

F. XIII und Blutverlust in der operativen Medizin – News from an Oldie

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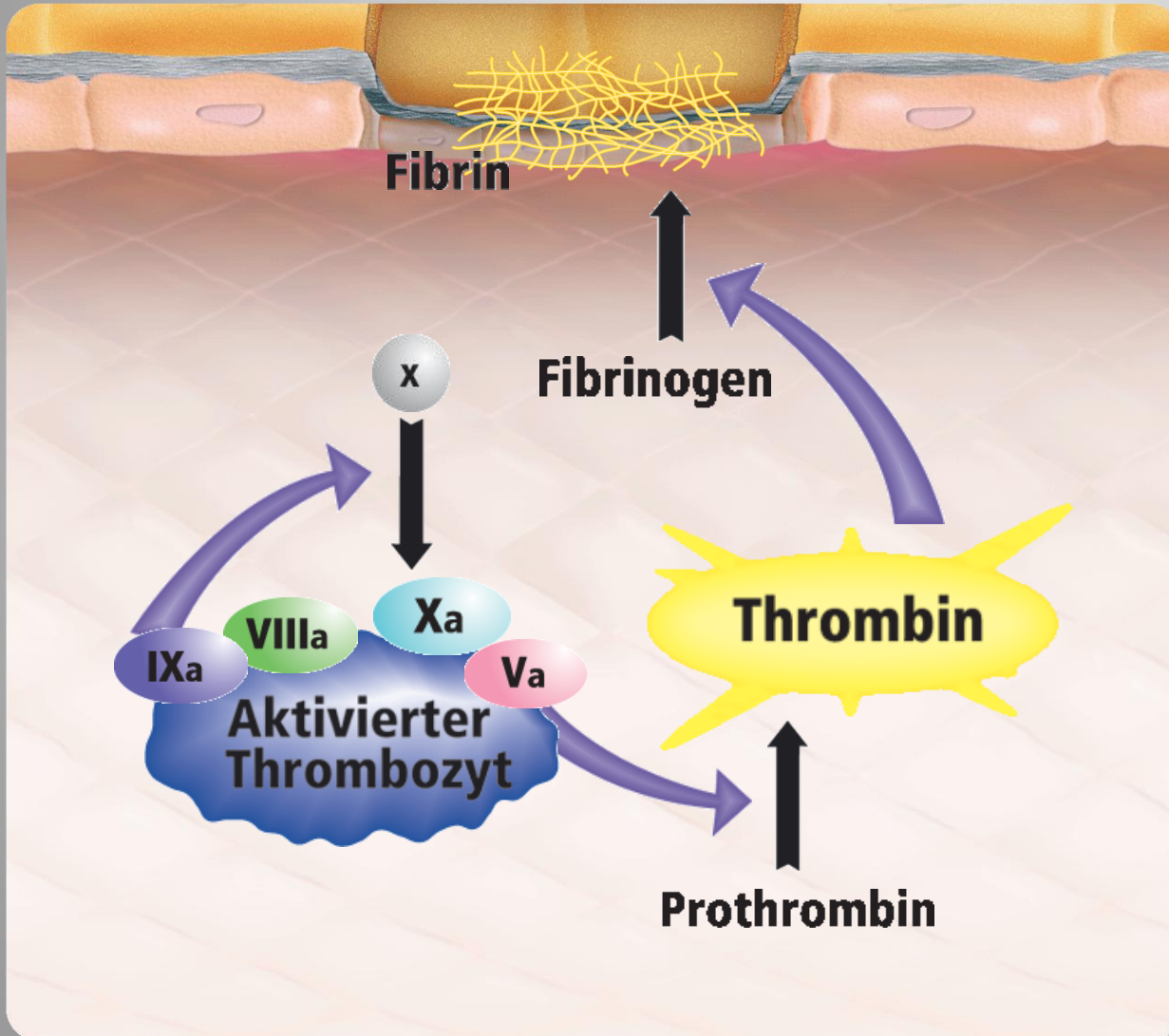
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Unexplained intraoperative coagulopathy: interventions due to bleeding

- cardiothorac. surgery: early revision 4.2 % Moulton, J Thorac Cardiovas Surg 1996, 111:1037
- OHS: repeat surgery for bleeding 3.6% Hall, Ann Thorac Cardiovasc Surg. 2001, 7:352
- aortic pseudoaneurysm 8.3 % Atik, J Thorac Cardiovas Surg , 2006, 132:379
- CPB "abnormal bleeding" 11 % Nuttal, Anesthesiology, 2001, 94:773
- laparosc. surgeries 4.1 % Schäfer, Am J Surg, 2000, 180:73
- TURP (blood loss > 1800 ml) 3.3 % Kolmert, Int Urol Nephrol, 1989, 21:47
- cystoscopic resection bladder cancer 2.8 % Collado, J Urol, 2000, 5:1529
- subdural heamtoma: reoperation "non-coagulopathic" patients 12%,
"coagulopathic" patients 41% Lee, Surg Neurol. 2004, 61:523

Cell based modell - Propagation

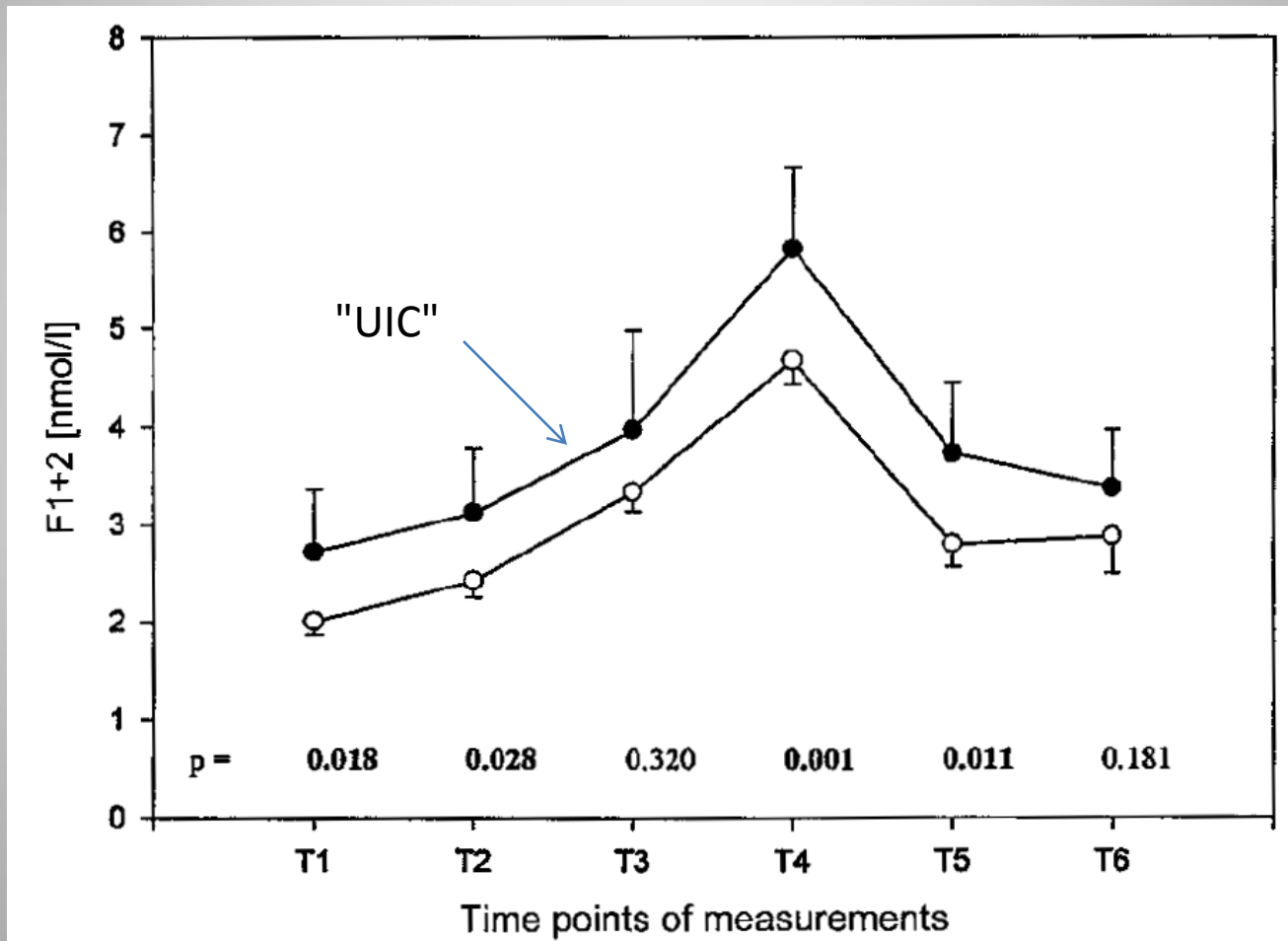


the FVIIIa/IXa complex activates FX on the surface of activated platelets

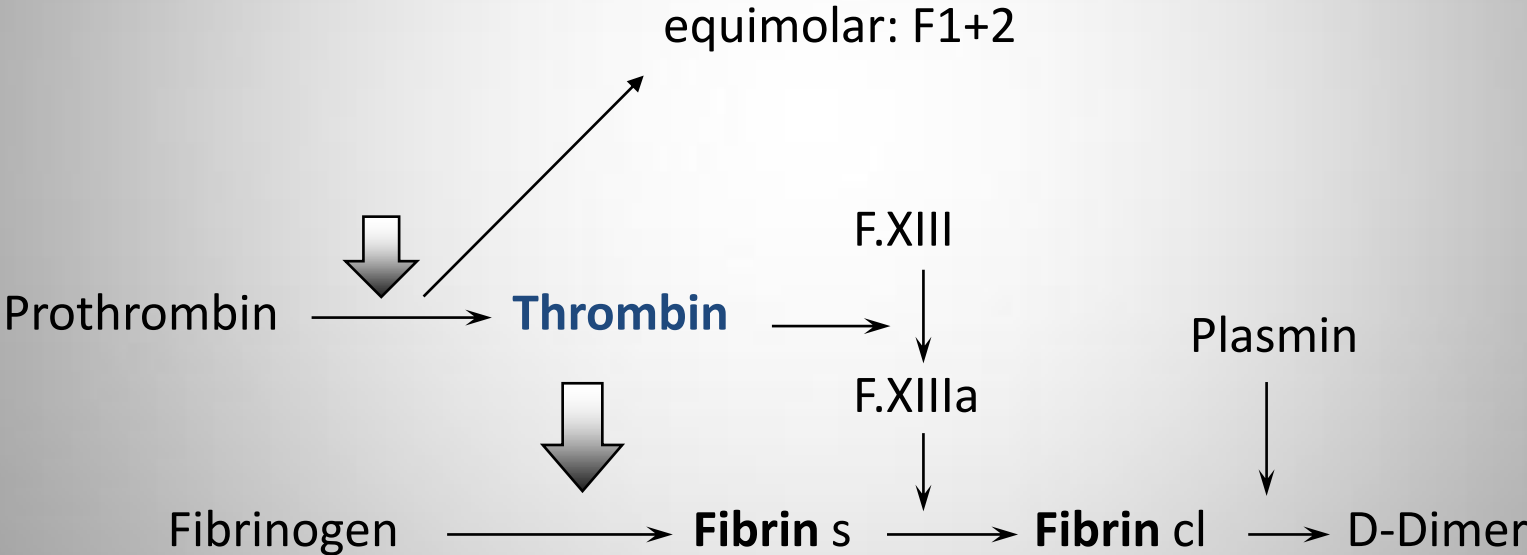
FXa in complex with FVa converts a large amount of prothombin to thrombin, leading to a “**thrombin burst**”

this “thrombin burst” leads to generation of a stable fibrin clot

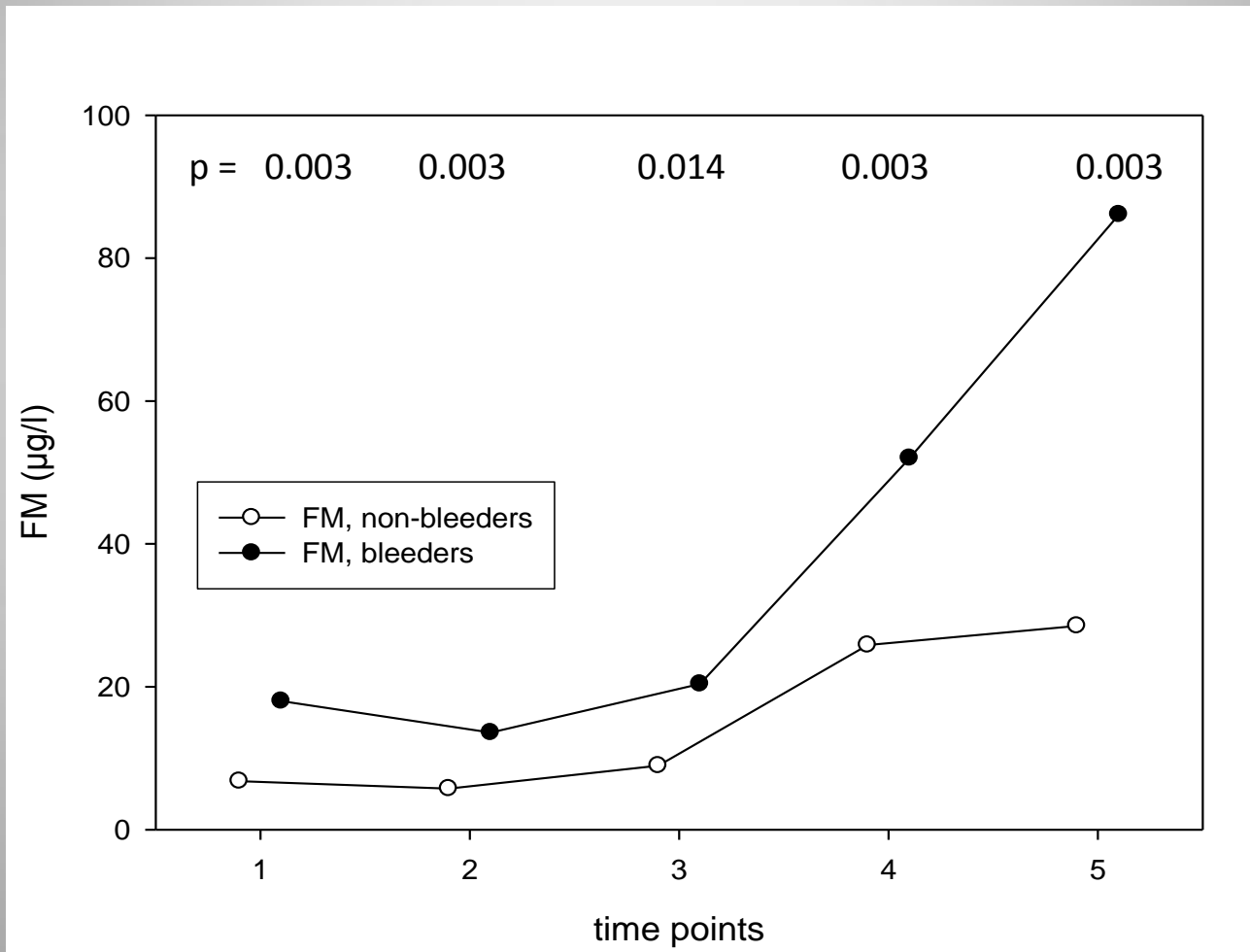
Prothrombin activation in patients without and with unexplained intraoperative coagulopathy ("UIC")



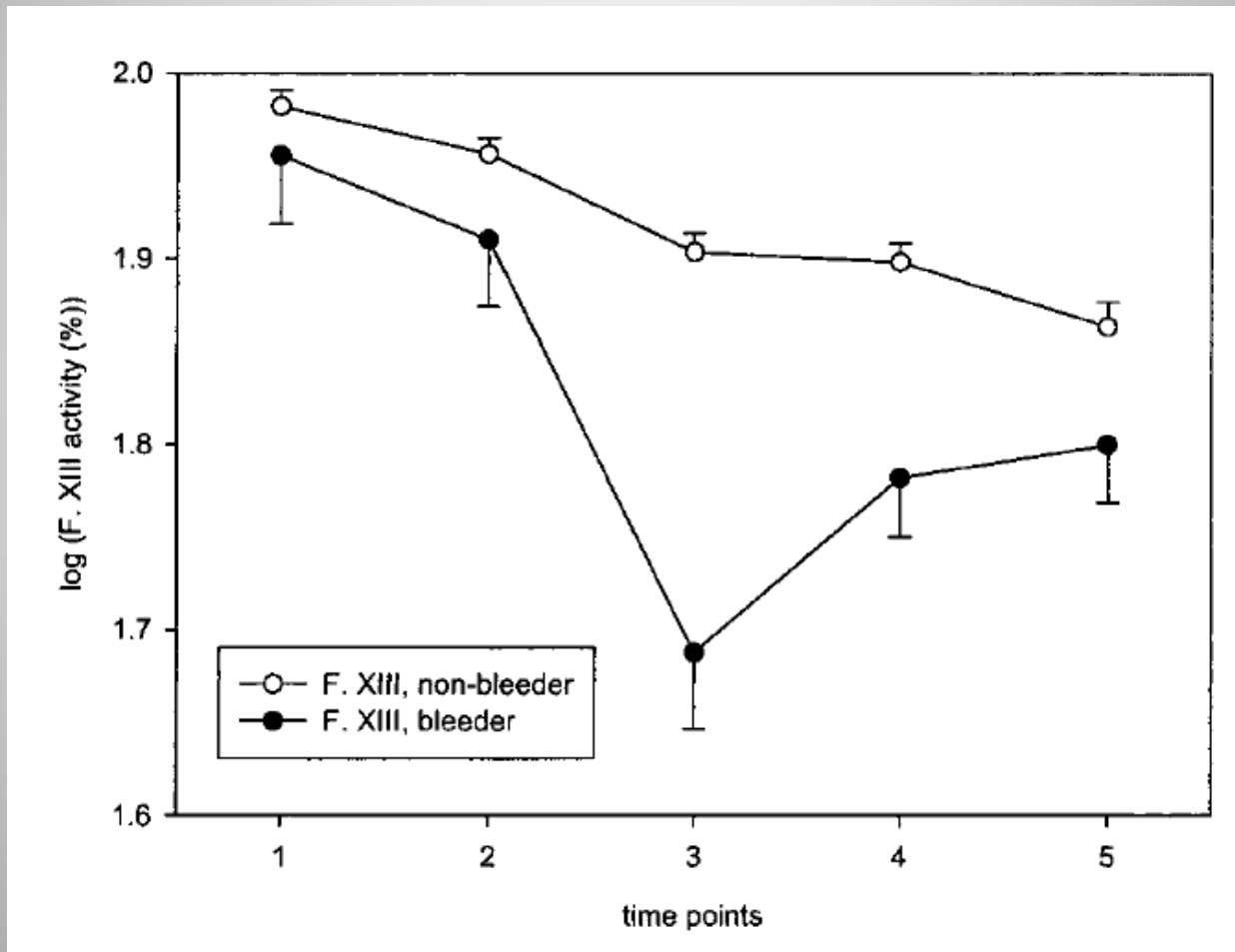
Pathophysiology of perioperative haemostasis – excursion to the end of the cascade



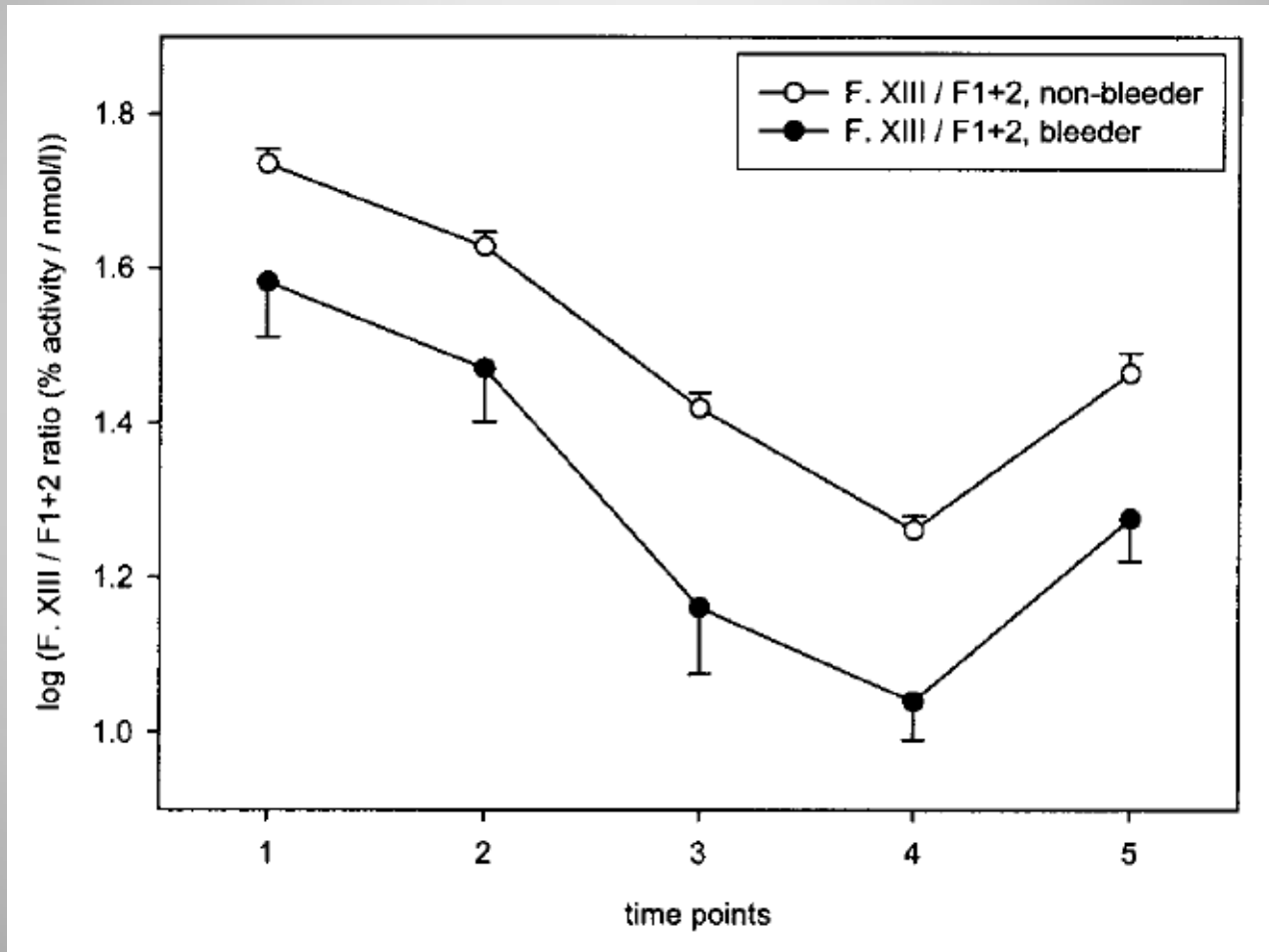
Patients with "unexplained" intraoperative coagulopathy: soluble fibrin, fibrin monomer



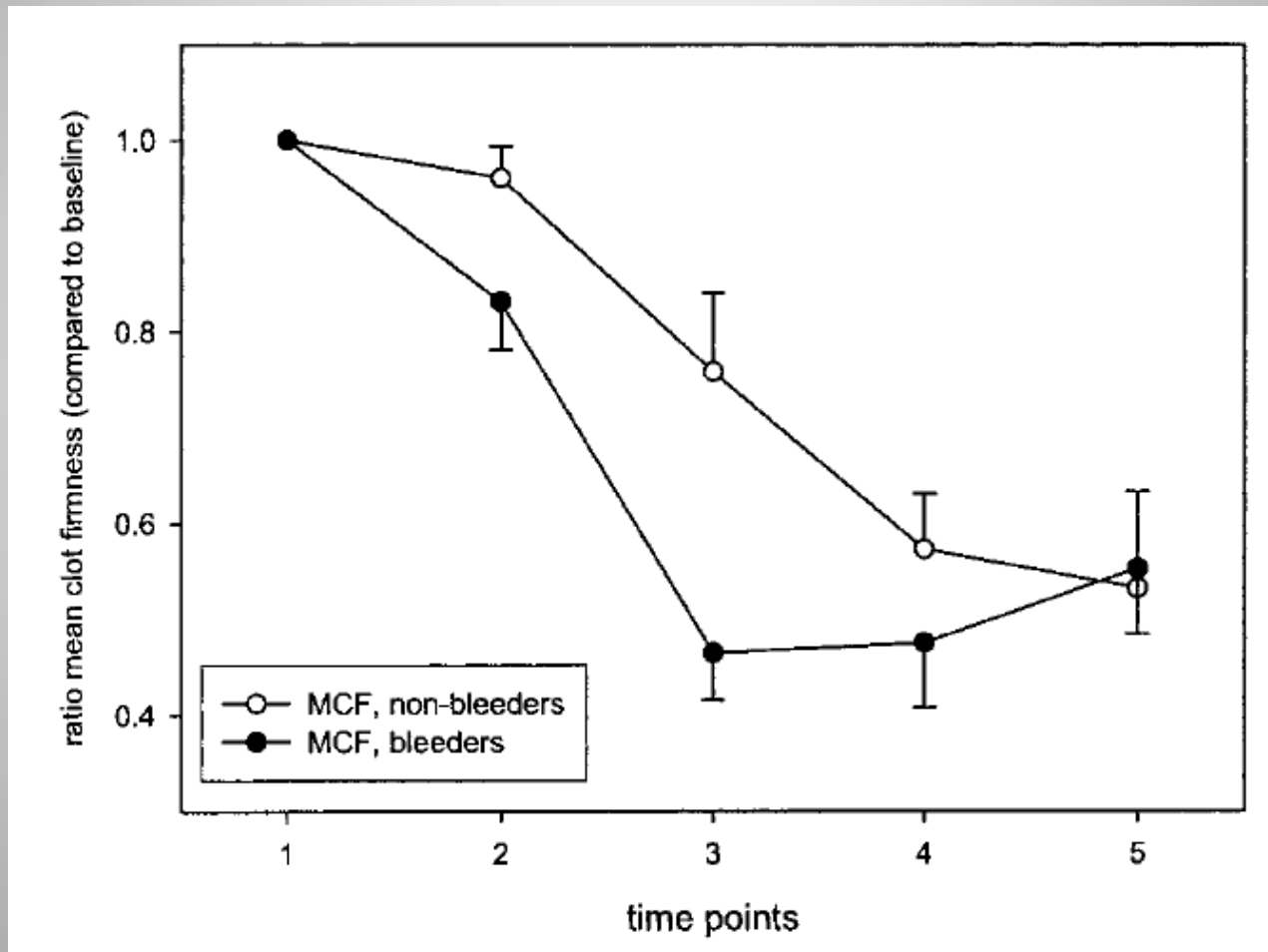
Course of F XIII in patients without and with unexplained intraoperative coagulopathy



Course of F XIII / F1+2 in patients without and with unexplained intraoperative coagulopathy



Course of clot firmness in patients without and with unexplained intraoperative coagulopathy



Dynamic clot properties with and without inhibition of F XIII

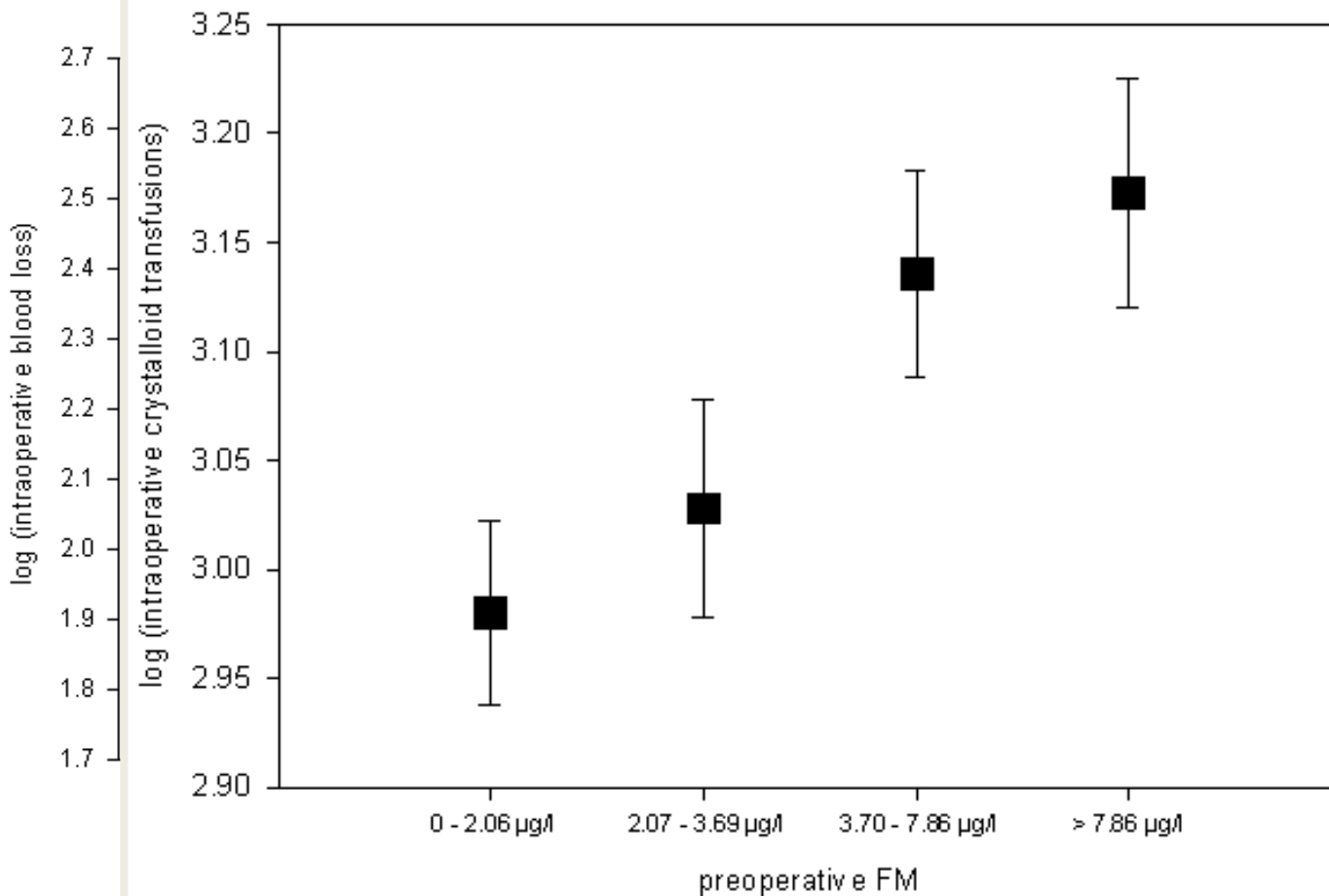
stiffness

fraction of energy
dissipated in
nonelastic processes

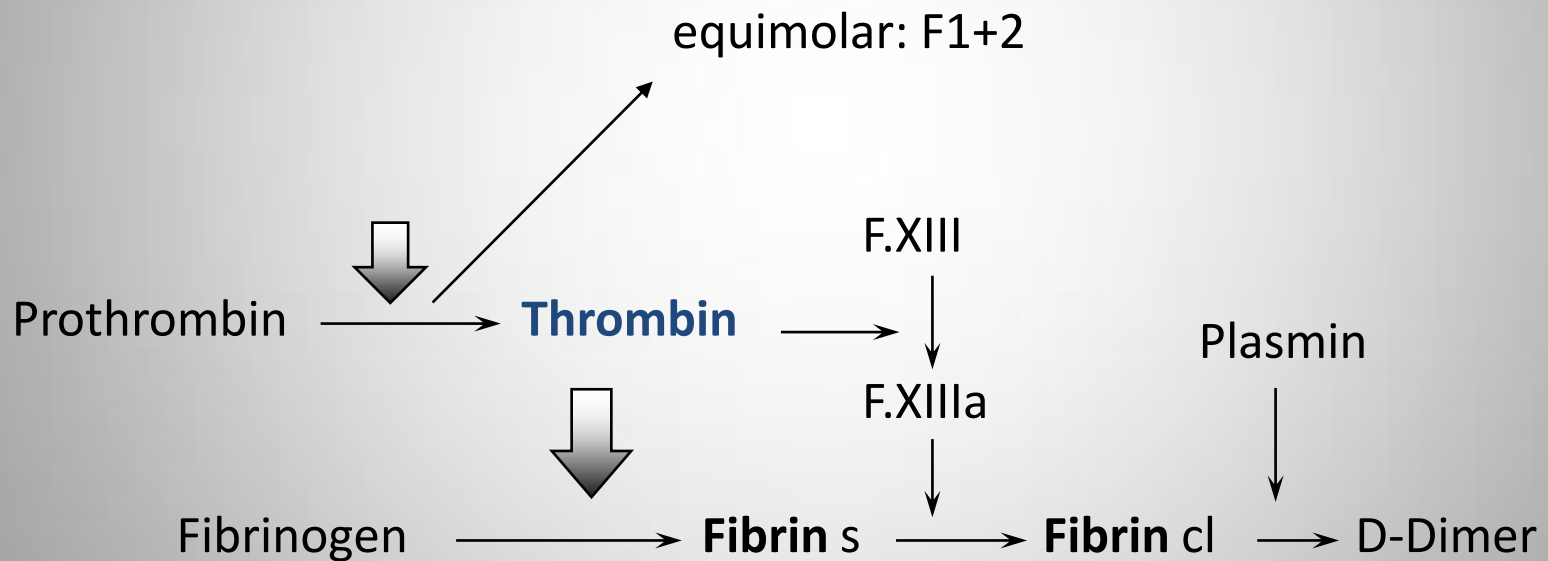
Fibrin clot	G' storage modulus, Pa	G'' loss modulus, Pa	G''/G' loss tangent tan δ
Clots without ligation	13.2 \pm 3.6	2.4 \pm 0.6	0.19
Clots with ligation	31.0 \pm 8.8	3.4 \pm 0.5	0.14

All parameters are significantly different with and without ligation;
 $P < 0.01$.

Pathophysiology of perioperative haemostasis – confirmation study of Fibrin Monomer as risk predictor of intraoperative blood loss

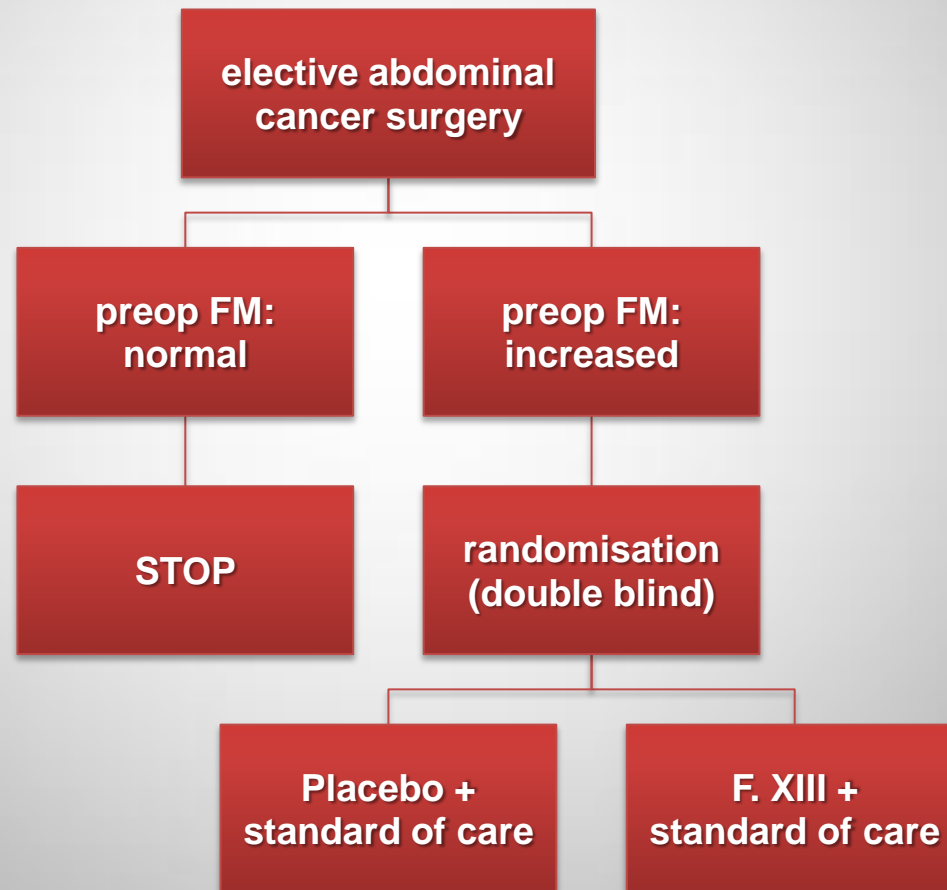


Pathophysiology of perioperative haemostasis – excursion to the end of the cascade



Factor XIII Substitution in Surgical Cancer Patients at High Risk for Intraoperative Bleeding

Wolfgang C. Korte, M.D.,* Christine Szadkowski, M.D.,† Anita Gähler, M.D.,‡ Konrad Gabi, M.D.,§
Edward Kownacki, Ph.D.,|| Monika Eder, B.M.A.,# Priska Degiacomi, B.M.A.,# Norbert Zoller, M.D.,# Jan Devay, M.S.,**
Jochen Lange, M.D.,†† Thomas Schnider, M.D.‡‡



F. XIII in high-risk patients (randomized, placebo-controlled, double blind)

blood loss

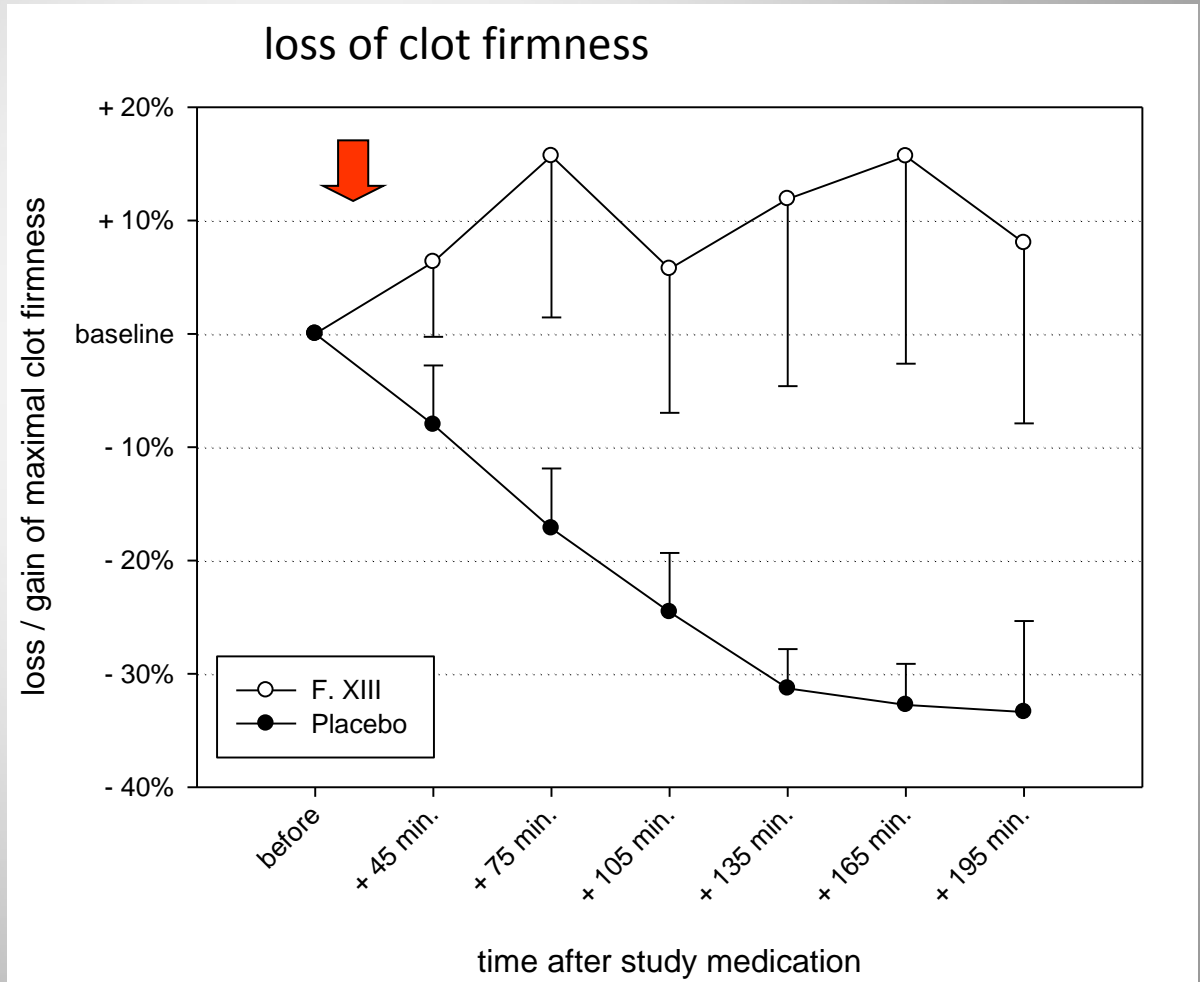
median blood loss:

- 29%

1050 ml (placebo)

750 ml (F. XIII)

p = 0.041



F. XIII in high-risk patients (randomized, placebo-controlled, double blind)

blood loss

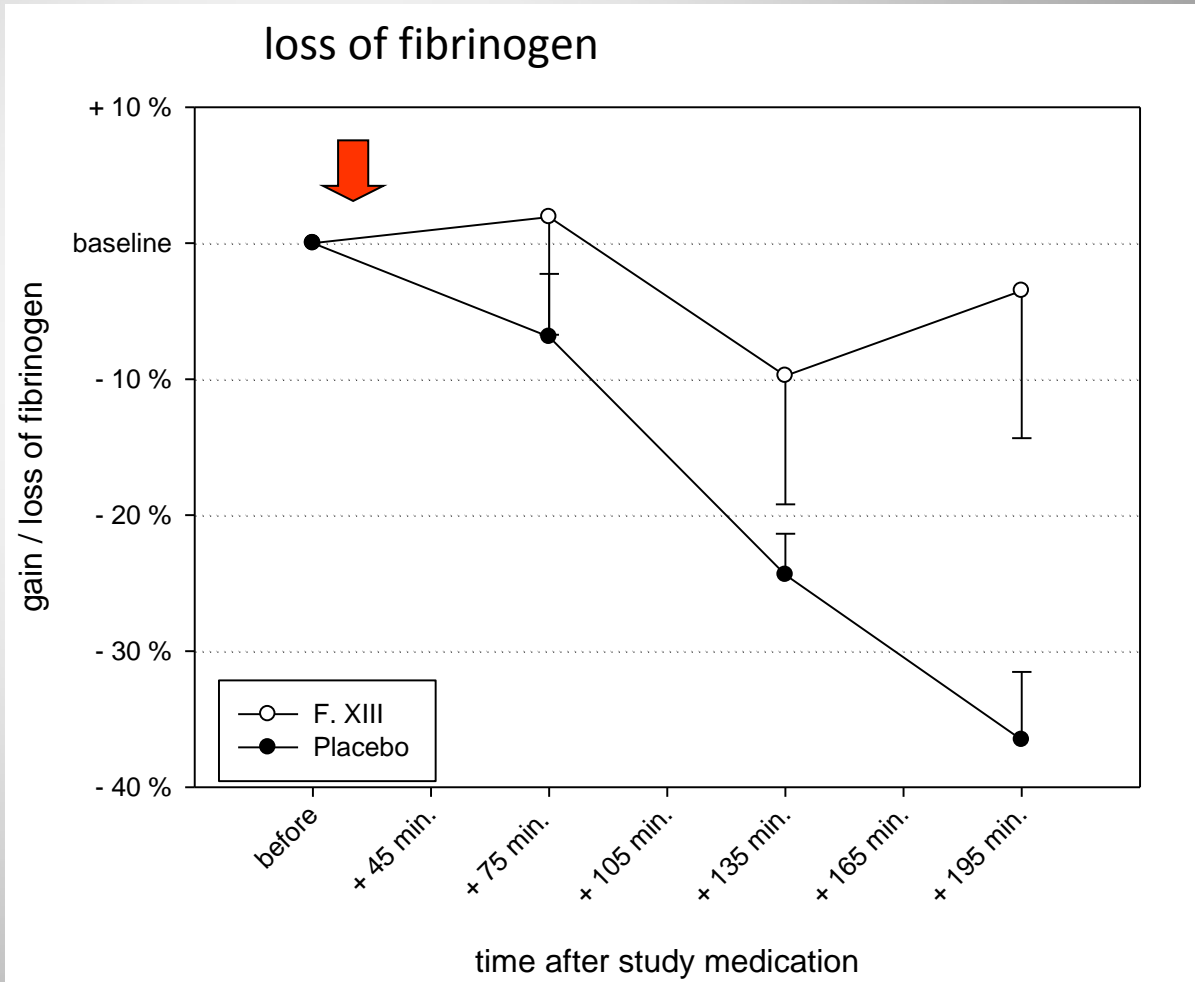
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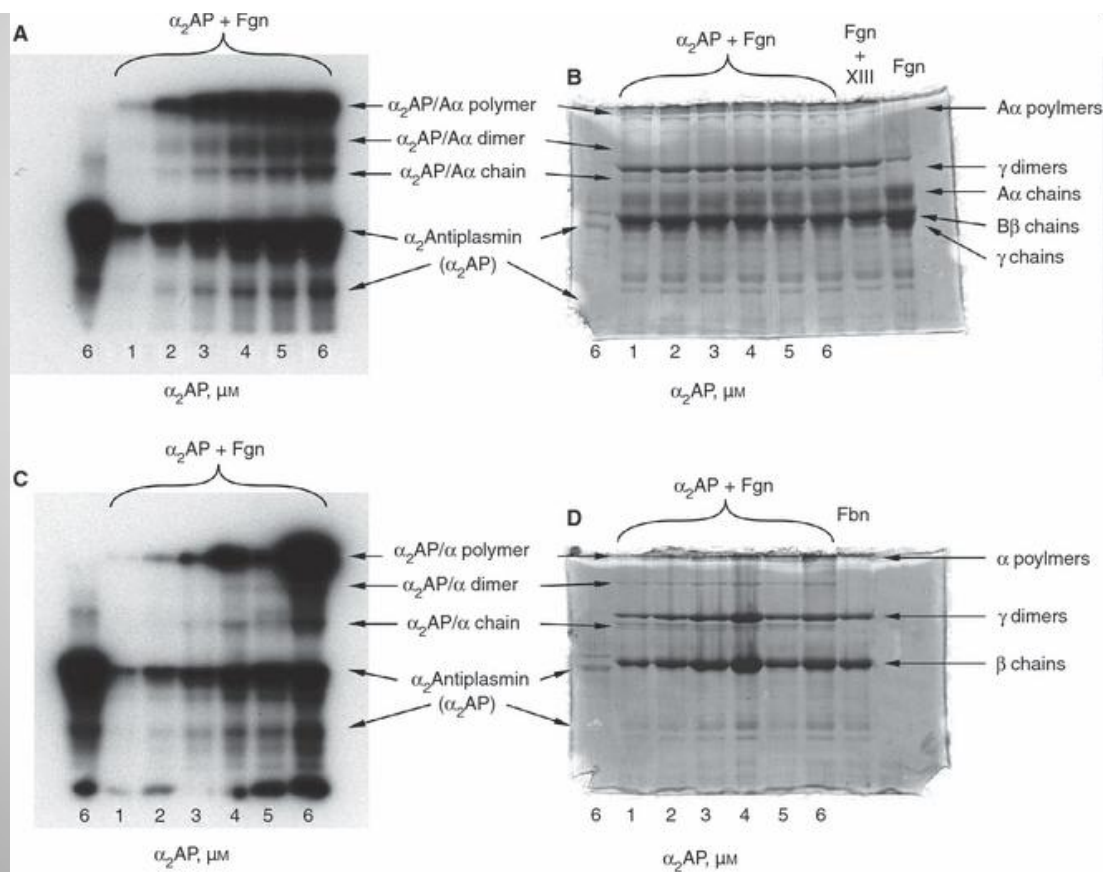
p = 0.041



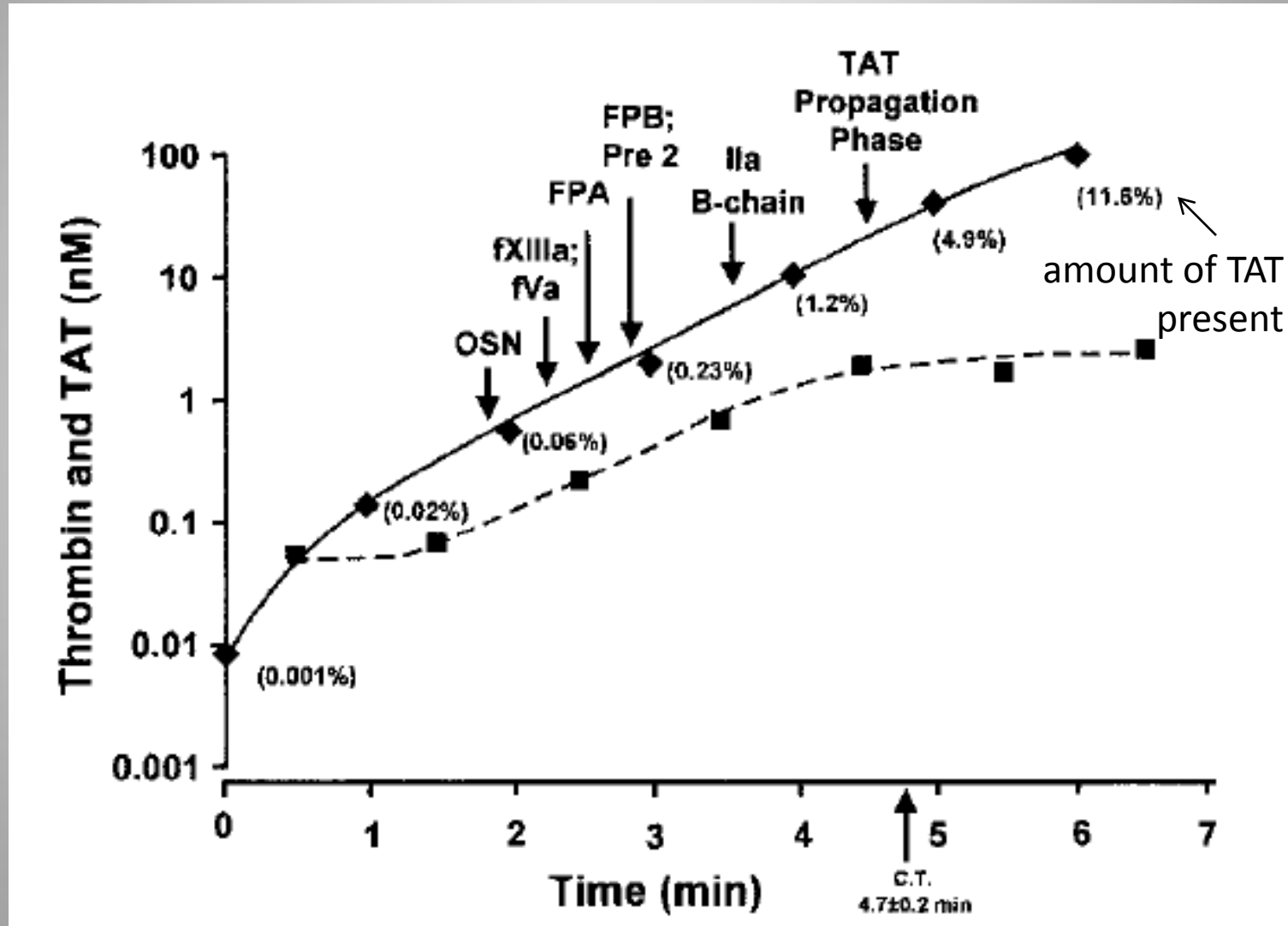
Evidence that α_2 -antiplasmin becomes covalently ligated to plasma fibrinogen in the circulation: a new role for plasma factor XIII in fibrinolysis regulation

M. W. MOESSON,* K. R. SIEBENLIST,† I. HERNANDEZ,* K. N. LEE,‡ P. A. McKEE‡ and P. A. McKEE‡

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Time course of initiation process



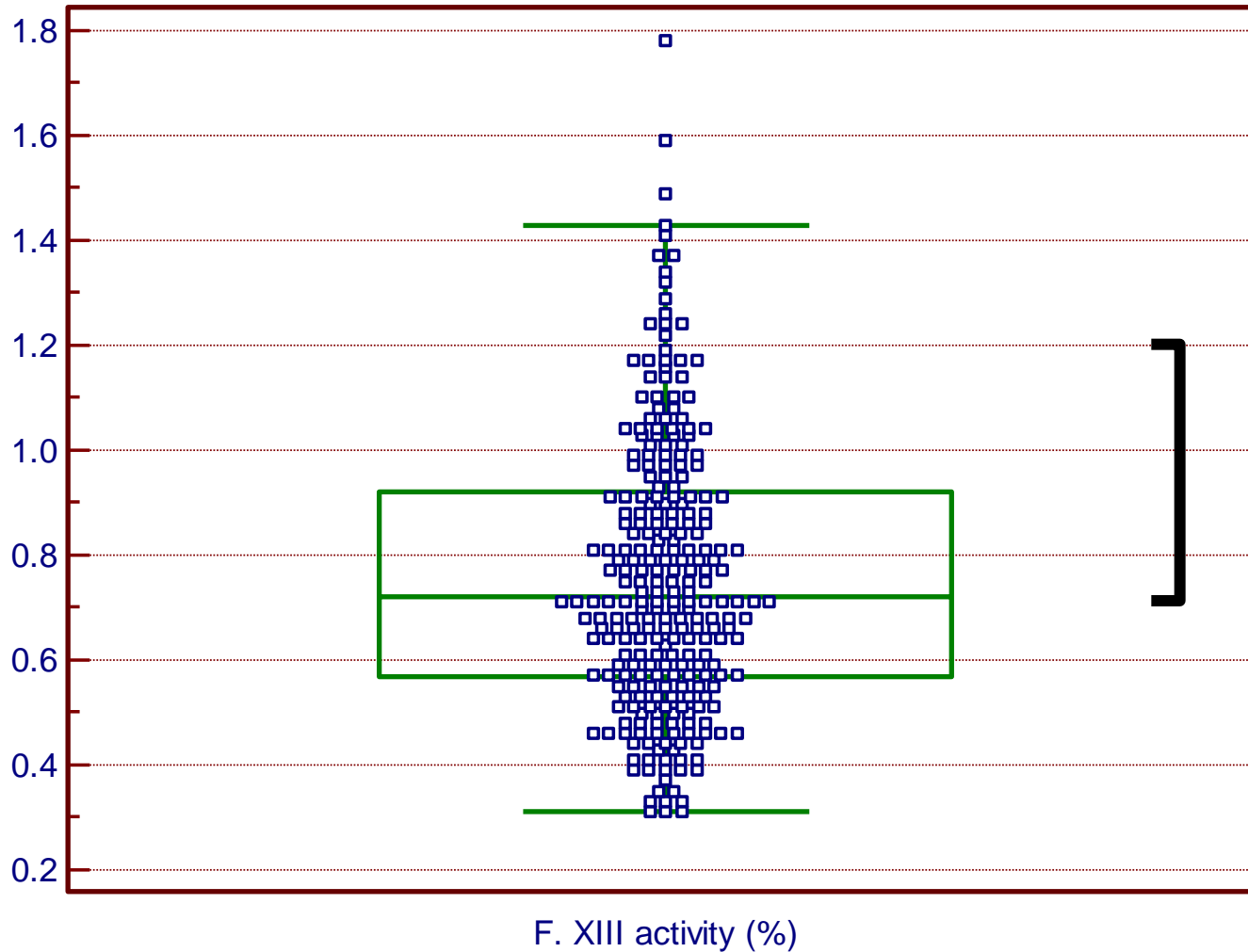
F XIII and postoperative hematoma in neurosurgery

TABLE 4. Postoperative Coagulation Parameters and Relative Risk for Postoperative Hematoma

Postoperative Coagulation Parameter	Relative Risk for Postoperative Hematoma	95% CI
Factor XIII < 60%	6.4	3.1–13.02
Platelet count < $150 \times 10^9/L$	3.0	1.5–5.77
Fibrinogen < 1.5 g/L	2.5	1.2–5.40

n = 876

Pathophysiology of perioperative haemostasis – prospective evaluation of postoperative F. XIII deficiency, St. Gallen SICU, n = 270



Pathophysiology of perioperative haemostasis – modulators of postoperative clot firmness (multivariate analysis)

	Coefficient	Std. Error	t	P	VIF
Constant	36.466	7.726		4.720	<0.001
Alter	0.0267	0.0286		0.935	0.351
BMI	0.0553	0.0863		0.641	0.523
ASA	0.0130	0.726		0.0179	0.986
Dauer	-0.00127	0.00385		-0.329	0.742
Temp Eintritt	0.165	0.442		0.373	0.710
ph	-0.308	2.291		-0.134	0.893
Hb	-0.0438	0.0274		-1.597	0.112
Tc	0.0428	0.00504		8.481	<0.001
Fibrinogen	1.984	0.343		5.779	<0.001
XIII	9.932	2.332		4.259	<0.001
Kristalloid	0.000296	0.000558	0.530	0.597	2.798
Kolloid	-0.00180	0.000671	-2.686	0.008	2.011

Pathophysiology of perioperative haemostasis – modulators of postoperative clot firmness (lowest quartile, multivariate analysis)

Ind. Variable	Coefficient	Standard Error	Wald Statistic	P value
Constant	12.780	22.105	0.334	0.563
Alter	-0.00542	0.0150	0.130	0.718
BMI	-0.0392	0.0573	0.468	0.494
ASA	-0.0384	0.367	0.0110	0.917
Dauer	0.000325	0.00176	0.0341	0.853
Temp Eintritt	-0.266	0.278	0.916	0.338
ph	0.185	2.825	0.00428	0.948
Hb	0.0132	0.0147	0.807	0.369
Tc	-0.0242	0.00534	20.543	<0.001
Fibrinogen	-0.193	0.290	0.441	0.507
XIII	-3.467	1.543	5.050	0.025
Kristalloid	-0.0000363	0.00028	0.0167	0.897
Kolloid	0.000770	0.00043	3.260	0.071

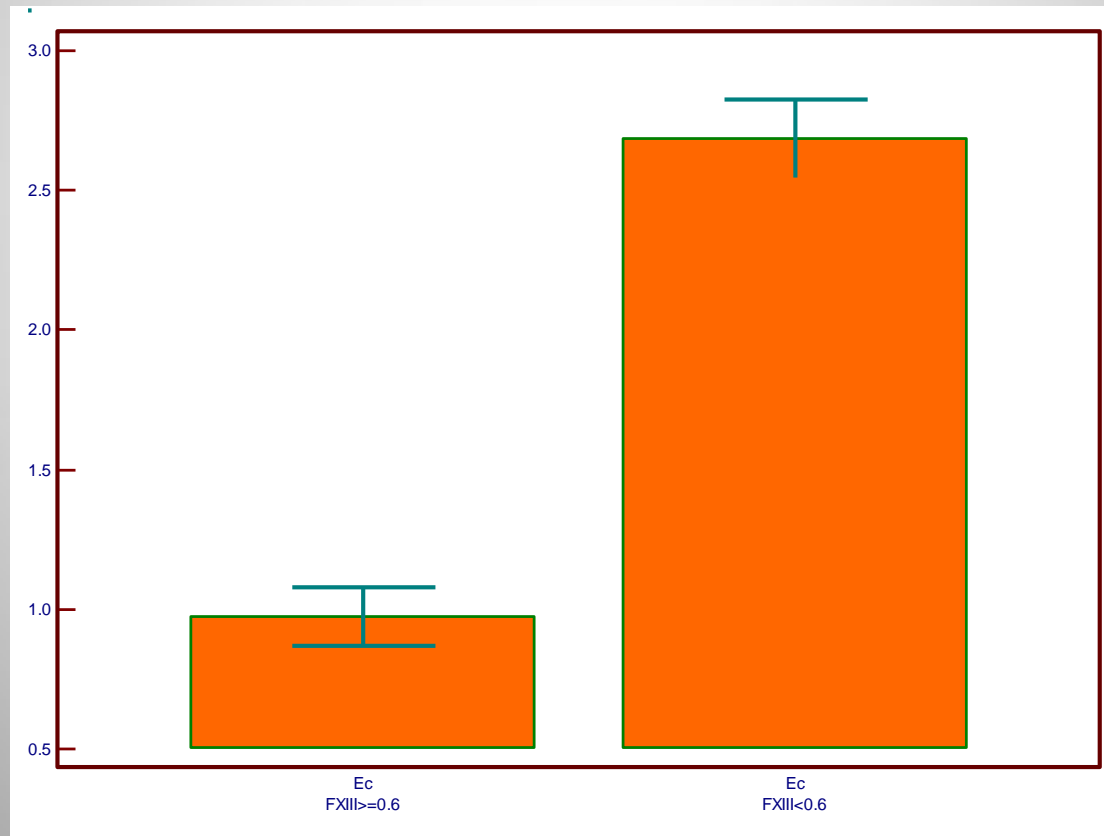
Multiple linear regression analysis on fibrinogen, platelet count, FXIII

outcome: number of red cell concentrates transfused
perioperatively , n = 485 (treatment episodes)

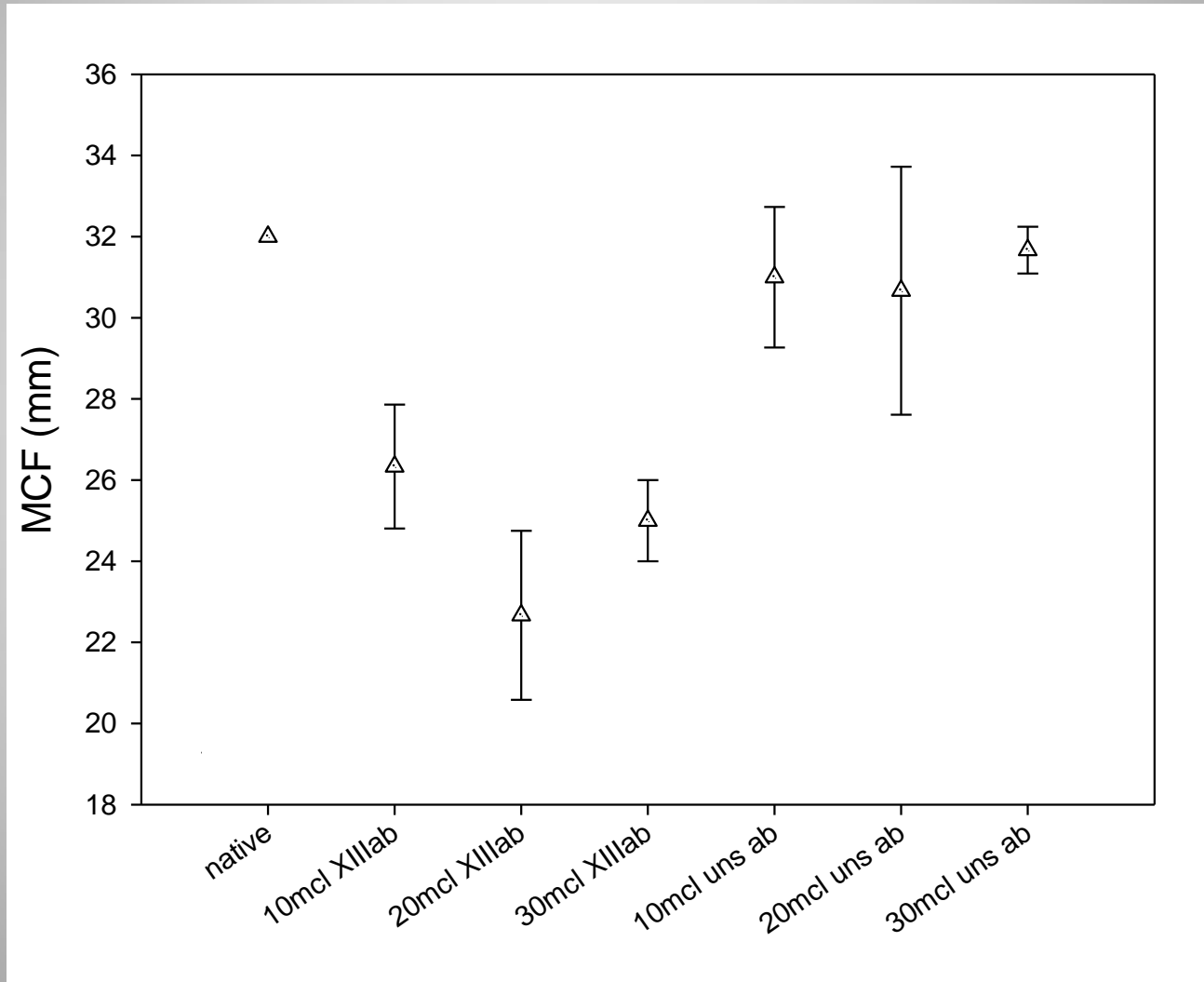
Independent variables	Coefficient	Std. Error	t	P
(Constant)	4.1057			
fibrinogen	-0.04727	0.06665	-0.709	0.4785
platelets	-0.0008731	0.0008532	-1.023	0.3066
FXIII	-3.0175	0.3079	-9.799	<0.0001

Perioperative use of red cell concentrates

n = 485 treatment episodes,
FXIII activity below vs above 60%



Results of F XIII inhibition in platelet inhibited* thrombelastography ("Fibtem")



*platelets present but unable to undergo shape change

Conclusions

- F XIII
 - increases clot firmness
 - decreases fibrinolytic and fibrinogenolytic effects
 - activated before fibrinogen is converted to fibrin monomers
- circulating F XIII
 - is important in haemostasis in the perioperative setting
 - a decision limit of 60% activity seems clinically relevant
 - FXIII deficiency (<60%) in the perioperative setting is **very** frequent
- increasing F XIII in at risk patients reduces blood loss
 - more clinical research (randomized controlled trials) needed



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<http://www.gth2012.org>