peak and Ila velocity obtained by thrombin generation tests in controls and patients with FXI deficiency. Results are showed with mean ± SD

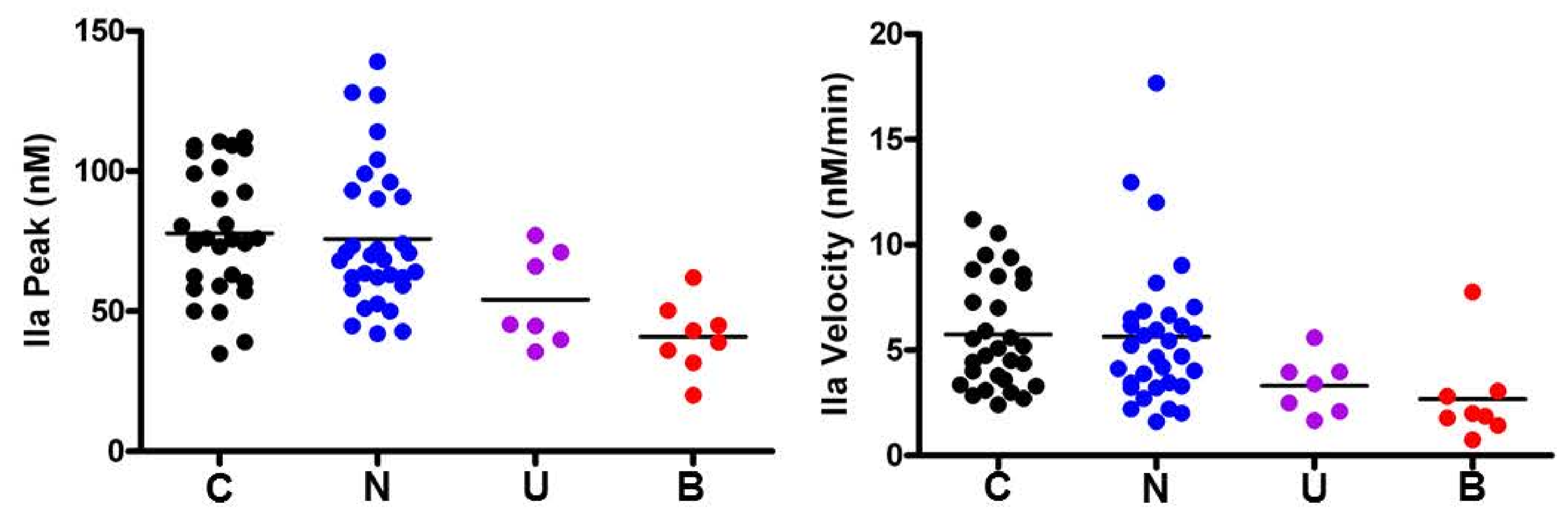


Figure 3, representation of Ila peak values (a.) and Ila velocity (b.) for each group of patients. C : controls; N : non bleeders ; U : undetermined ; and B : bleeders.

- Patients with FXI deficiency exhibited a low thrombin peak and a decreased velocity (Table1).
- Non bleeders exhibited similar thrombin generation results compared to controls' (Table1,figure 3, table 2)
- In 8 patients exhibiting severe bleeding tendency, independently of their FXI level, a dramatically impaired thrombin generation was observed. Peak and thrombin generation velocity results were significantly lower than those observed in non-bleeders (Table 1,figure 3, table 2).

T-test Mann-Whitney	Controls vs. Non bleeders	Controls vs. Undetermined	Controls vs. bleeders	Non bleeders vs. Bleeders
Ila Peak (nM)	p = 0,43	p = 0,02	p < 0,0001	p = 0,0002
Ila Velocity (nM.min <sup>-1</sup> )	p = 0,64	p = 0,02	p = 0,0005	p = 0,0019

Table 2. Mann-Whitney t-tests were performed to compare the mean values of Ila peak and Ila velocity between groups.

## CONCLUSIONS

- FXI activity does not perfectly reflect the bleeding risk of patients
- We confirmed our previous findings in this larger series of patients . **Low velocity and low thrombin peak were the main parameters suggesting a higher bleeding risk<sup>3</sup>.**
- Association of thrombin generation test in PRP and personal clinical history could better predict the bleeding risk

## REFERENCES:

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