What I need to treat our bleeding patients properly

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IRCCS Policlinico S.Donato

Disclosures

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Haemonetics
Werfen-IL
Haemosonics
Roche Diagnostics
CSL Behring
Livanova
Medtronic

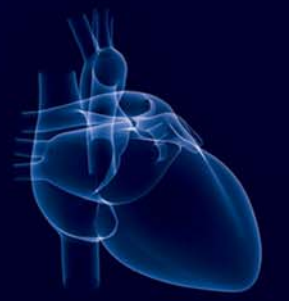
THE PRE-REQUISITE: A BLEEDING PATIENT

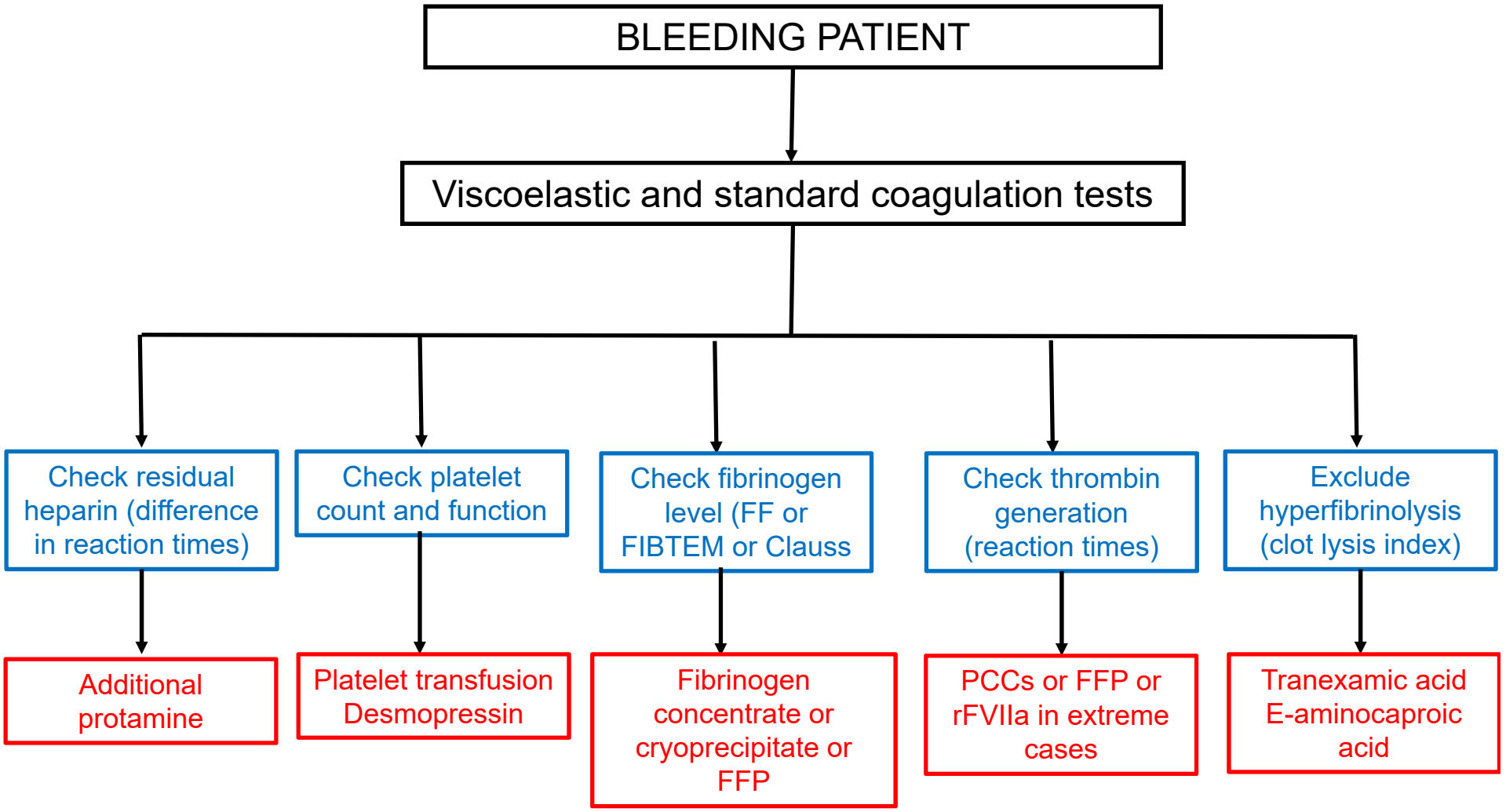
- The PPV of point-of-care or standard coagulation tests is very poor (< 10%) for prediction of bleeding
- Therefore, routine application of these tests and the consequent algrothms should be avoided
- Tests and algorithms should be applied only in:

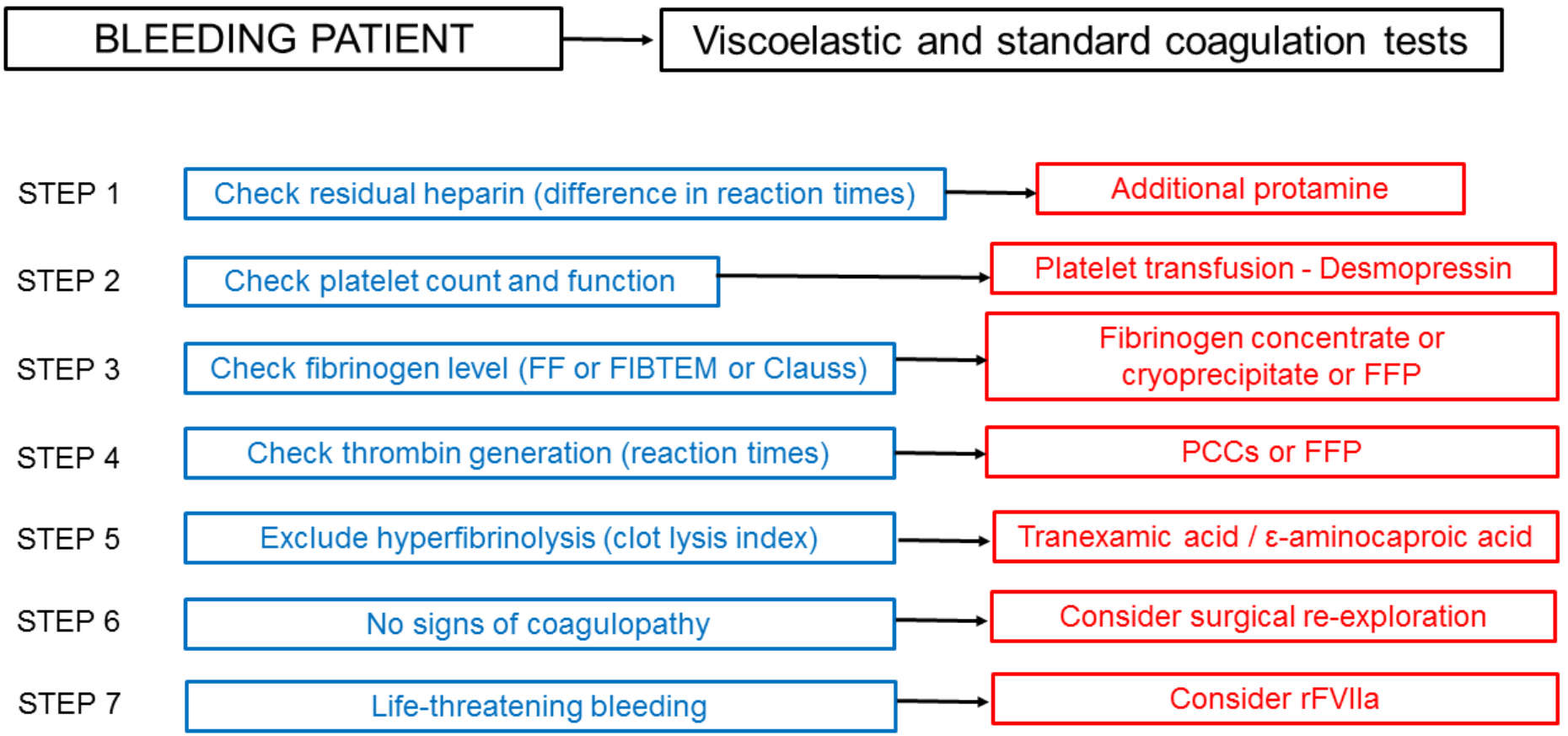
a) Patients at very high risk of bleeding due to their characteristics (drugs on board; low platelet count; known coagulopathy) or to the procedure (aortic dissection, very complex surgery)
b) Evidence of microvascular bleeding in the OR
c) Evidence of excessive chest drain blood loss in the ICU

THE CORRECT WAY: A STEP-BY STEP RULE OUT

- The NPV of point-of-care tests is very high: > 95%
- Therefore, instead of ruling in the different bleeding causes, a ruling-out approach should be followed
- Vertical algorithms run better than horizantal ones
- The order of approach to the different bleeding causes is important, and depends on (a) the easiness of the therapeutic approach and (b) the probability of the different causes (i.e. platelet dysfunction more likely than low coagulation factors)




BLEEDING PATIENT
Viscoelastic and standard coagulation tests
Check residual heparin (difference in reaction times)
Check platelet count and function
Check fibrinogen level (FF or FIBTEM or Clauss
Check thrombin generation (reaction times)
Exclude hyperfibrinolysis (clot lysis index)
Additional protamine
Platelet transfusion Desmopressin
Fibrinogen concentrate or cryoprecipitate or FFP
PCCs or FFP or rFVIIa in extreme cases
Tranexamic acid E-aminocaproic acid


BLEEDING PATIENT
Viscoelastic and standard coagulation tests
STEP 1
Check residual heparin (difference in reaction times)
Additional protamine
STEP 2
Check platelet count and function
Platelet transfusion - Desmopressin
STEP 3
Check fibrinogen level (FF or FIBTEM or Clauss)
Fibrinogen concentrate or cryoprecipitate or FFP
STEP 4
Check thrombin generation (reaction times)
PCCs or FFP
STEP 5
Exclude hyperfibrinolysis (clot lysis index)
Tranexamic acid / ε-aminocaproic acid
STEP 6
No signs of coagulopathy
Consider surgical re-exploration
STEP 7
Life-threatening bleeding
Consider rFVIIa


CENTRIFUGE IEC CL10
QUANTRA
TEG
Haemonetics
02723
Werfen

A VISCOELASTIC TESTS-BASED ALGORITHM (TEG-ROTEM)

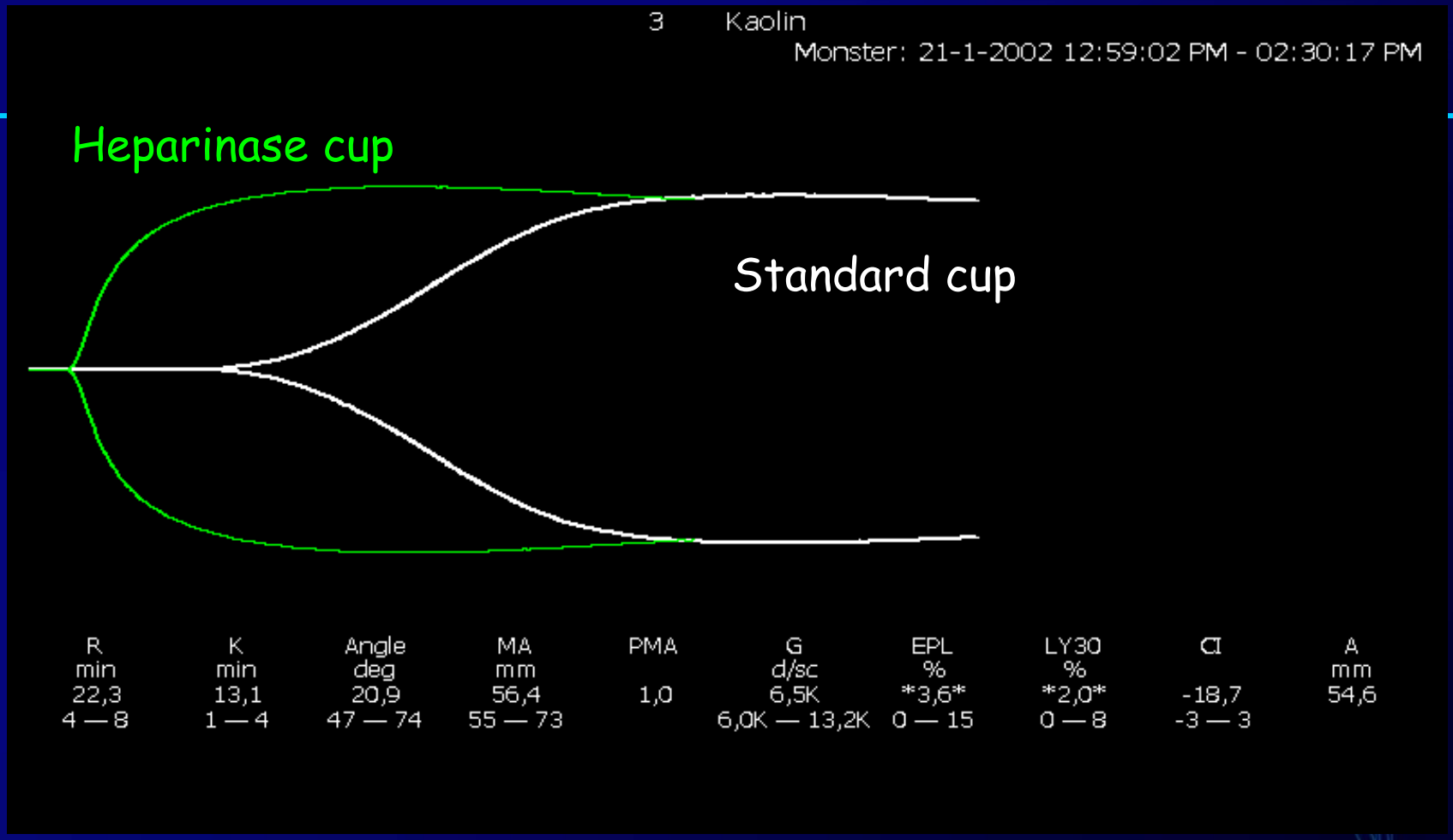
Rule-out residual heparin

Yes

Protamine supplementation

No

Proceed to step 2



FORGET THE ACT

A VISCOELASTIC TESTS-BASED ALGORITHM (TEG-ROTEM)

Rule-out low platelet count/function

Yes

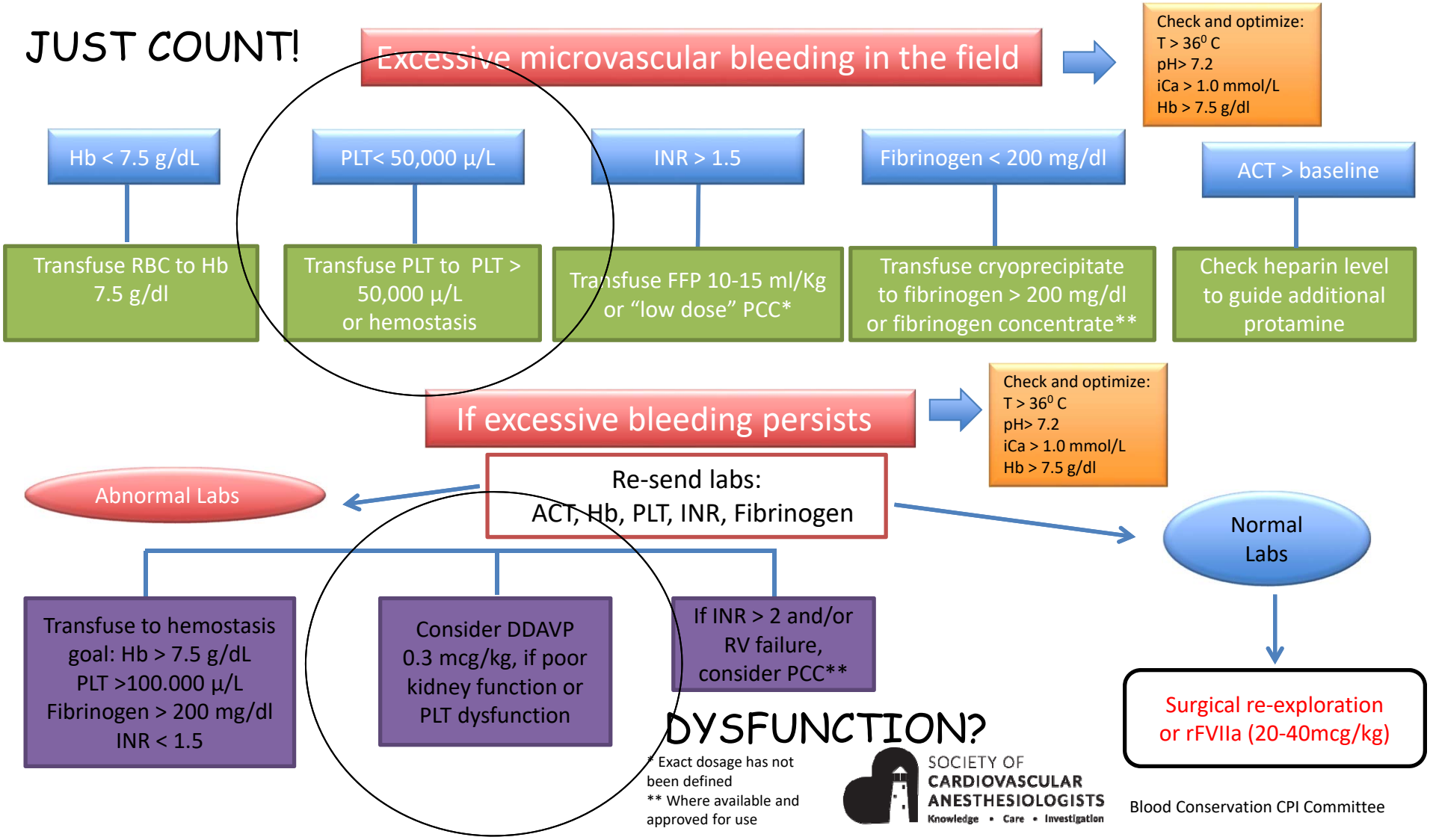
Platelet concentrate transfusion and/or DDAVP

No

Proceed to step 3

Cardiac Surgery Intraoperative Targeted Transfusion Algorithm
Non-TEG/ROTEM directed

Consider: Anti-fibrinolytics, ANH, mini-circuits, retrograde autologous priming, or ultrafiltration and the use of red cell salvage using centrifugation
Before coming Off CPB: measure Hb, platelet count, fibrinogen level and heparin-corrected INR



* Exact dosage has not been defined
** Where available and approved for use

SOCIETY OF CARDIOVASCULAR ANESTHESIOLOGISTS
Knowledge • Care • Investigation

Blood Conservation CPI Committee

European Journal of Cardio-Thoracic Surgery 53 (2018) 79–111
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EACTS/EACTA GUIDELINES

2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery

The Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA)

Authors/Task Force Members: Domenico Pagano* (EACTS Chairperson) (UK), Milan Milojevic (Netherlands), Michael I. Meesters[a] (Netherlands), Umberto Benedetto (UK), Daniel Bolliger[a] (Switzerland), Christian von Heymann[a] (Germany), Anders Jeppsson (Sweden), Andreas Koster[a] (Germany), Ruben L. Osnabrugge (Netherlands), Marco Ranucci[a] (Italy), Hanne Berg Ravn[a] (Denmark), Alexander B.A. Vonk (Netherlands), Alexander Wahba (Norway), Christa Boer[a,*] (EACTA Chairperson) (Netherlands)

Document Reviewers: Moritz W.V. Wyler von Ballmoos (USA), Mate Petricevic (Croatia), Arie Pieter Kappetein (Netherlands), Miguel Sousa-Uva (Portugal), Georg Trummer (Germany), Peter M. Rosseel[a] (Netherlands), Michael Sander[a] (Germany), Pascal Colson[a] (France), Adrian Bauer[b] (Germany)

In the bleeding patient with a low-fibrinogen level (<1.5 g/l), fibrinogen substitution may be considered to reduce postoperative bleeding and transfusions.	IIb	B	[216–218]
In patients where bleeding is related to coagulation factor deficiency, PCC or FFP administration should be considered to reduce bleeding and transfusions.	IIa	B	[219, 220]
The prophylactic use of DDAVP to reduce bleeding is not recommended.	III	B	[221, 222]
In bleeding patients with platelet dysfunction on the basis of an inherited or acquired bleeding disorder, the use of DDAVP should be considered to reduce bleeding and the requirement for transfusions.	IIa		
The prophylactic use of rFVIIa to prevent bleeding is not recommended.	III	B	[223]
In patients with refractory, non-surgical bleeding, off-label use of rFVIIa may be considered to reduce bleeding.	IIb	B	[224]

NO CUT-OFF VALUES

Recommendations	Class[a]	Level[b]	Ref[c]
Implementation of a PBM protocol for the bleeding patient is recommended.	I	C	
The use of PRBCs of all ages is recommended, because the storage time of the PRBCs does not affect the outcomes.	I	A	[259, 260]
The use of leucocyte-depleted PRBCs is recommended to reduce infectious complications.	I	B	[261]
Pooled solvent detergent FFP may be preferred to standard FFP to reduce the risk of TRALI.	IIb	B	[262]
Perioperative treatment algorithms for the bleeding patient based on viscoelastic POC tests should be considered to reduce the number of transfusions.	IIa	B	[263–265]
It is recommended that one transfuse PRBCs on the basis of the clinical condition of the patient rather than on a fixed haemoglobin threshold.	I	B	[266, 267]
A haematocrit of 21–24% may be considered during CPB when an adequate DO_2 (>273 ml O_2/min/m^2) level is maintained.	IIb	B	[268]
Platelet concentrate should be transfused in bleeding patients with a platelet count below 50 (10^9/l) or patients on antiplatelet therapy with bleeding complications.	IIa	C	

ONLY COUNT

EJA

Eur J Anaesthesiol 2017; **34**:332–395

GUIDELINES

Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology

First update 2016

Sibylle A. Kozek-Langenecker, Aamer B. Ahmed, Arash Afshari, Pierre Albaladejo, Cesar Aldecoa, Guidrius Barauskas, Edoardo De Robertis, David Faraoni, Daniela C. Filipescu, Dietmar Fries, Thorsten Haas, Matthias Jacob, Marcus D. Lancé, Juan V.L. Pitarch, Susan Mallett, Jens Meier, Zsolt L. Molnar, Niels Rahe-Meyer, Charles M. Samama, Jakob Stensballe, Philippe J.F. Van der Linden, Anne J. Wikkelsø, Patrick Wouters, Piet Wyffels and Kai Zacharowski

7.5. Plasma and platelet transfusion

Recommendations

We recommend against the use of plasma transfusion for pre-procedural correction of mild-to-moderately elevated INR. **1C**

We recommend early and targeted treatment of coagulation factor deficiencies in the plasma. Sources of coagulation factors are coagulation factor concentrates, cryoprecipitate or high volumes of plasma, depending on the clinical situation, type of bleeding, type of deficiency and resources provided. **1B**

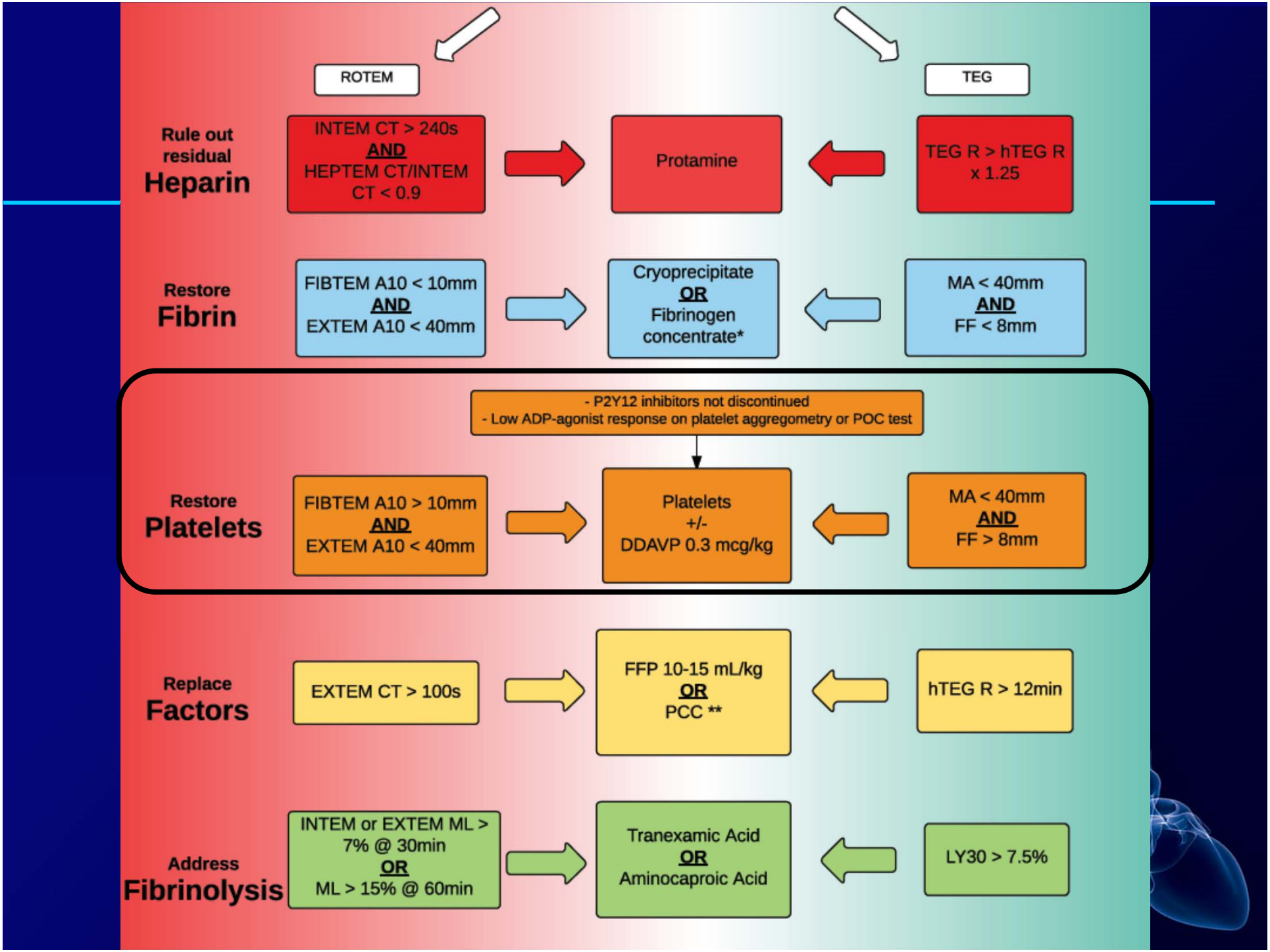
In the treatment of acquired coagulation factor deficiency, we suggest the consideration of a ratio-driven protocol (RBC:plasma:platelet concentrates) early in uncontrolled massive bleeding outside the trauma setting followed by a goal-directed approach as soon as possible. **2C**

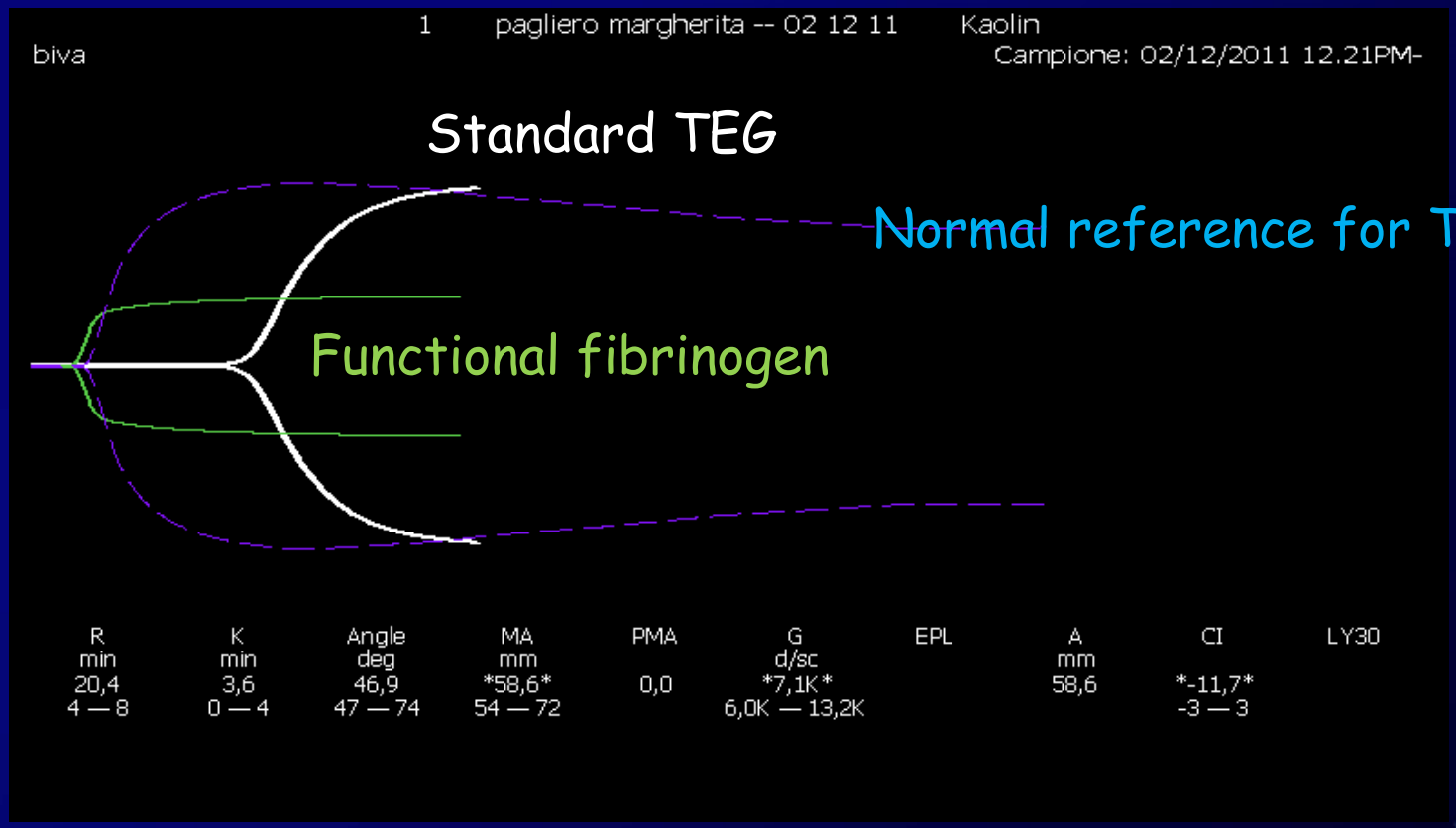
We suggest coagulation factor concentrates for the primary treatment of acquired coagulation factor deficiency due to their high efficacy and their minimal infectiousness. **2C**

We recommend against indiscriminate use of plasma transfusion in perioperative bleeding management. **1C**

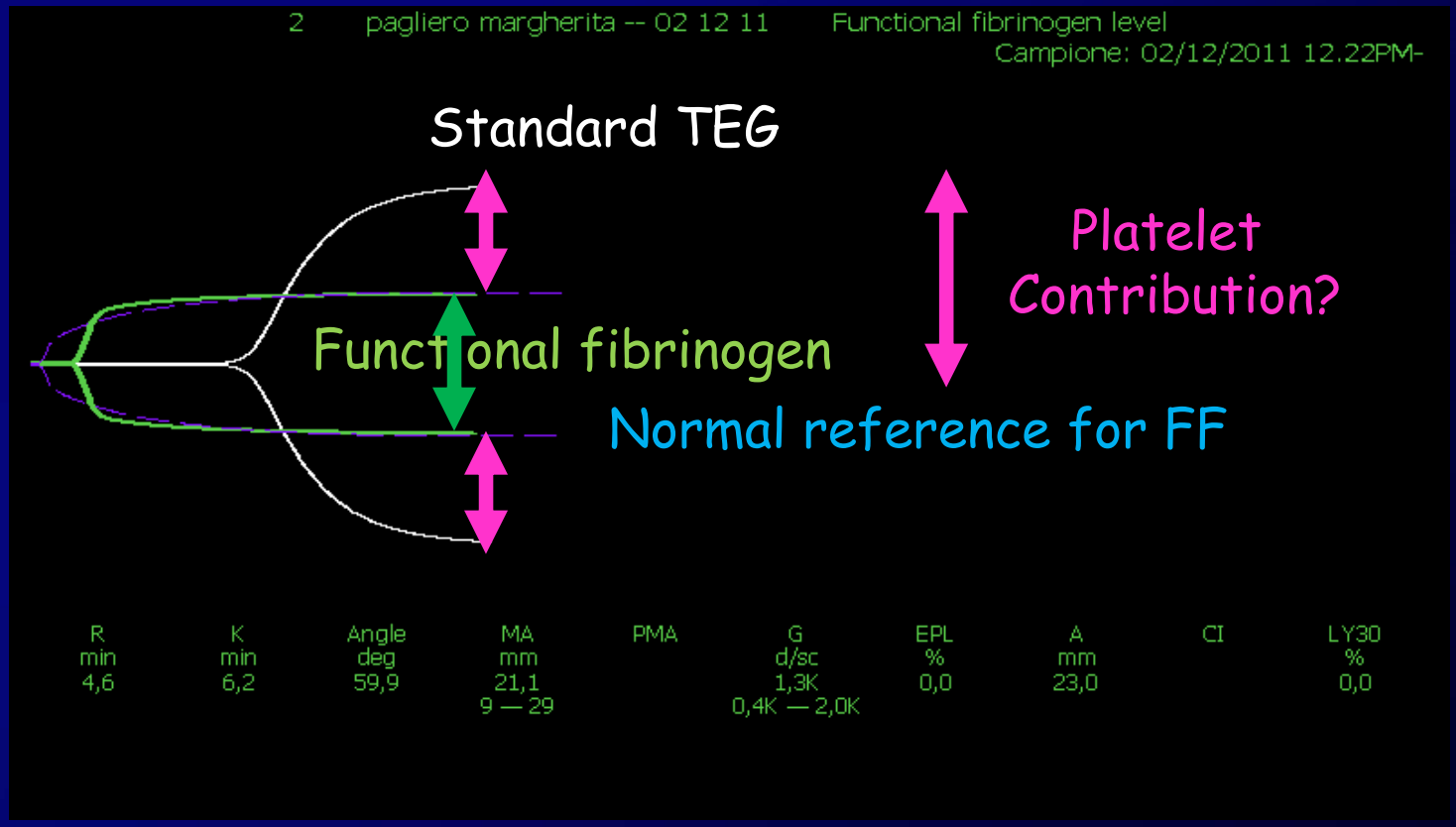
We suggest platelet concentrate transfusion in bleeding situati
clearly related to antiplatelet drugs or thrombocytopaenia l
than $50 \times 10^9\ l^{-1}$. **2C**

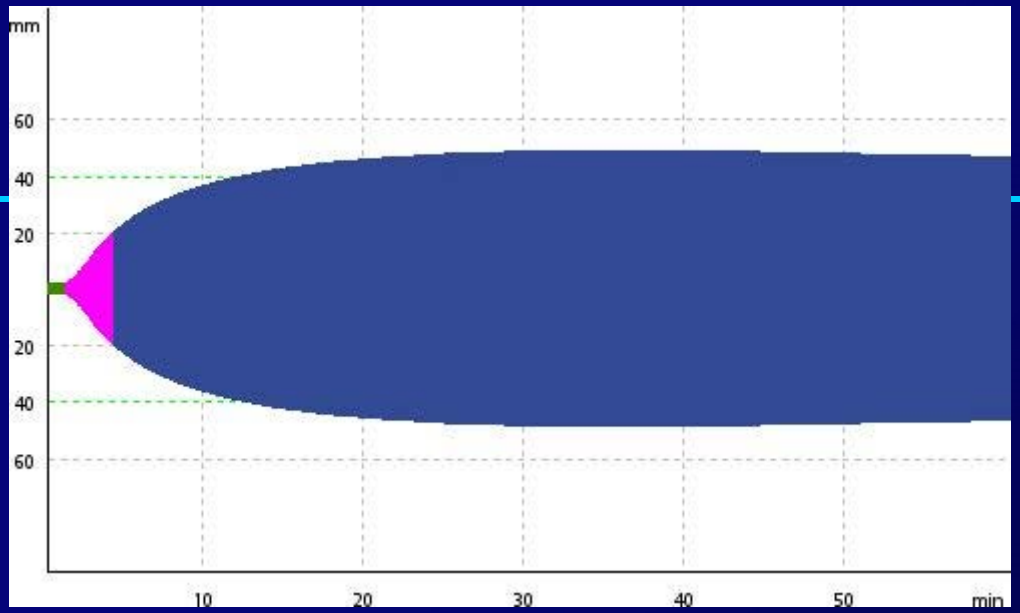
COUNT ONLY
NO CUT-OFF
VALUES


ROTEM
TEG
Rule out residual Heparin
INTEM CT > 240s AND HEPTEM CT/INTEM CT < 0.9
Protamine
TEG R > hTEG R x 1.25
Restore Fibrin
FIBTEM A10 < 10mm AND EXTEM A10 < 40mm
Cryoprecipitate OR Fibrinogen concentrate*
MA < 40mm AND FF < 8mm
- P2Y12 inhibitors not discontinued
- Low ADP-agonist response on platelet aggregometry or POC test
Restore Platelets
FIBTEM A10 > 10mm AND EXTEM A10 < 40mm
Platelets +/- DDAVP 0.3 mcg/kg
MA < 40mm AND FF > 8mm
Replace Factors
EXTEM CT > 100s
FFP 10-15 mL/kg OR PCC **
hTEG R > 12min
Address Fibrinolysis
INTEM or EXTEM ML > 7% @ 30min OR ML > 15% @ 60min
Tranexamic Acid OR Aminocaproic Acid
LY30 > 7.5%


1 pagliero margherita -- 02 12 11 Kaolin
biva
Campione: 02/12/2011 12.21PM-
Standard TEG
Normal reference for TEG
Functional fibrinogen
R min 20,4 4 — 8
K min 3,6 0 — 4
Angle deg 46,9 47 — 74
MA mm *58,6* 54 — 72
PMA 0,0
G d/sc *7,1K* 6,0K — 13,2K
EPL
A mm 58,6
CI *-11,7* -3 — 3
LY30

FALSE: roughly indicative of count, not of function
because thrombin (kaolin-dependent) always activates platelets





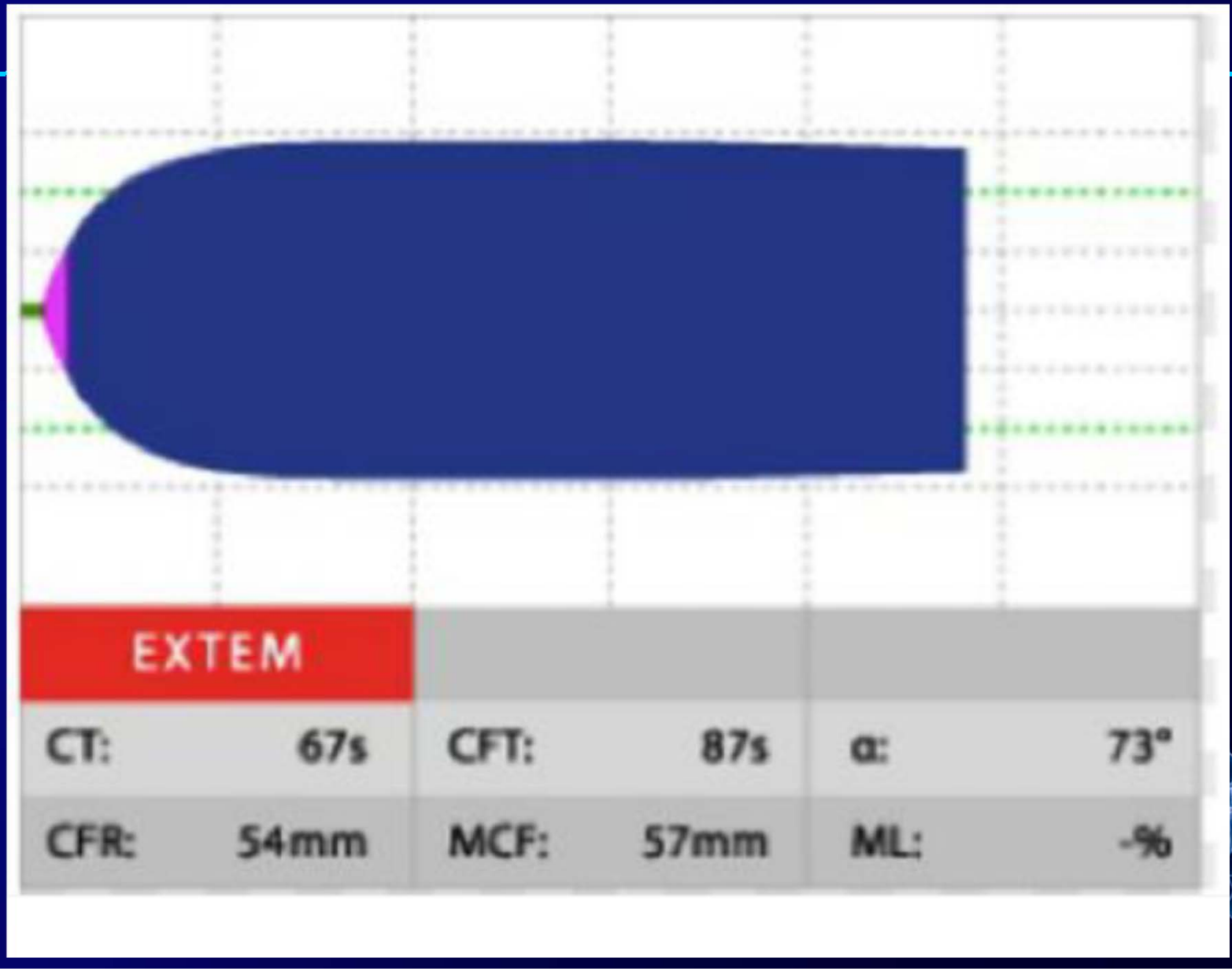
EXTEM

MCF 49
Range (50-72)

MCF 6
Range (9-25)

FIBTEM

ROTEM EXTEM



EXTEM					
CT:	67s	CFT:	87s	α:	73°
CFR:	54mm	MCF:	57mm	ML:	-%

A normal Rotem-Fibtem

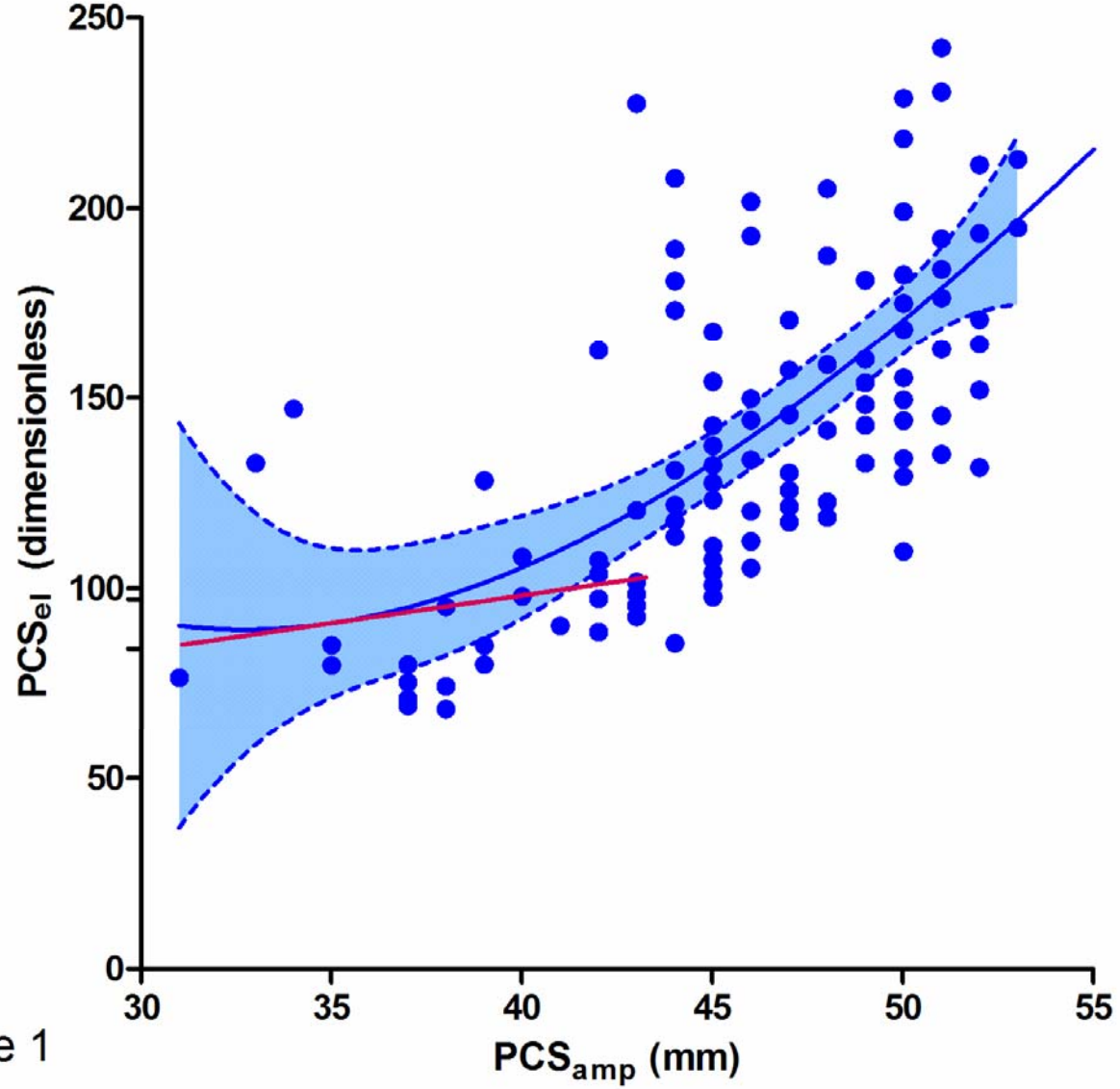

250
200
150
100
50
0
30
35
40
45
50
55
PCSel (dimensionless)
PCSamp (mm)

Figure 1

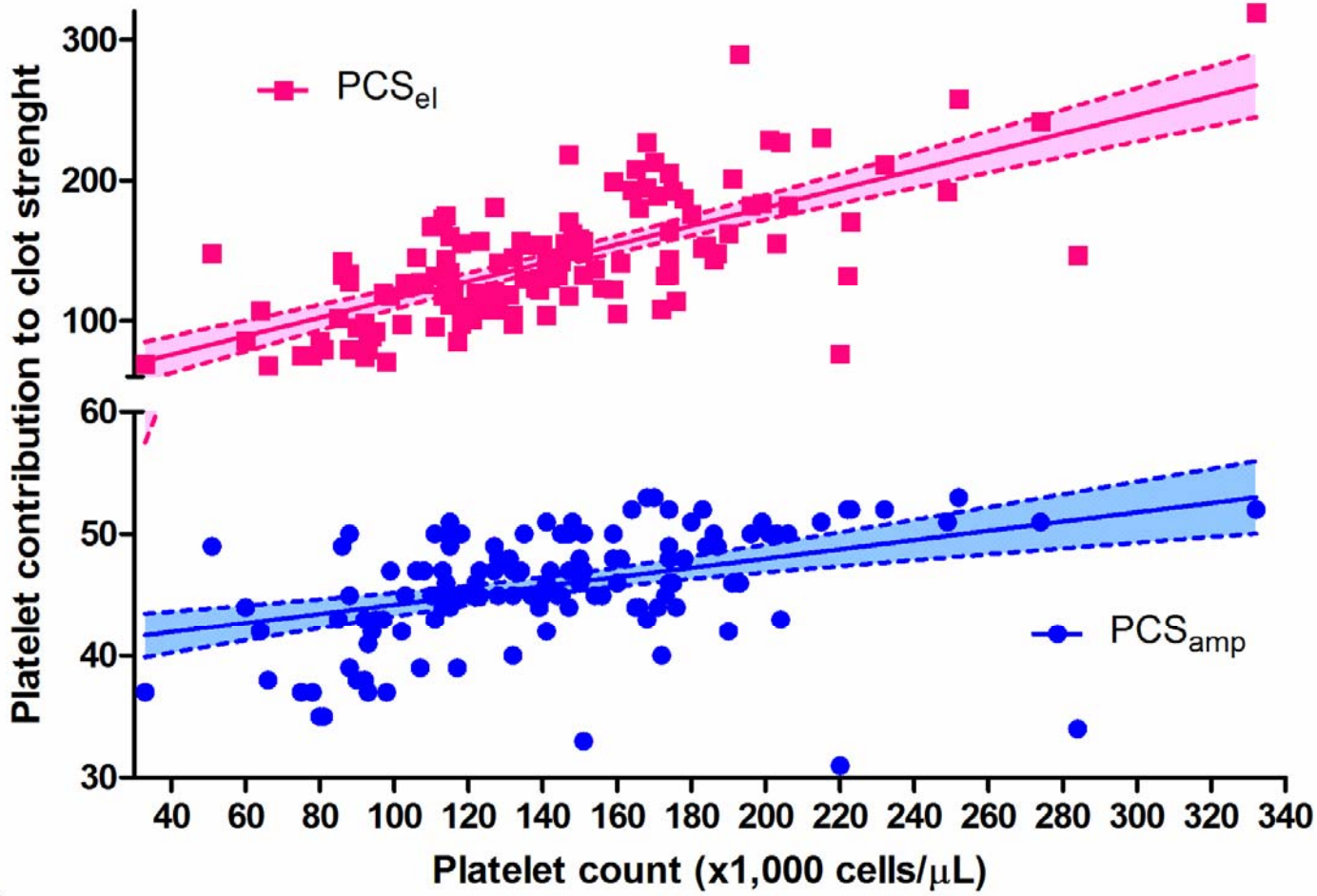

Platelet contribution to clot strenght
300
200
100
60
50
40
30
PCS$_{el}$
PCS$_{amp}$
40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340
Platelet count (x1,000 cells/μL)

Figure 2

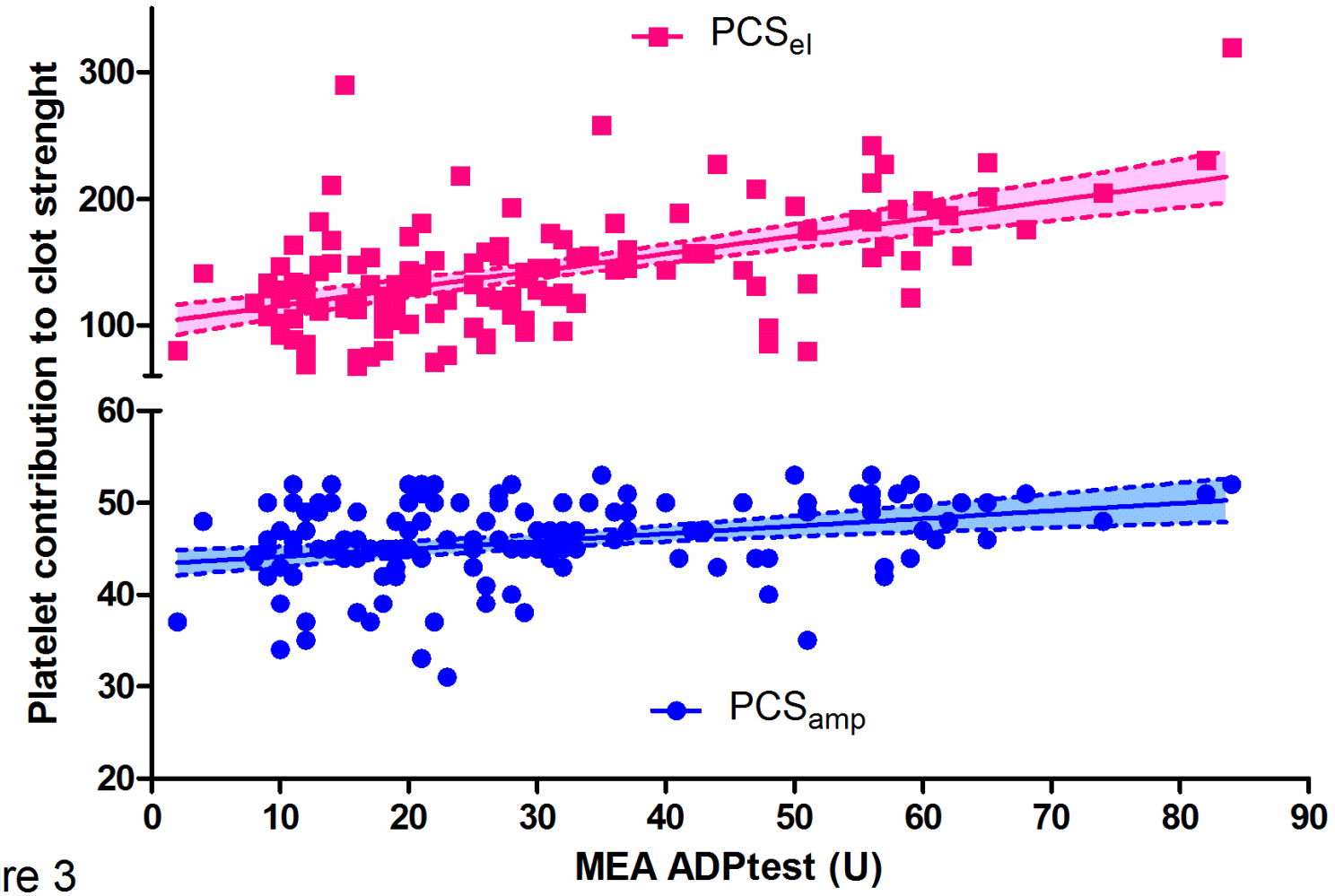

PCS$_{el}$
PCS$_{amp}$
Platelet contribution to clot strenght
MEA ADPtest (U)
300
200
100
60
50
40
30
20
0
10
20
30
40
50
60
70
80
90

Figure 3

MULTIVARIABLE ANALYSIS

Platelet count and ADP-dependent platelet function are independently associated with PCSel

Platelet count explains 36% of the PCSel variance, Platelet function explains 14%

Overall, the model explains 50% of the PCSel variance

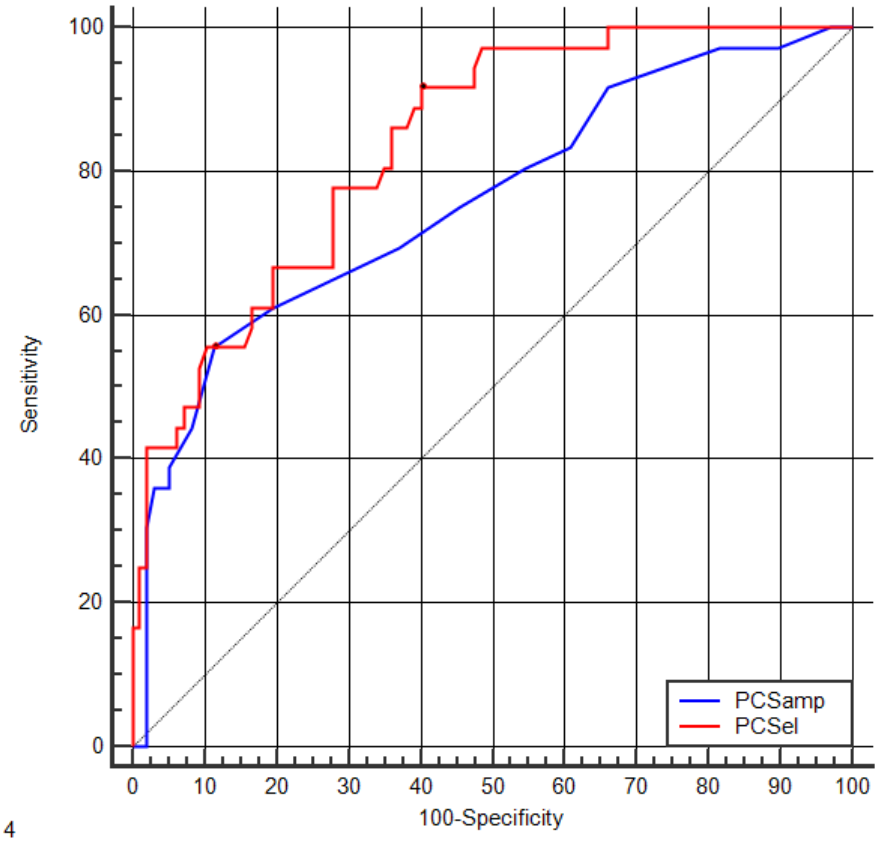


Figure 4

DISCRIMINATION (AUC) FOR LOW PLATELET COUNT (< 100,000) OR FUNCTION (ADPtest<12 U) IS VERY GOOD (0.837)

QUANTRA Hemostasis Analyzer

Point-of-Care Coagulation Monitoring

Dr. **Ekaterina Baryshnikova**, Biol.PhD

San Donato Milanese, Italy

Results display: the dial view

Our study

30 patients undergoing cardiac surgery (any kind)

QUANTRA compared with ROTEM, Multiplate and standard lab

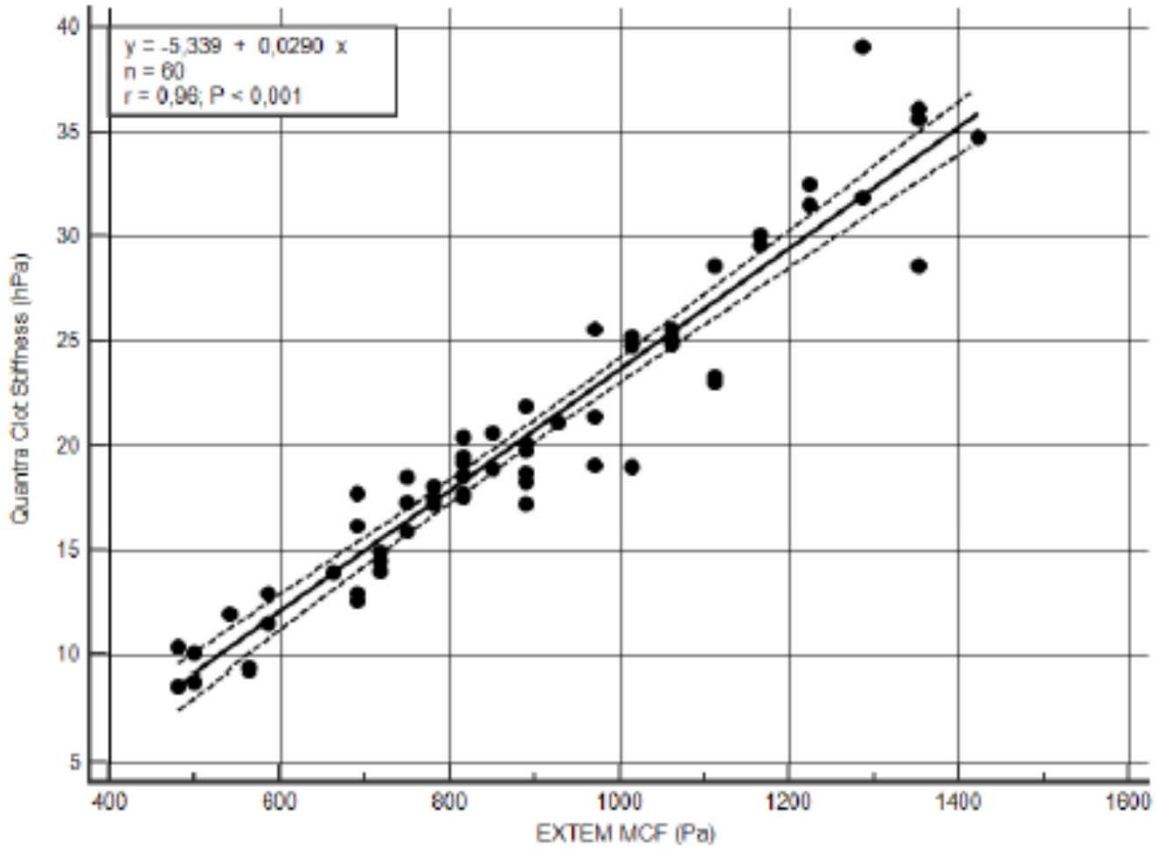
2 time points:

PRE (after induction, before incision)

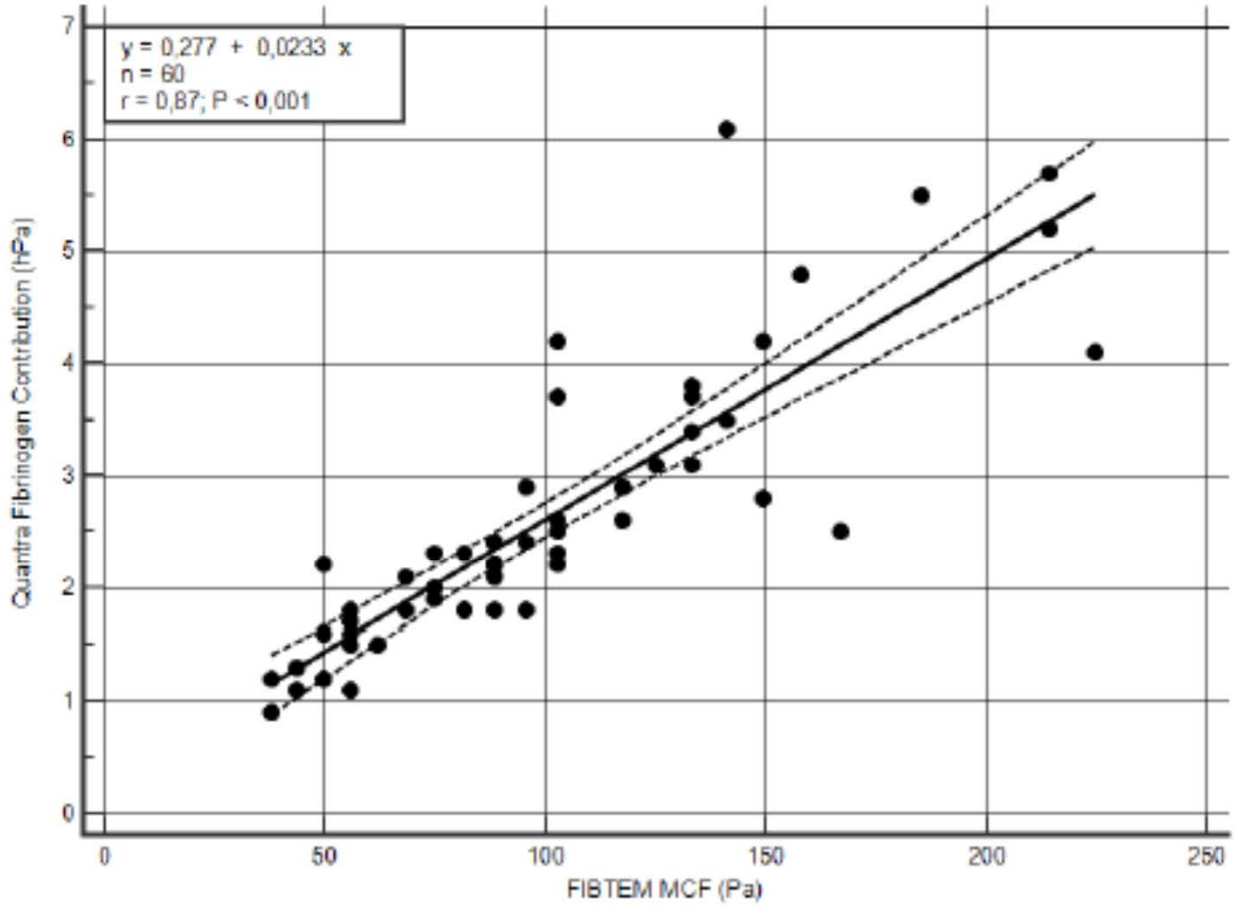
POST (after heparin reversal)

→ **NO/weak correlation of Qplus CT and INTEM CT/aPTT**

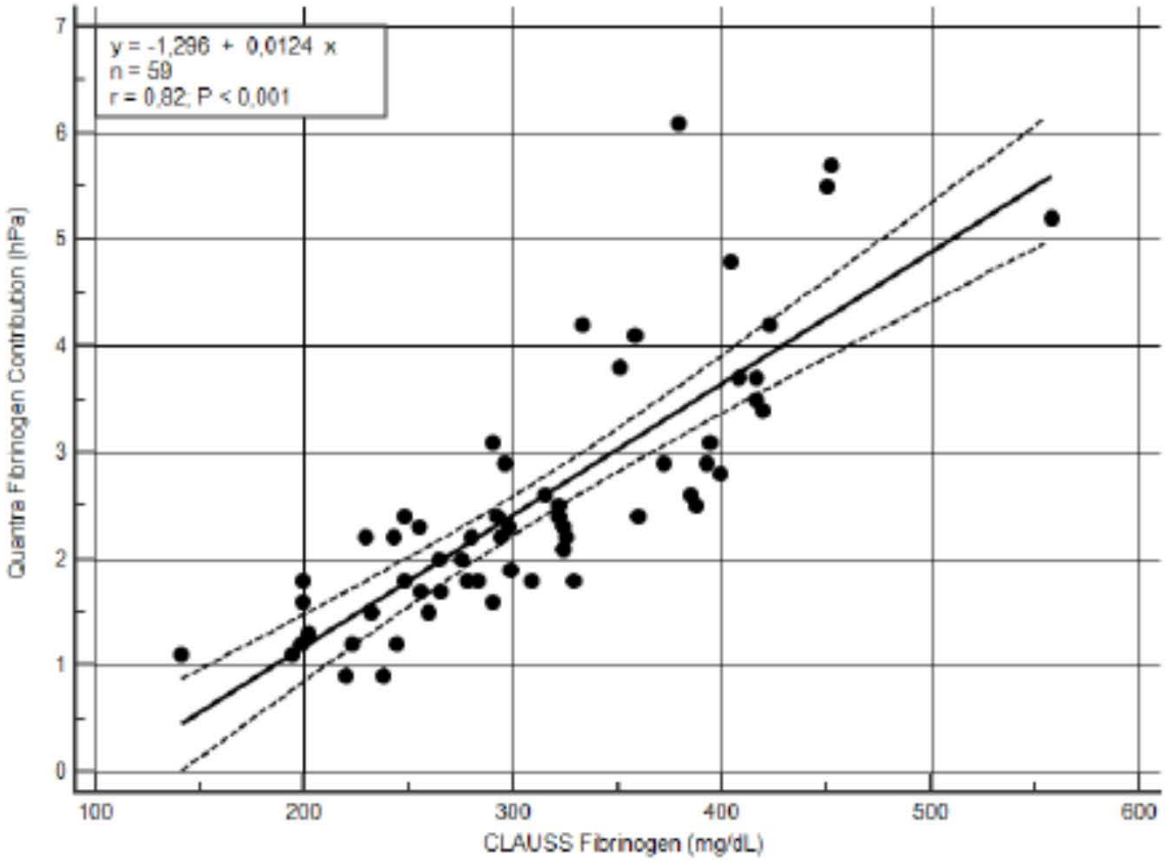
A Quantra clot stiffness vs. EXTEM Maximum Clot Firmness – All samples

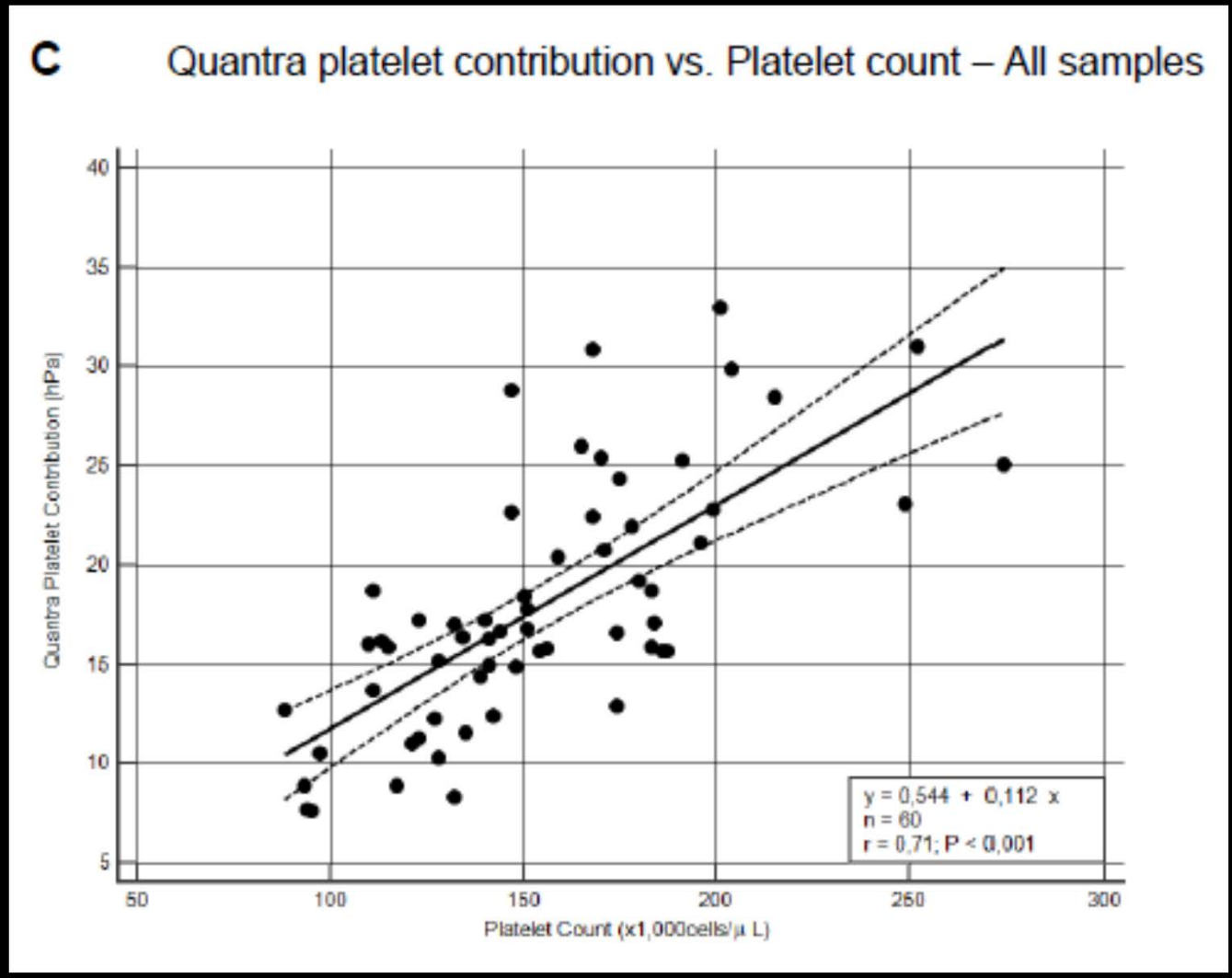


A Quantra fibrinogen contribution vs. FIBTEM Maximum Clot Firmness – All samples

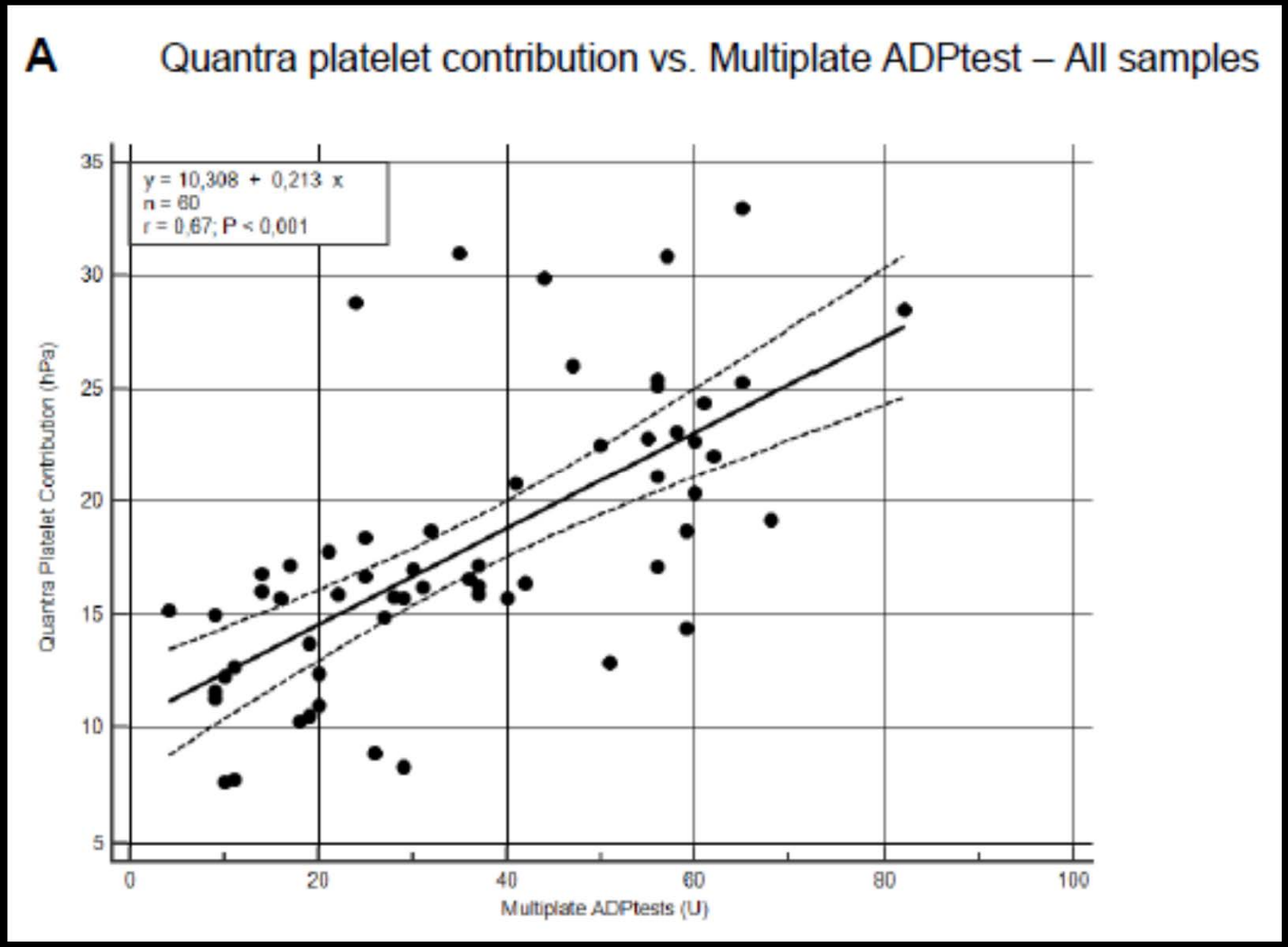


A Quantra fibrinogen contribution vs. Clauss Fibrinogen Concentration – All samples




C
Quantra platelet contribution vs. Platelet count – All samples
Quantra Platelet Contribution [hPa]
40
35
30
25
20
15
10
5
50
100
150
200
250
300
Platelet Count (x1,000cells/μ L)
y = 0,544 + 0,112 x
n = 60
r = 0,71; P < 0,001

Platelet Contribution related to ADP **platelet function**?



independently associated at multivariable analysis

PLATFORM

- Prospective cohort study
- Registered at Clinicaltrials.gov
- Adult patients
- 1-year data collection
- Exclusion: emergency surgery; unwillingness to participate; unavailability of reagents; unavailability of study staff
- Externally funded by Roche Diagnostics

PLATFORM

PATIENT POPULATION:

494 subjects

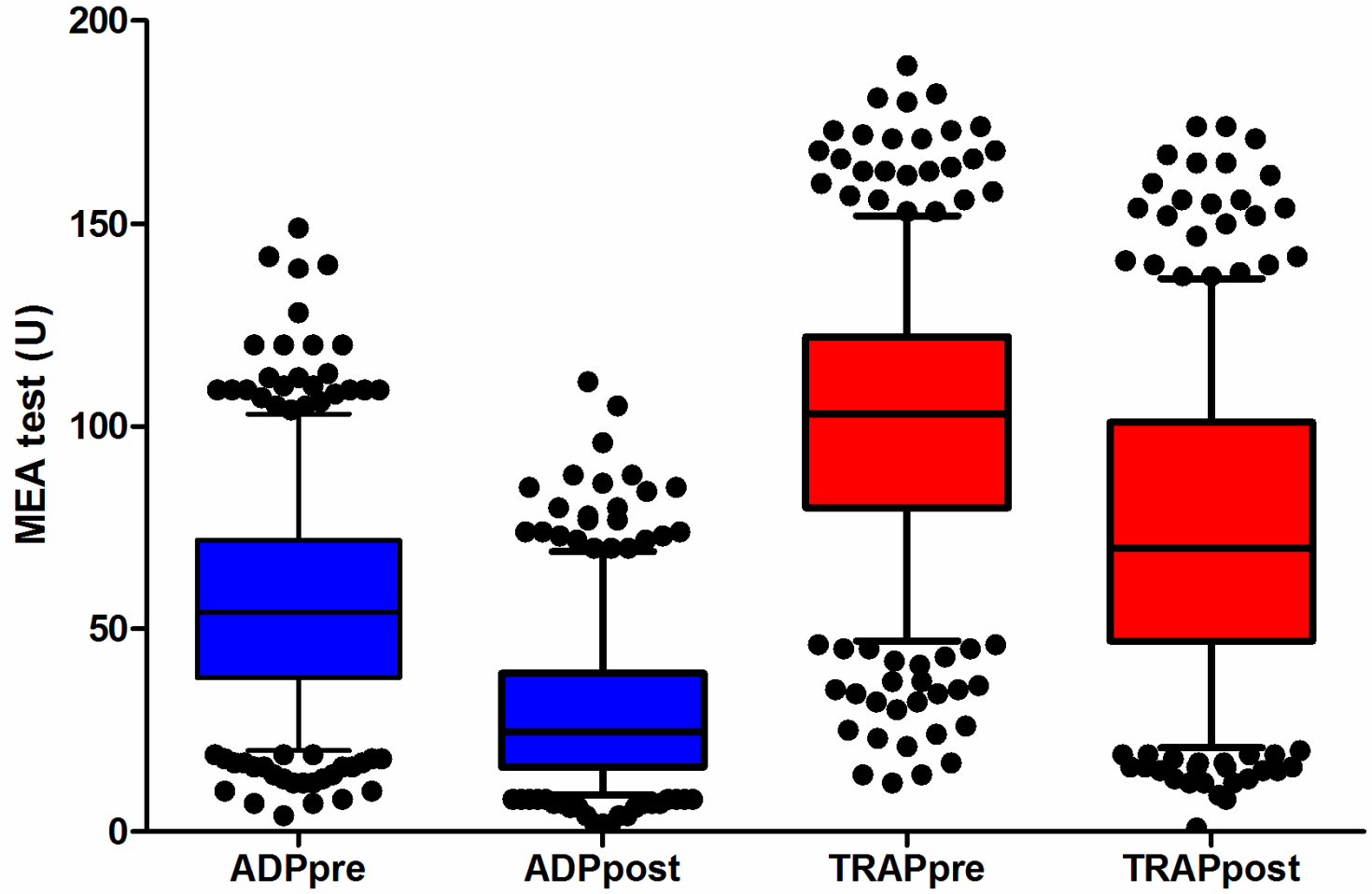
DEFINITIONS:

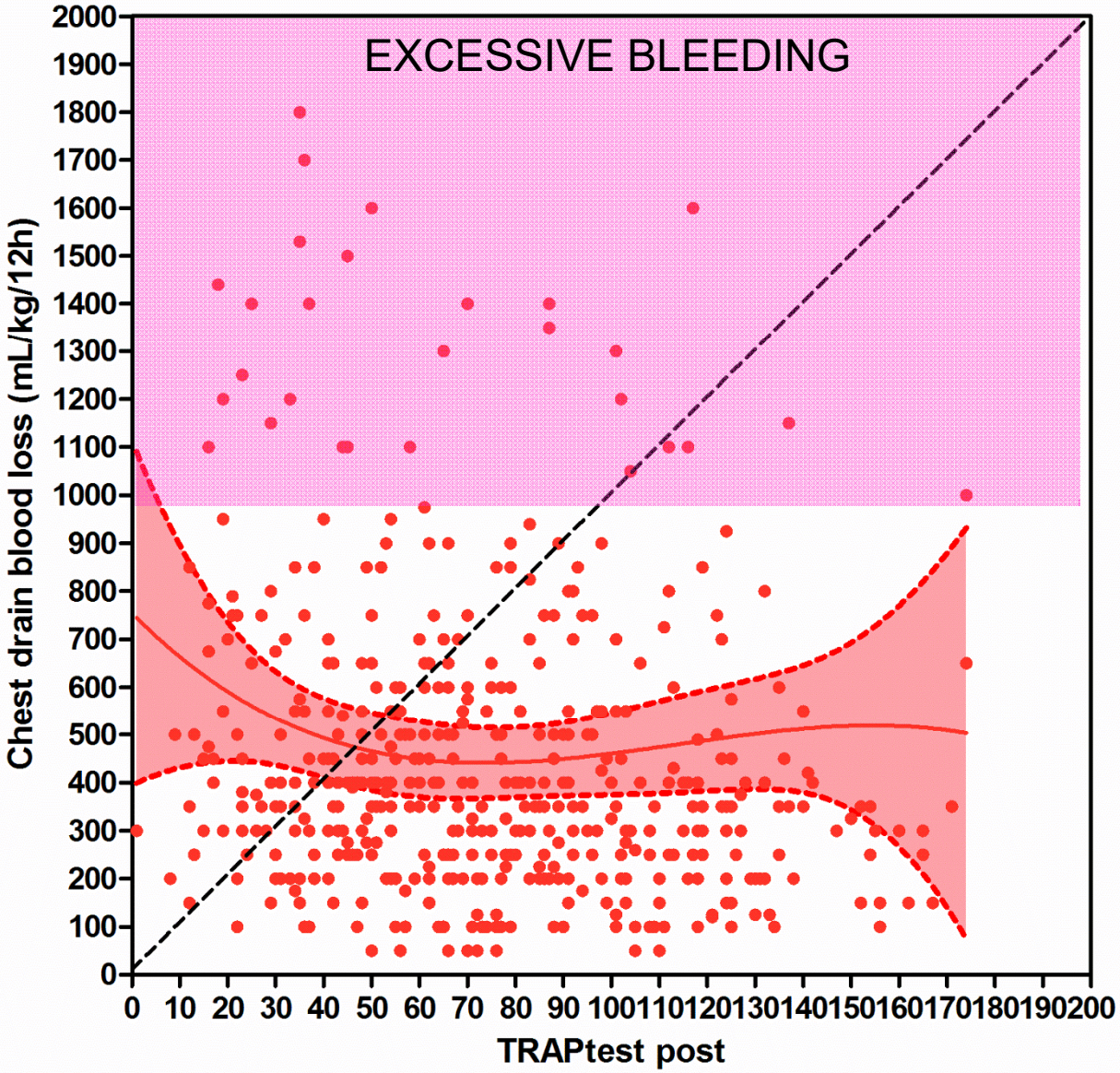
Bleeding: chest drain blood loss 12-hours

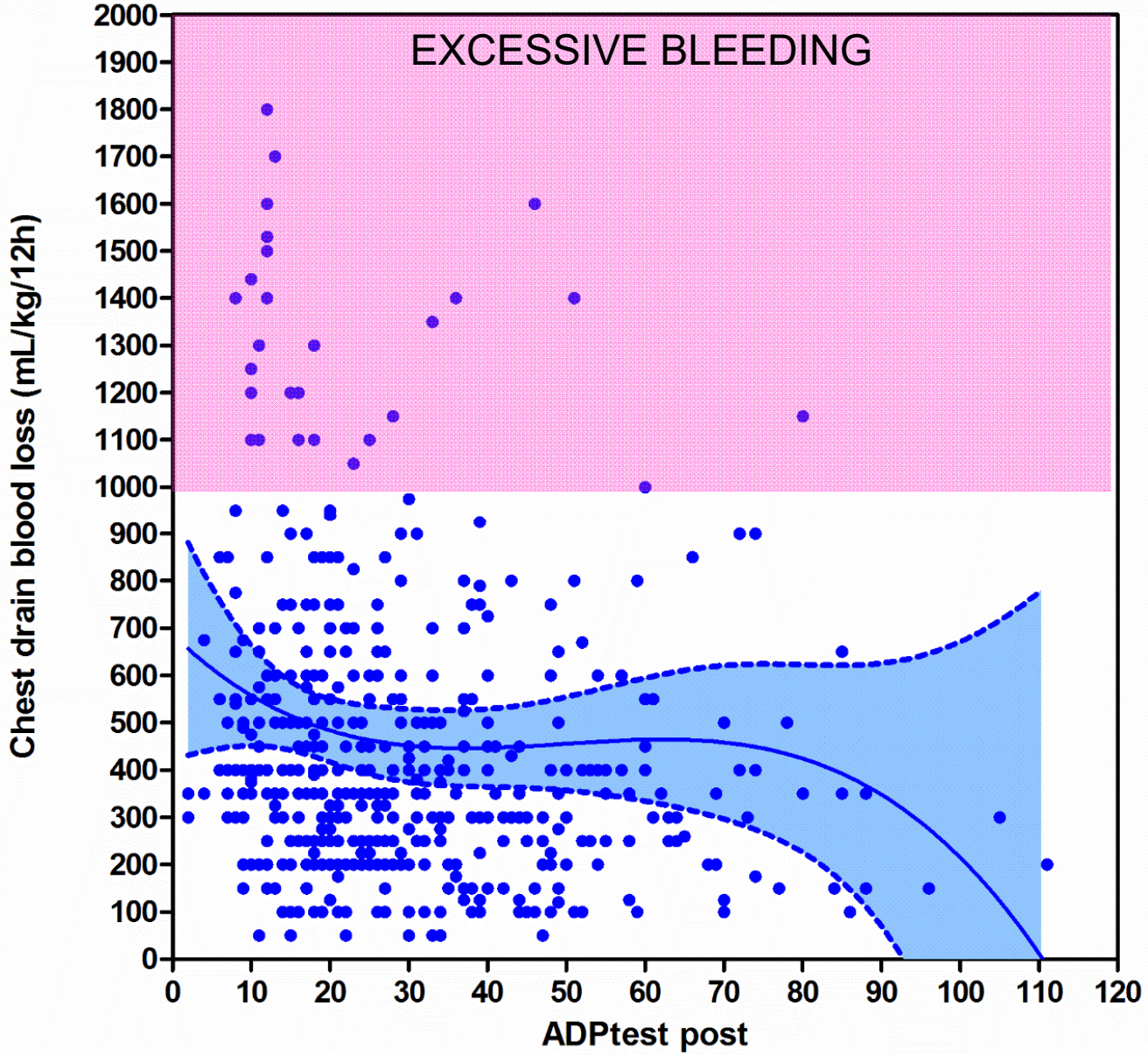
Excessive Bleeding: according to the UDPB, > 1,000 mL/12 h and/or surgical revision

Measurements

- aPTT, INR, Platelet count the day before surgery
- aPTT, INR, fibrinogen (Clauss), Platelet count at the arrival in the ICU
- ADPtest and TRAPtest MEA (Multiplate) preoperatively, in the OR
- ADPtest and TRAPtest MEA (Multiplate) post-protamine, in the OR


MEA test (U)
200
150
100
50
0
ADPpre
ADPpost
TRAPpre
TRAPpost


EXCESSIVE BLEEDING
Chest drain blood loss (mL/kg/12h)
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200
TRAPtest post


EXCESSIVE BLEEDING
Chest drain blood loss (mL/kg/12h)
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
0
10
20
30
40
50
60
70
80
90
100
110
120
ADPtest post

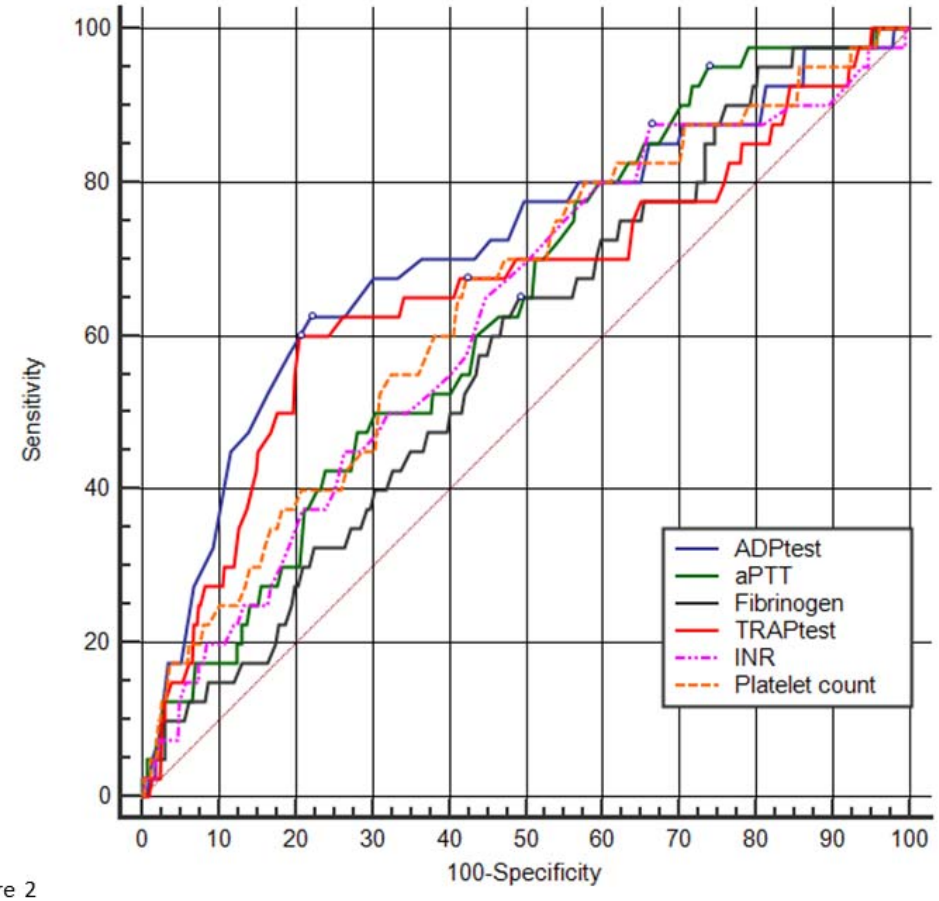


Figure 2

AUC ADP: 0.716

AUC TRAP: 0.630

POST-PROTAMINE ADPtest
Rate of events: 8.3%

CUT-OFF VALUE (U)	PPV	NPV
4	27.7	88.2
6	33.8	89.4
8	41.7	89.6
10	36.0	90.4
12	34.7	92.2
14	30.6	92.8
16	27.9	93.8
18	23.2	94.0
20	20.7	93.9

A VISCOELASTIC TESTS-BASED ALGORITHM (TEG-ROTEM)

Rule-out low fibrinogen levels

Yes

FIBRINOGEN CONCENTRATE SUPPLEMENTATION

No

Proceed to step 4

POSTOPERATIVE

- Should we supplement with fibrinogen the patient after CPB?
- If yes, when (trigger value?)
- If yes, to reach what level (target value?)
- If yes, how much?

Fibrinogen deficiency

- Due to dilution and consumption
- Rare in routine cardiac surgery
- Factor activity becomes critical below 30%
- More common in long (> 2 hours) pump run
- Associated to extensive use of cell-saver
- Common in aortic surgery
- Common in aortic dissection

ORIGINAL RESEARCH

Randomized, Double-Blinded, Placebo-Controlled Trial of Fibrinogen Concentrate Supplementation After Complex Cardiac Surgery

Marco Ranucci, MD; Ekaterina Baryshnikova, PhD (Biol.); Giulia Beatrice Crapelli, MD; Niels Rahe-Meyer, MD; Lorenzo Menicanti, MD; Alessandro Frigiola, MD; for the Surgical Clinical Outcome REsearch (SCORE) Group*

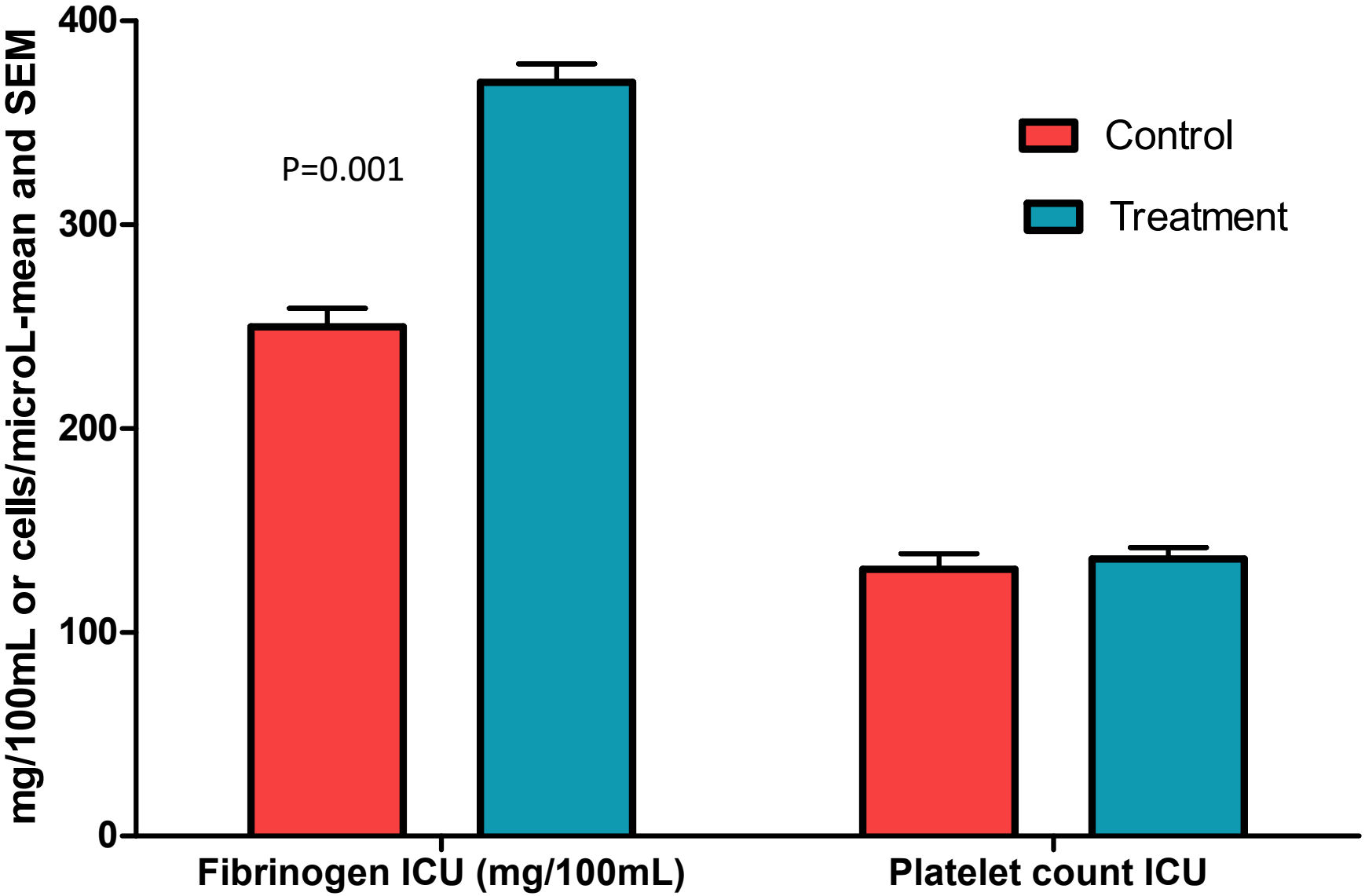
Background—Postoperative bleeding after heart operations is still a common finding, leading to allogeneic blood products transfusion. Fibrinogen and coagulation factors deficiency are possible determinants of bleeding. The experimental hypothesis of this study is that a first-line fibrinogen supplementation avoids the need for fresh frozen plasma (FFP) and reduces the need for any kind of transfusions.

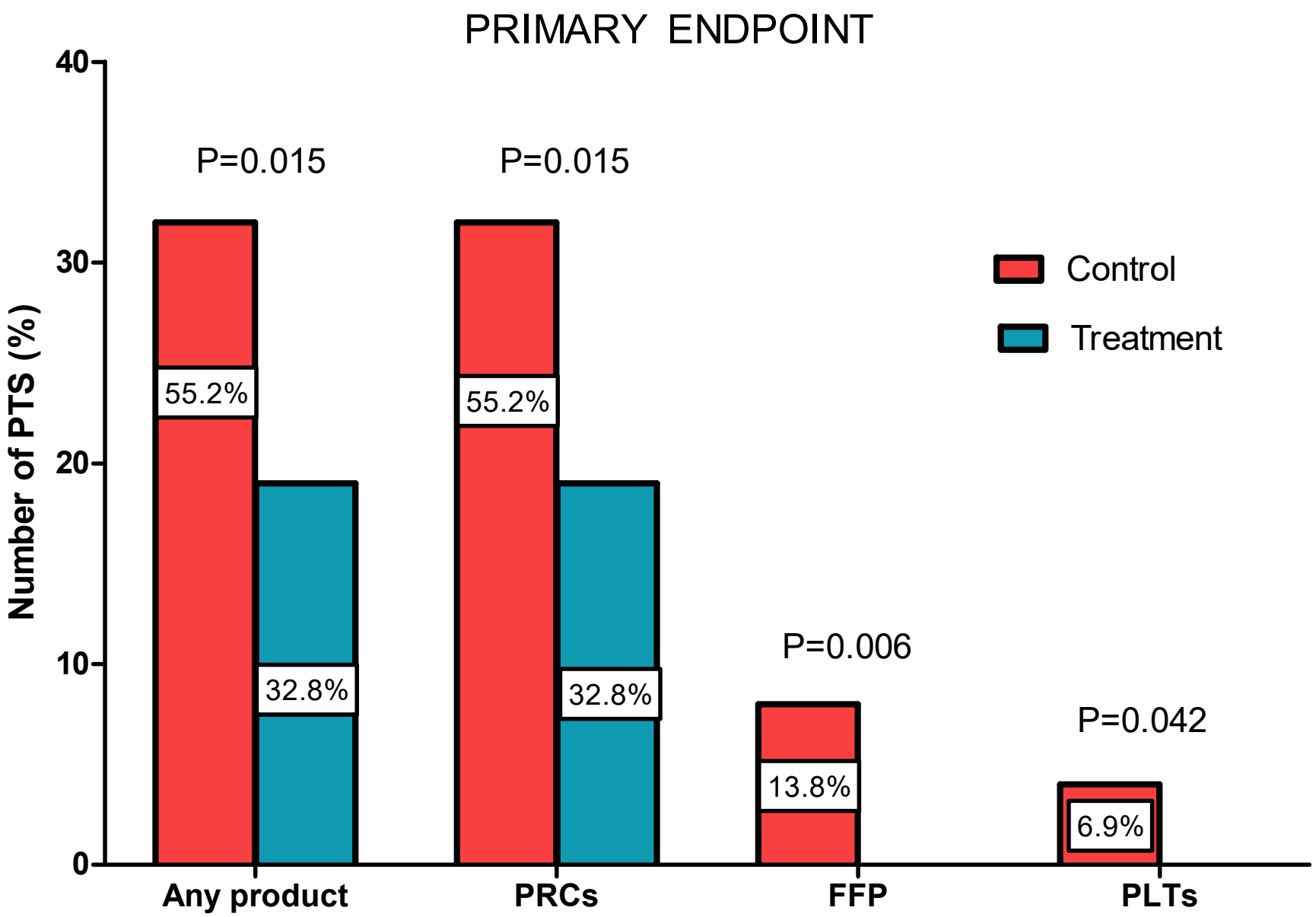
Methods and Results—This was a single-center, prospective, randomized, placebo-controlled, double-blinded study. One-hundred sixteen patients undergoing heart surgery with an expected cardiopulmonary bypass duration >90 minutes were admitted to the study. Patients in the treatment arm received fibrinogen concentrate after protamine administration; patients in the control arm received saline solution. In case of ongoing bleeding, patients in the treatment arm could receive prothrombin complex concentrates (PCCs) and those in the control arm saline solution. The primary endpoint was avoidance of any allogeneic blood product. Patients in the treatment arm had a significantly lower rate of any allogeneic blood products transfusion (odds ratio, 0.40; 95% confidence interval, 0.19 to 0.84, P=0.015). The total amount of packed red cells and FFP units transfused was significantly lower in the treatment arm. Postoperative bleeding was significantly (P=0.042) less in the treatment arm (median, 300 mL; interquartile range, 200 to 400 mL) than in the control arm (median, 355 mL; interquartile range, 250 to 600 mL).

Conclusions—Fibrinogen concentrate limits postoperative bleeding after complex heart surgery, leading to a significant reduction in allogeneic blood products transfusions. No safety issues were raised.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01471730. **(*J Am Heart Assoc.* 2015;4: e002066 doi: 10.1161/JAHA.115.002066)**

Key Words: cardiopulmonary bypass • fibrinogen • hemorrhage • surgery

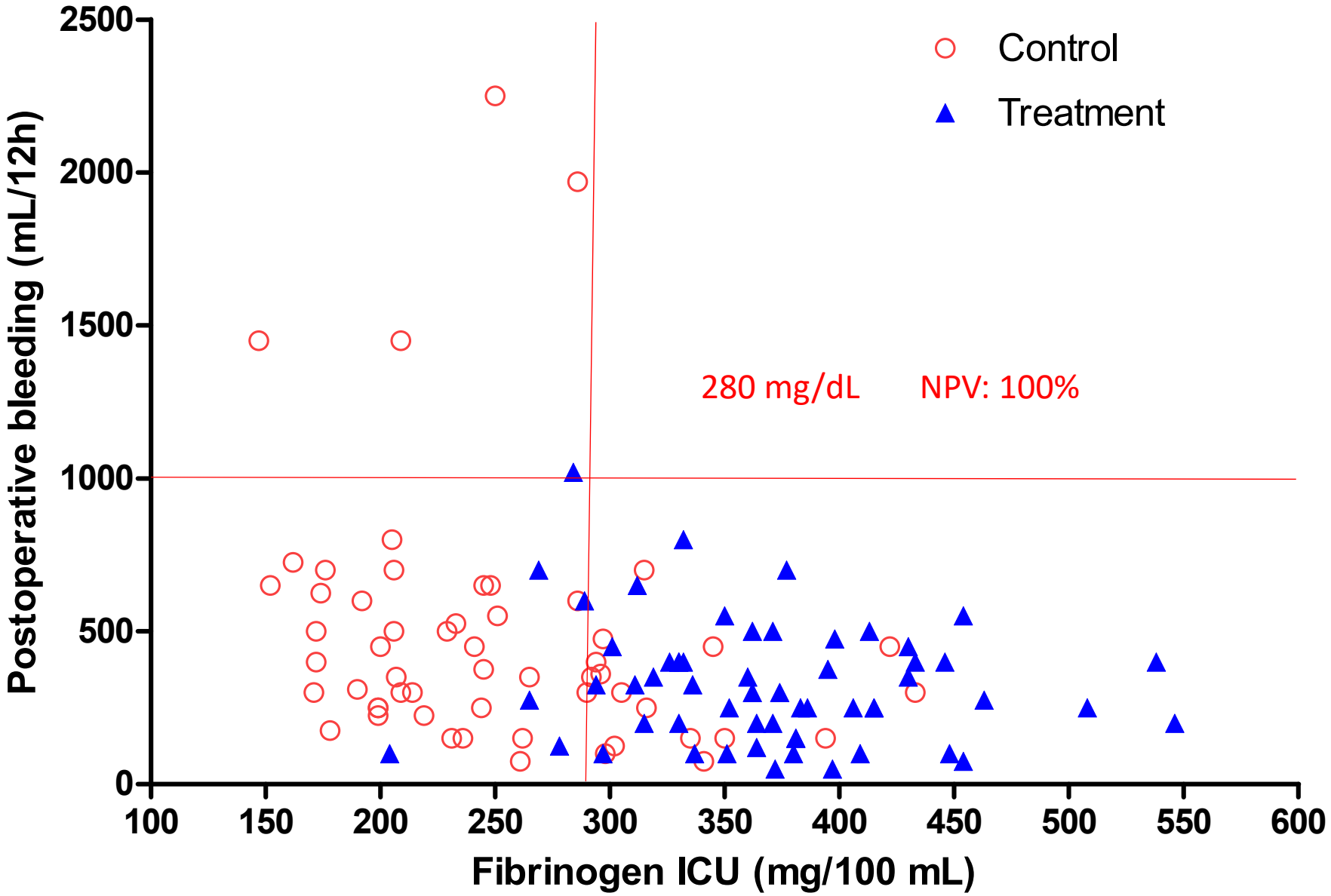

400
300
200
100
0
mg/100mL or cells/microL-mean and SEM
P=0.001
Control
Treatment
Fibrinogen ICU (mg/100mL)
Platelet count ICU

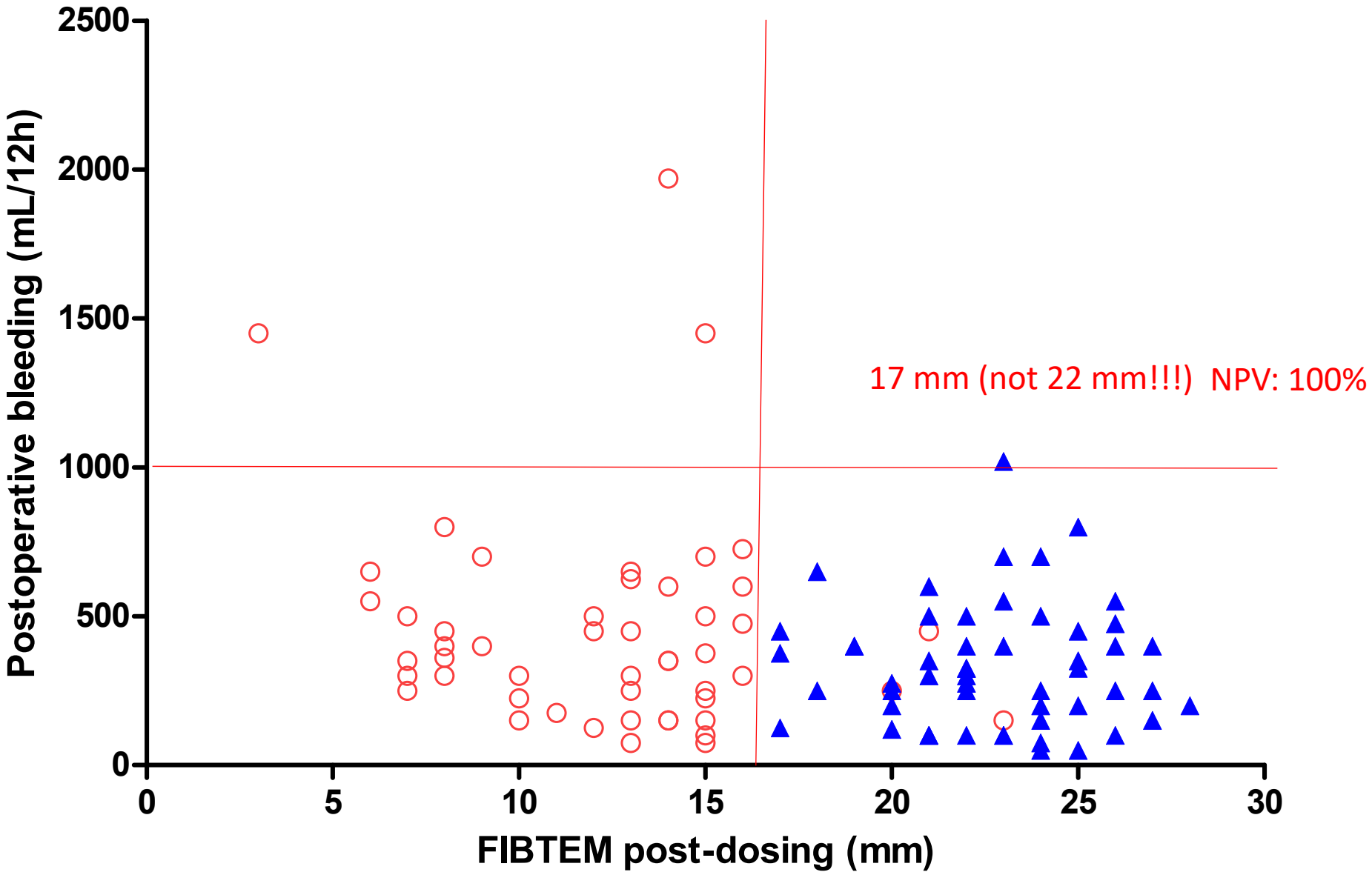

PRIMARY ENDPOINT
Number of PTS (%)
40
30
20
10
0
P=0.015
P=0.015
P=0.006
P=0.042
55.2%
32.8%
55.2%
32.8%
13.8%
6.9%
Control
Treatment
Any product
PRCs
FFP
PLTs

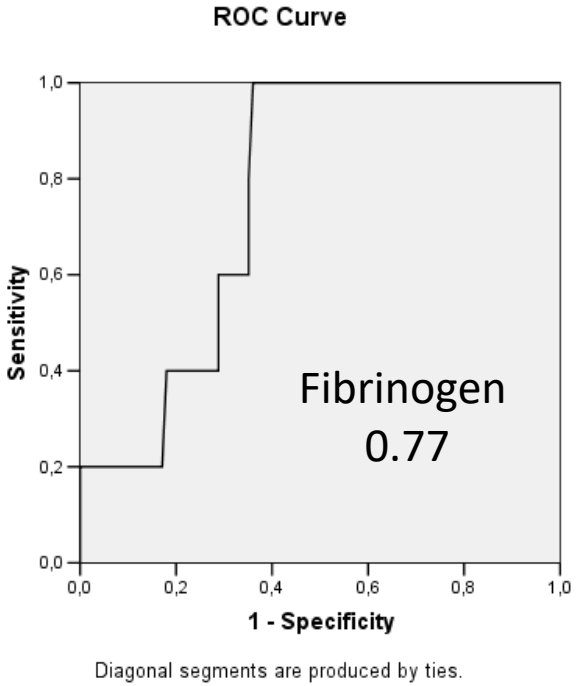
OXFORD UNIVERSITY PRESS | BJA British Journal of Anaesthesia

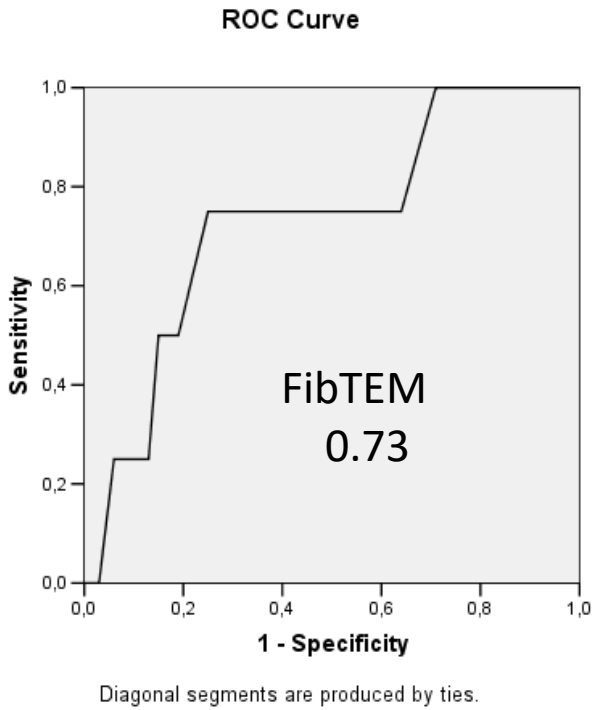
FIBRINOGEN SUPPLEMENTATION AFTER CARDIAC SURGERY: INSIGHTS FROM THE ZERO-PLASMA TRIAL (ZEPLAST)

Journal:	*British Journal of Anaesthesia*
Manuscript ID:	Draft
Manuscript Type:	Clinical Investigation
Date Submitted by the Author:	n/a
Complete List of Authors:	Ranucci, Marco; IRCCS Policlinico San Donato, Cardiothoracic Anesthesia and ICU Baryshnikova, Ekaterina; IRCCS Policlinico San Donato, Cardiothoracic Anesthesia
Key Words:	CARDIOVASCULAR ANAESTHESIA, Complications - haemorrhage, fibrinogen


Control
Treatment
280 mg/dL
NPV: 100%
Postoperative bleeding (mL/12h)
2500
2000
1500
1000
500
0
100
150
200
250
300
350
400
450
500
550
600
Fibrinogen ICU (mg/100 mL)


Postoperative bleeding (mL/12h)
2500
2000
1500
1000
500
0
0
5
10
15
20
25
30
FIBTEM post-dosing (mm)
17 mm (not 22 mm!!!) NPV: 100%





PREDICTION FOR SEVERE BLEEDING (> 1,000 mL)

CUT-OFF VALUES:	Fibrinogen 285 mg/100 mL	Sensitivity 80%, Specificity 65%
	FIBTEM 13.5 mm	Sensitivity 80%, Specificity 72%

FIBRINOGEN LEVELS AFTER CARDIAC SURGERY: ASSOCIATION WITH POSTOPERATIVE BLEEDING, TRIGGER VALUES, AND TARGET VALUES

Marco Ranucci, MD, FESC, Valeria Pistuddi, Ekaterina Baryshnikova, PhD (Biol),

Paolo Bianchi (MD)

Department of Cardiothoracic and Vascular Anesthesia and ICU

IRCCS Policlinico San Donato, San Donato Milanese (Milan) ITALY

Text word count: 4,724

Abstract word count: 242

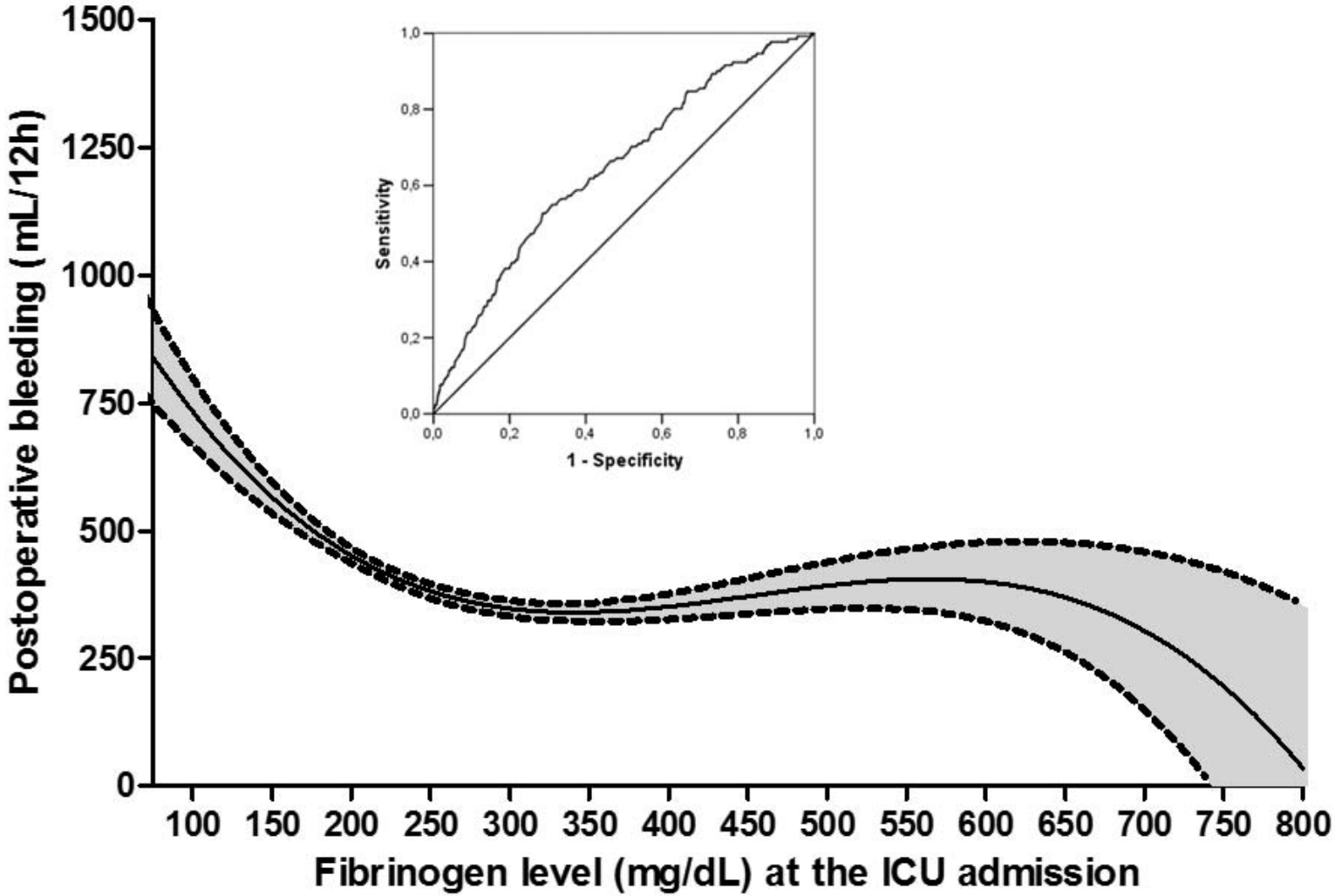

Postoperative bleeding (mL/12h)
1500
1250
1000
750
500
250
0
100 150 200 250 300 350 400 450 500 550 600 650 700 750 800
Fibrinogen level (mg/dL) at the ICU admission
Sensitivity
1,0
0,8
0,6
0,4
0,2
0,0
0,0 0,2 0,4 0,6 0,8 1,0
1 - Specificity

Figure 1

Table 4. Levels of negative and positive predictive values at different cut-off values of postoperative fibrinogen

Fibrinogen level	All cases (N=2,800)			Excluding patients with other isolated factors (N=2,051)		
	PPV	NPV	P	PPV	NPV	P
75 mg/dL	100%	95.4%	0.002	100%	95.0%	0.003
100 mg/dL	67%	95.4%	0.006	67%	95.0%	0.007
115 mg/dL	50%	95.4%	0.012	50%	95.0%	0.014
125 mg/dL	20%	95.4%	0.076	20%	95.0%	0.088
150 mg/dL	15%	95.6%	0.002	15%	95.2%	0.004
175 mg/dL	10%	95.9%	0.001	10%	95.9%	0.001
200 mg/dL	9.1%	96.4%	0.001	9.1%	96.4%	0.001
225 mg/dL	7.7%	96.9%	0.001	7.7%	97.0%	0.001
250 mg/dL	6.4%	97.0%	0.001	6.9%	97.3%	0.001
275 mg/dL	5.8%	97.2%	0.001	6.4%	97.5%	0.001
300 mg/dL	5.6%	98.0%	0.001	6.2%	98.5%	0.001

Trigger

Target

NPV: negative predictive value; PPV: positive predictive value.

FIBTEM INCREASE: 10 mm

Table 4. Levels of negative and positive predictive values at different cut-off values of postoperative fibrinogen

Fibrinogen level	All cases (N=2,800)			Excluding patients with other isolated factors (N=2,051)		
	PPV	NPV	P	PPV	NPV	P
75 mg/dL	100%	95.4%	0.002	100%	95.0%	0.003
100 mg/dL	67%	95.4%	0.006	67%	95.0%	0.007
115 mg/dL	50%	95.4%	0.012	50%	95.0%	0.014
125 mg/dL	20%	95.4%	0.076	20%	95.0%	0.088
150 mg/dL	15%	95.6%	0.002	15%	95.2%	0.004
175 mg/dL	10%	95.9%	0.001	10%	95.9%	0.001
200 mg/dL	9.1%	96.4%	0.001	9.1%	96.4%	0.001
225 mg/dL	7.7%	96.9%	0.001	7.7%	97.0%	0.001
250 mg/dL	6.4%	97.0%	0.001	6.9%	97.3%	0.001
275 mg/dL	5.8%	97.2%	0.001	6.4%	97.5%	0.001
300 mg/dL	5.6%	98.0%	0.001	6.2%	98.5%	0.001

NPV: negative predictive value; PPV: positive predictive value.

Fibtem 4

Fibtem 14

IN THE BLEEDING PATIENT……

Table 4. Levels of negative and positive predictive values at different cut-off values of postoperative fibrinogen

Fibrinogen level	All cases (N=2,800)			Excluding patients with other isolated factors (N=2,051)		
	PPV	NPV	P	PPV	NPV	P
75 mg/dL	100%	95.4%	0.002	100%	95.0%	0.003
100 mg/dL	67%	95.4%	0.006	67%	95.0%	0.007
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175 mg/dL	10%	95.9%	0.001	10%	95.9%	0.001
200 mg/dL	9.1%	96.4%	0.001	9.1%	96.4%	0.001
225 mg/dL	7.7%	96.9%	0.001	7.7%	97.0%	0.001
250 mg/dL	6.4%	97.0%	0.001	6.9%	97.3%	0.001
275 mg/dL	5.8%	97.2%	0.001	6.4%	97.5%	0.001
300 mg/dL	5.6%	98.0%	0.001	6.2%	98.5%	0.001

NPV: negative predictive value; PPV: positive predictive value.

Fibtem 6-7

Fibtem 14

tration is not recommended.			
In the bleeding patient with a low-fibrinogen level (<1.5 g/l), fibrinogen substitution may be considered to reduce postoperative bleeding and transfusions.	IIb	B	[216–218]

A VISCOELASTIC TESTS-BASED ALGORITHM (TEG-ROTEM)

Rule-out low soluble coagulation factors levels

Yes

PCC supplementation (better 4-factors) rFVIIa (life-threatening bleeding)

No

Proceed to step 5

Factors deficiency

- Due to dilution and consumption
- Rare in routine cardiac surgery
- Factor activity becomes critical below 30%
- More common in long (> 2 hours) pump run
- Associated to extensive use of cell-saver
- Common in aortic surgery
- Common in aortic dissection

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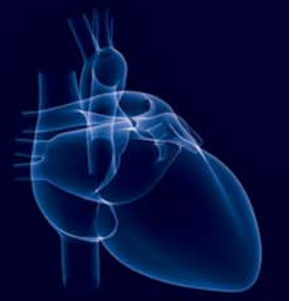
journal homepage: www.elsevier.com/locate/thromres

Regular Article

Plasma activity of individual coagulation factors, hemodilution and blood loss after cardiac surgery: A prospective observational study

Lisa Ternström [a,d], Vladimir Radulovic [b], Martin Karlsson [a,d], Fariba Baghaei [b], Monica Hyllner [a], Anders Bylock [c], Kenny M. Hansson [c], Anders Jeppsson [a,d,*]

[a] Department of Cardiovascular Surgery and Anesthesia, Sahlgrenska University Hospital, Gothenburg, Sweden
[b] Department of Medicine/Hematology and Coagulation Disorders, Sahlgrenska University Hospital, Gothenburg, Sweden
[c] AstraZeneca AB, Mölndal, Sweden
[d] Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden



		r	p
Fibrinogen	Preop	-0.19	0.15
	2 h Postop	-0.33	0.019
FII	Preop	-0.11	0.42
	2 h Postop	-0.22	0.12
FV	Preop	0.04	0.79
	2 h Postop	-0.14	0.34
FVII	Preop	0.04	0.76
	2 h Postop	-0.06	0.66
FVIII	Preop	-0.06	0.65
	2 h Postop	-0.07	0.61
FIX	Preop	-0.09	0.52
	2 h Postop	-0.15	0.29
FX	Preop	0.04	0.78
	2 h Postop	-0.17	0.24
FXI	Preop	-0.12	0.39
	2 h Postop	-0.22	0.12
FXIII	Preop	-0.34	0.009
	2 h Postop	-0.41	0.003

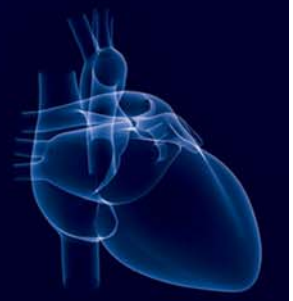
Factors deficiency

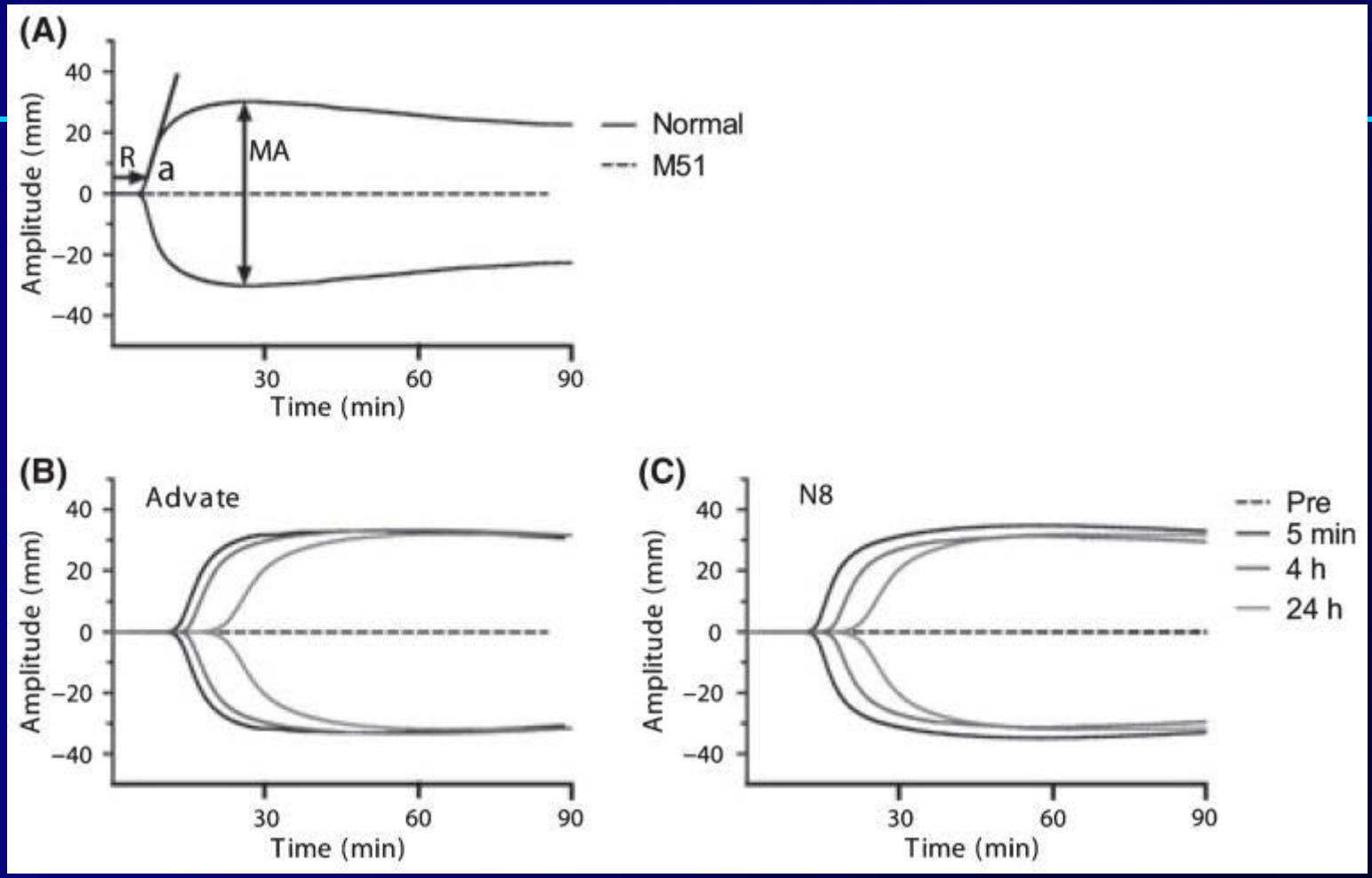
- LEADS TO DECREASED THROMBIN GENERATION

FACTORS ACTING BEFORE THE GEL POINT

Everything acting before the GEL POINT is directly or indirectly related to a poor thrombin generation or direct thrombin inhibition

- Congenital coagulation disorders
- Poor liver synthesis/consumption
- Heparin
- Warfarin
- Direct thrombin inhibitors

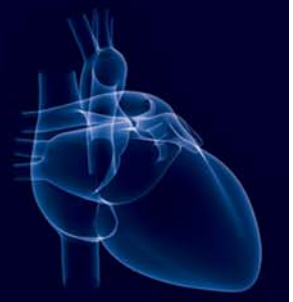


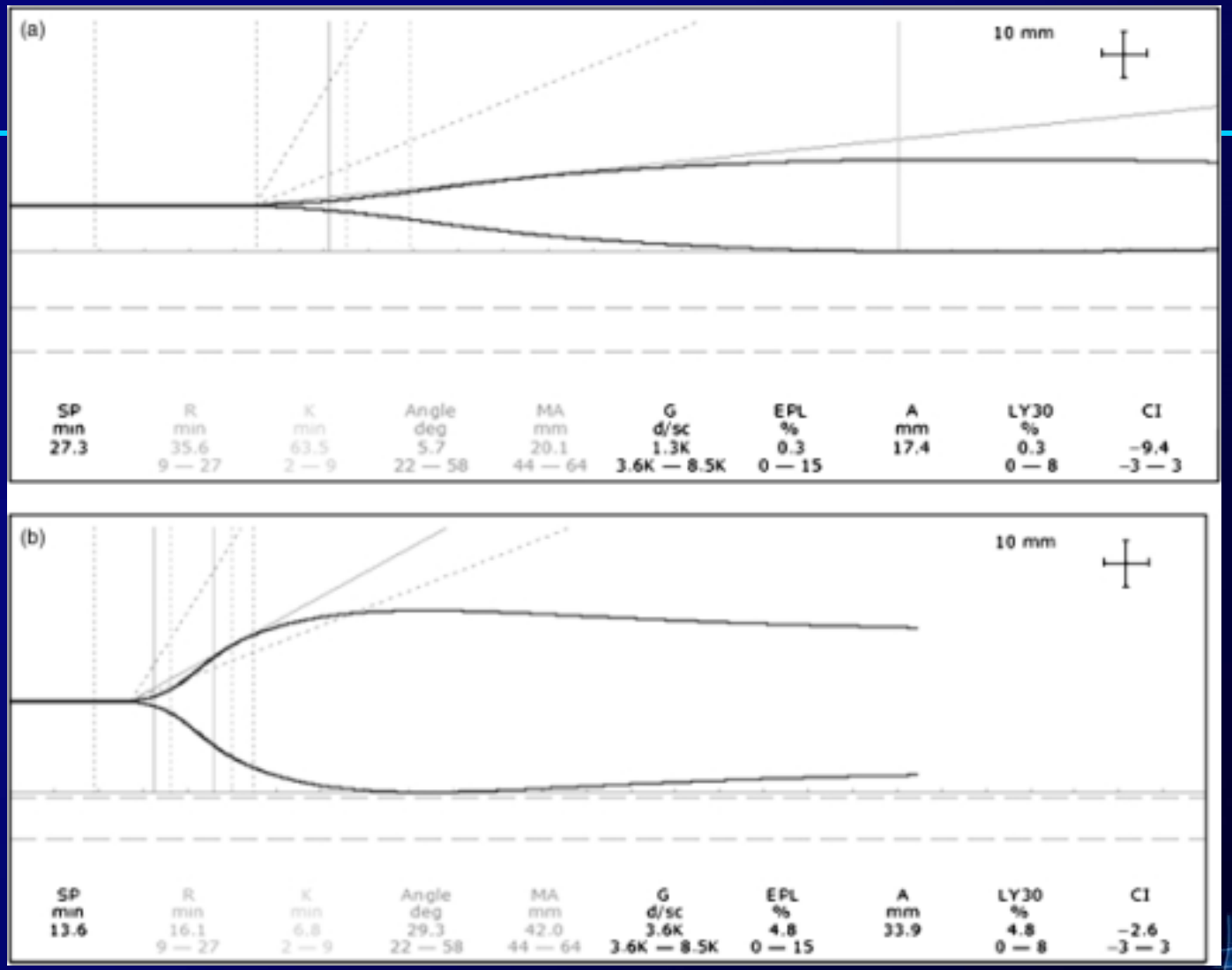

(A)
40
20
0
−20
−40
Amplitude (mm)
R
a
MA
30
60
90
Time (min)
Normal
M51
(B)
Advate
40
20
0
−20
−40
Amplitude (mm)
30
60
90
Time (min)
(C)
N8
40
20
0
−20
−40
Amplitude (mm)
30
60
90
Time (min)
Pre
5 min
4 h
24 h

FACTORS ACTING BEFORE THE GEL POINT

Everything acting before the GEL POINT is directly or indirectly related to a poor thrombin generation or direct thrombin inhibition

- Congenital coagulation disorders
- Poor liver synthesis/consumption
- Heparin
- Warfarin
- Direct thrombin inhibitors

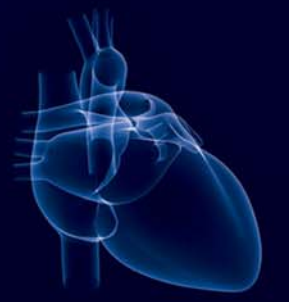



(a)
10 mm
SP
min
27.3
R
min
35.6
9 — 27
K
min
63.5
2 — 9
Angle
deg
5.7
22 — 58
MA
mm
20.1
44 — 64
G
d/sc
1.3K
3.6K — 8.5K
EPL
%
0.3
0 — 15
A
mm
17.4
LY30
%
0.3
0 — 8
CI
−9.4
−3 — 3
(b)
10 mm
SP
min
13.6
R
min
16.1
9 — 27
K
min
6.8
2 — 9
Angle
deg
29.3
22 — 58
MA
mm
42.0
44 — 64
G
d/sc
3.6K
3.6K — 8.5K
EPL
%
4.8
0 — 15
A
mm
33.9
LY30
%
4.8
0 — 8
CI
−2.6
−3 — 3

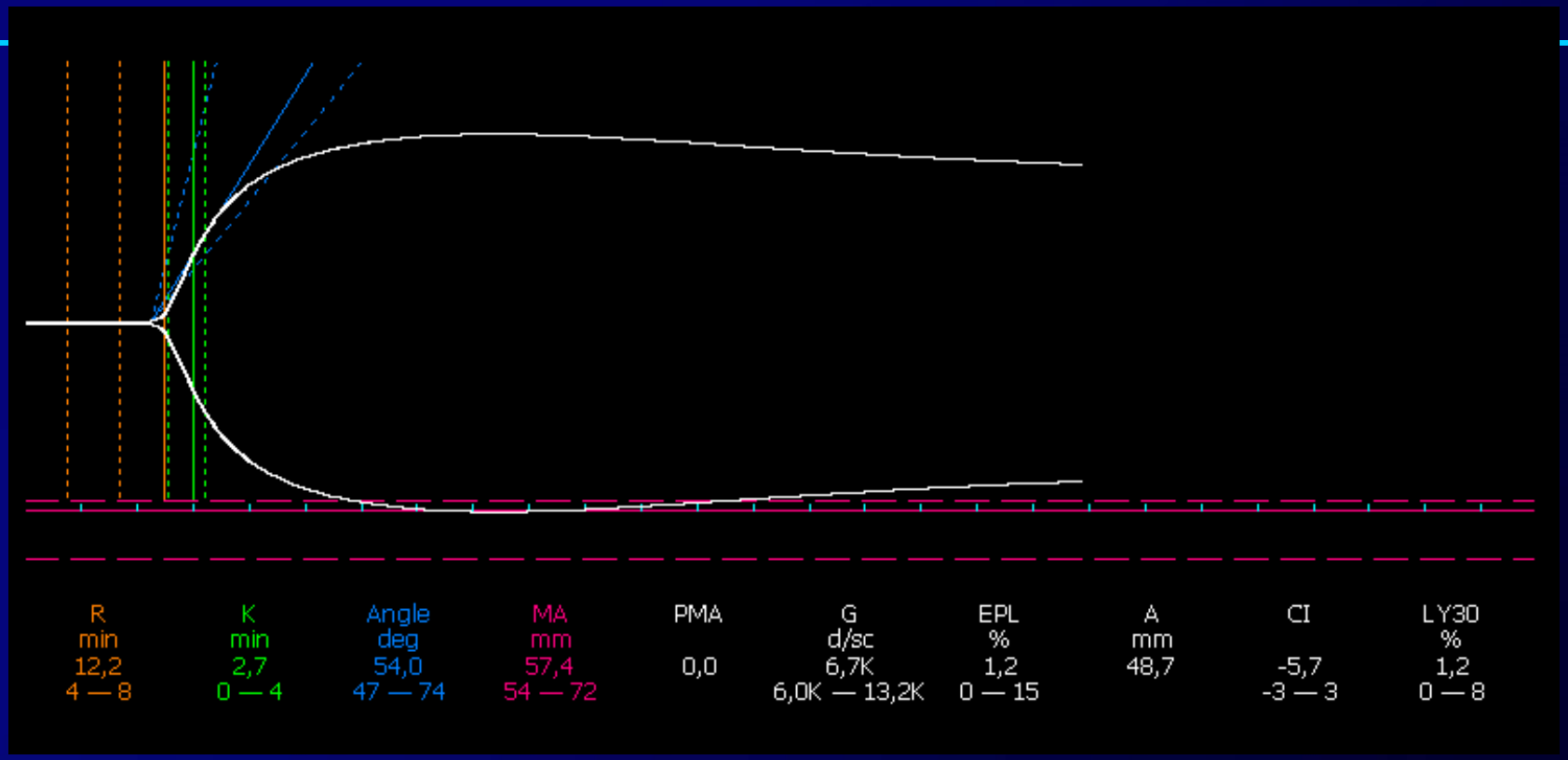
FACTORS ACTING BEFORE THE GEL POINT

Everything acting before the GEL POINT is directly or indirectly related to a poor thrombin generation or direct thrombin inhibition

- Congenital coagulation disorders
- Poor liver synthesis/consumption
- Heparin
- Warfarin
- Direct thrombin inhibitors

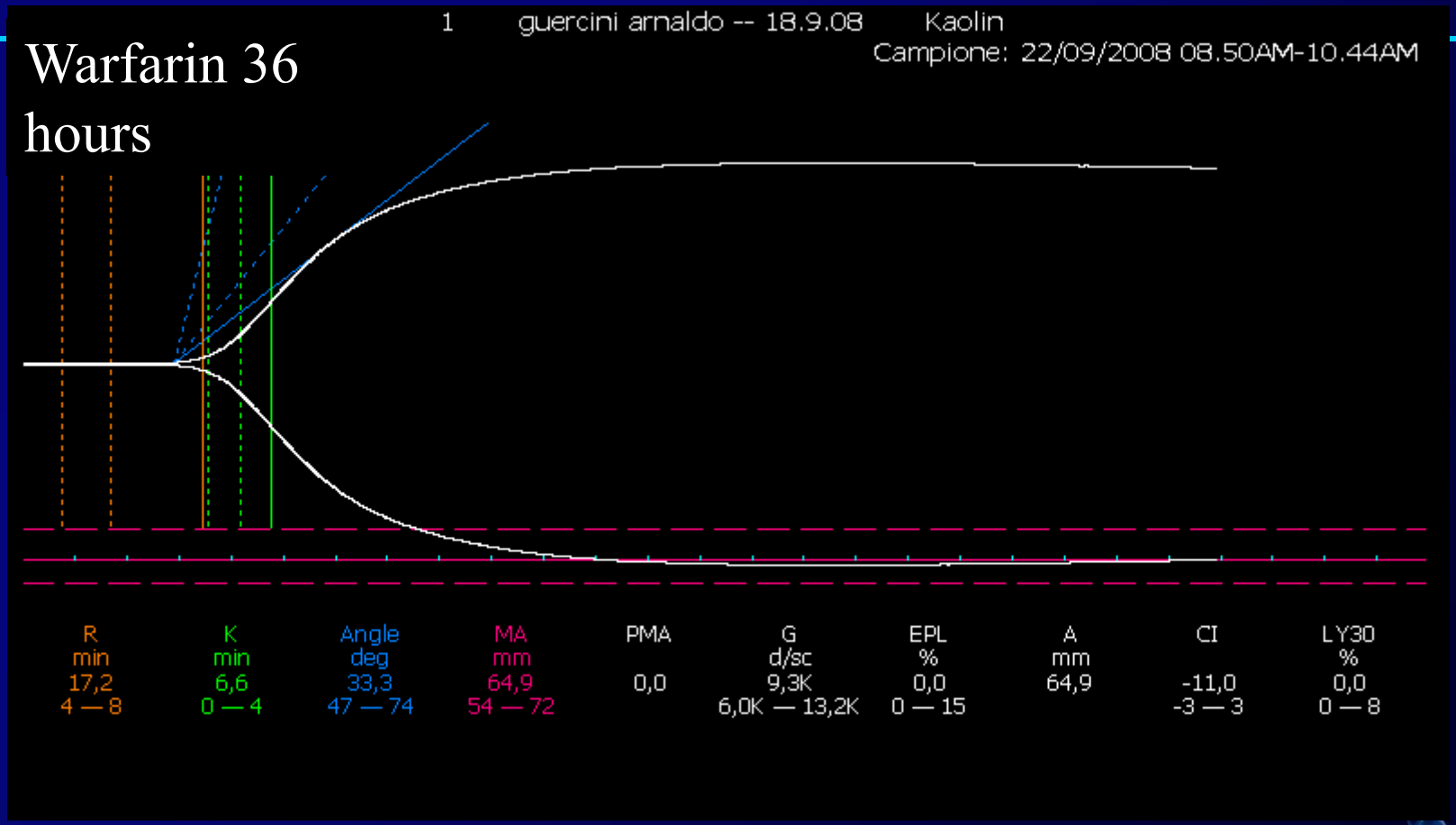


WARFARIN

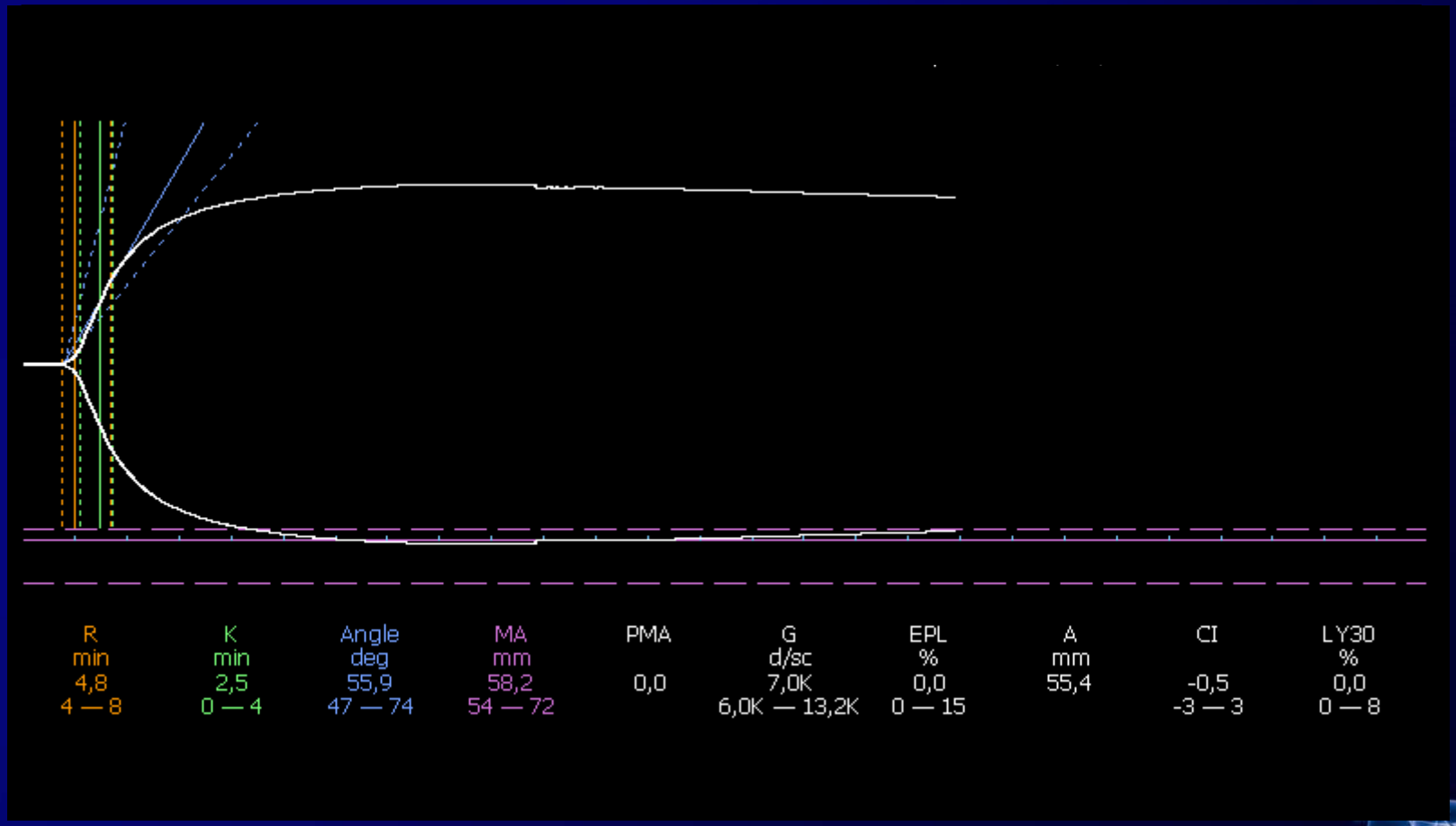


R	K	Angle	MA	PMA	G	EPL	A	CI	LY30
min	min	deg	mm		d/sc	%	mm		%
12,2	2,7	54,0	57,4	0,0	6,7K	1,2	48,7	-5,7	1,2
4 — 8	0 — 4	47 — 74	54 — 72		6,0K — 13,2K	0 — 15		-3 — 3	0 — 8

Warfarin 36 hours



PCCs 25IU/Kg

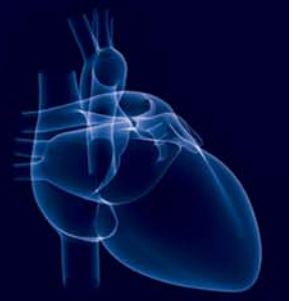


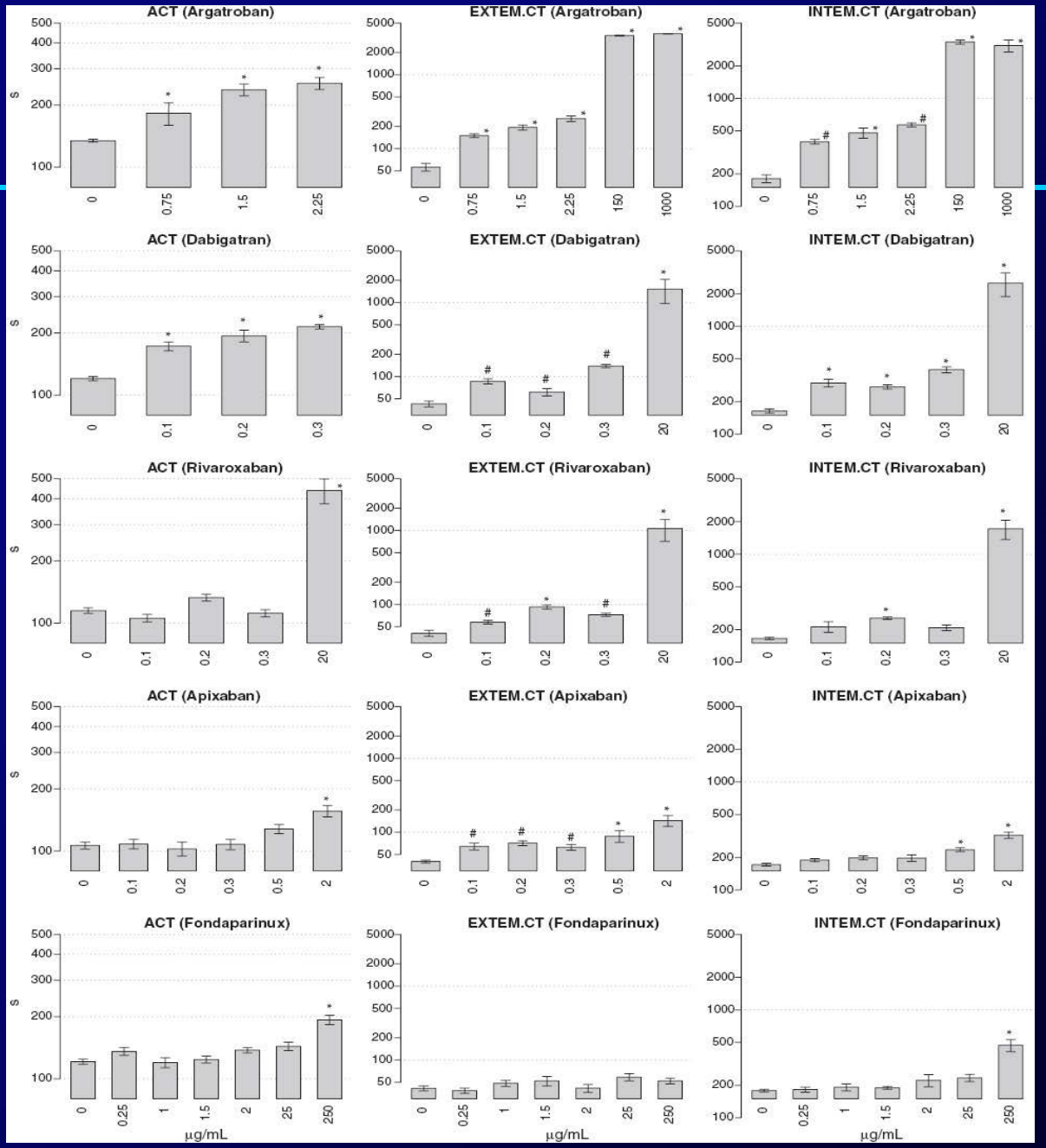
R	K	Angle	MA	PMA	G	EPL	A	CI	LY30
min	min	deg	mm		d/sc	%	mm		%
4,8	2,5	55,9	58,2	0,0	7,0K	0,0	55,4	-0,5	0,0
4 — 8	0 — 4	47 — 74	54 — 72		6,0K — 13,2K	0 — 15		-3 — 3	0 — 8

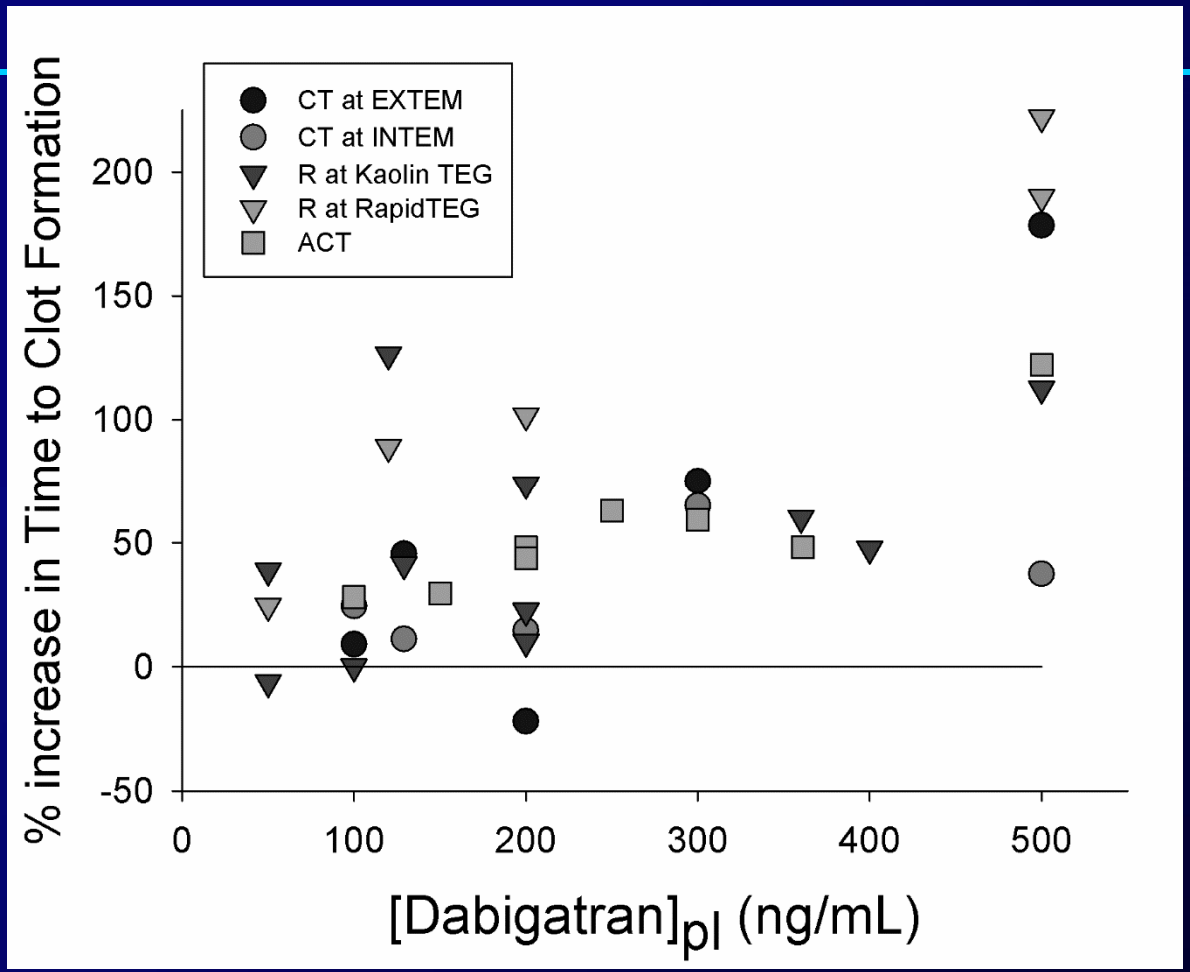
FACTORS ACTING BEFORE THE GEL POINT

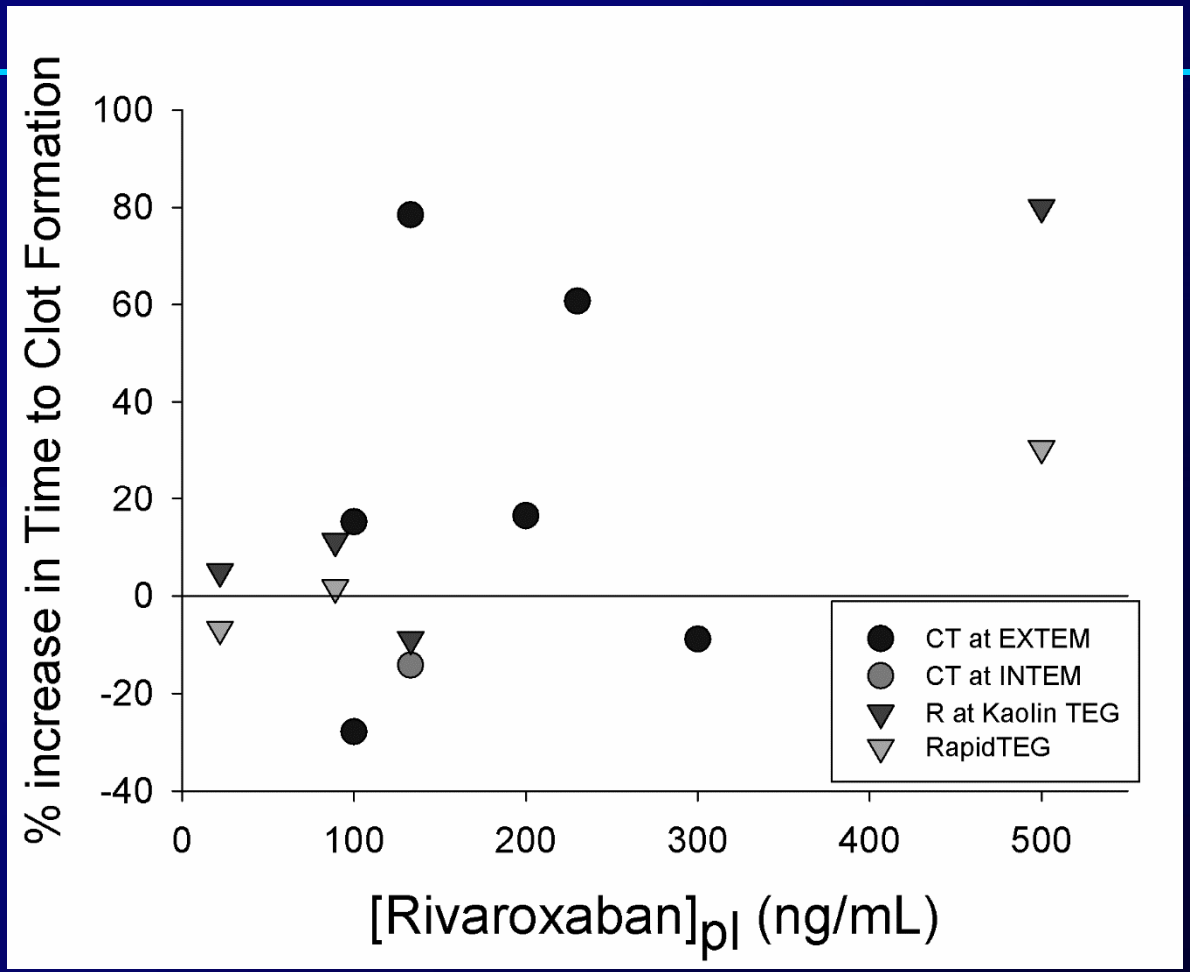
Everything acting before the GEL POINT is directly or indirectly related to a poor thrombin generation or direct thrombin inhibition

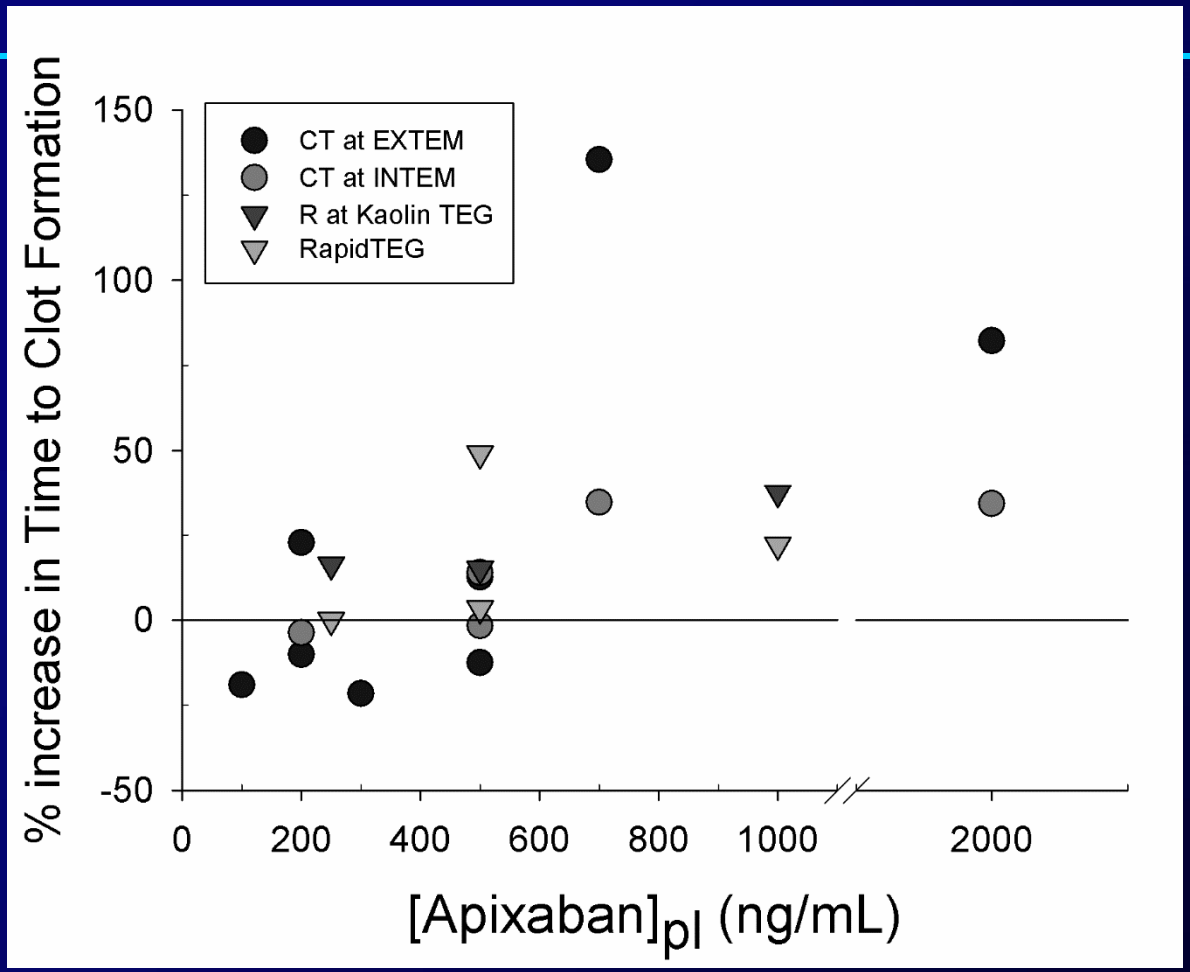
- Congenital coagulation disorders
- Poor liver synthesis/consumption
- Heparin
- Warfarin
- Direct thrombin inhibitors




ACT (Argatroban)
EXTEM.CT (Argatroban)
INTEM.CT (Argatroban)
ACT (Dabigatran)
EXTEM.CT (Dabigatran)
INTEM.CT (Dabigatran)
ACT (Rivaroxaban)
EXTEM.CT (Rivaroxaban)
INTEM.CT (Rivaroxaban)
ACT (Apixaban)
EXTEM.CT (Apixaban)
INTEM.CT (Apixaban)
ACT (Fondaparinux)
EXTEM.CT (Fondaparinux)
INTEM.CT (Fondaparinux)
s
µg/mL


CT at EXTEM
CT at INTEM
R at Kaolin TEG
R at RapidTEG
ACT
% increase in Time to Clot Formation
200
150
100
50
0
-50
0
100
200
300
400
500
[Dabigatran]pl (ng/mL)


% increase in Time to Clot Formation
100
80
60
40
20
0
-20
-40
0
100
200
300
400
500
[Rivaroxaban]pl (ng/mL)
CT at EXTEM
CT at INTEM
R at Kaolin TEG
RapidTEG


% increase in Time to Clot Formation
150
100
50
0
-50
0
200
400
600
800
1000
2000
CT at EXTEM
CT at INTEM
R at Kaolin TEG
RapidTEG
[Apixaban]pl (ng/mL)

A VISCOELASTIC TESTS-BASED ALGORITHM (TEG-ROTEM)

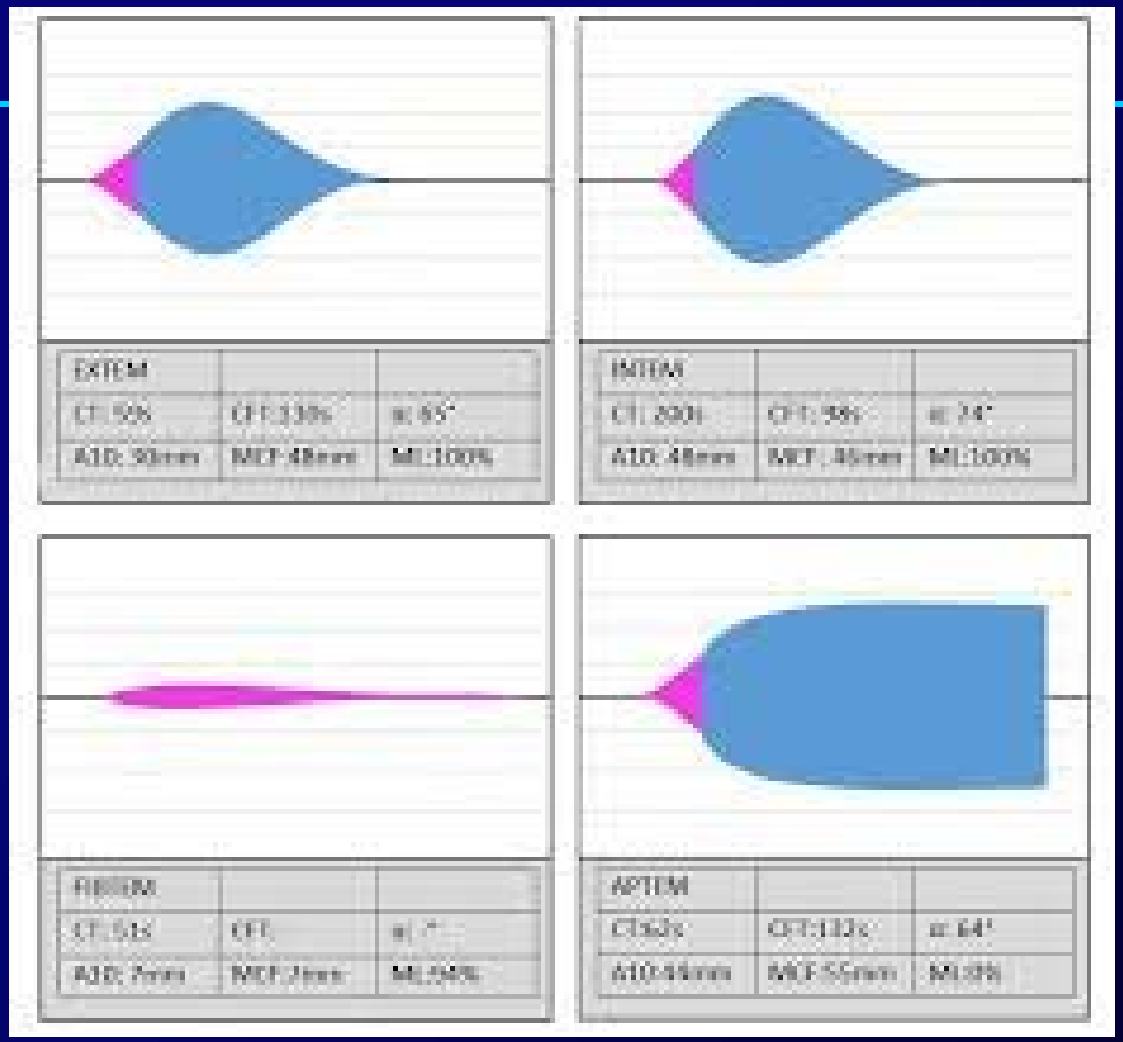
Rule-out hyperfibrinolysis

Yes

TRANEXAMIC ACID
FIBRINOGEN CONCENTRATE

No

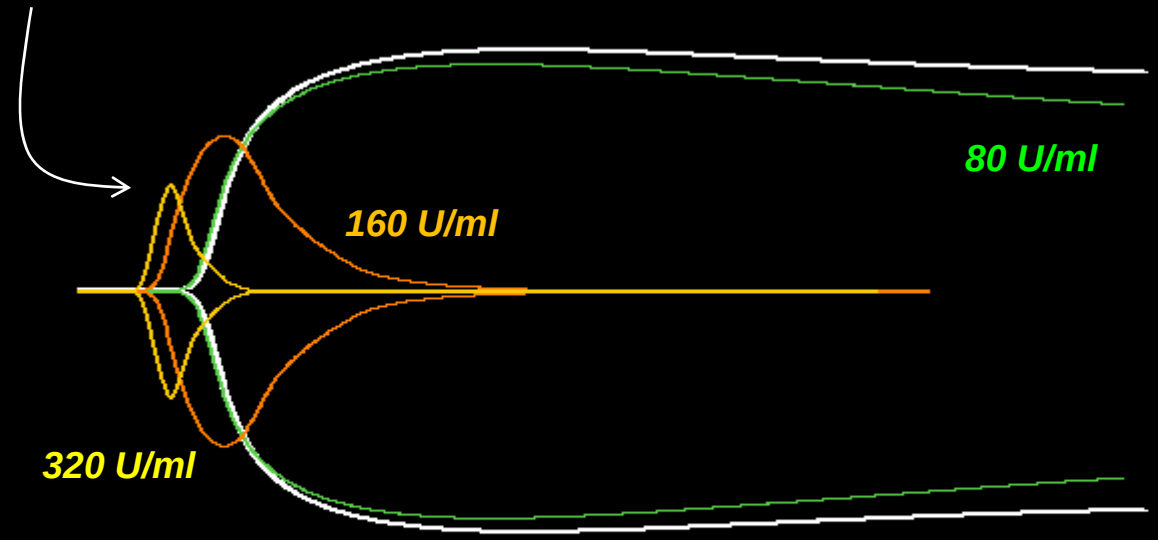
Proceed to step 6


EXTEM
CT: 50s
CFT:330s
α: 65°
A10: 50mm
MCF:48mm
ML:100%
INTEM
CT: 200s
CFT: 90s
α: 74°
A10: 48mm
MCF: 46mm
ML:100%
FIBTEM
CT: 51s
CFT:
α: °
A10: 7mm
MCF:7mm
ML:98%
APTEM
CT:62s
CFT:132s
α: 64°
A10:44mm
MCF:55mm
ML:0%

UKIF-TEG

our experience

UKIF-TEG MA* not comparable to *C - MA



***low* susceptibility**

R	K	Angle	MA	G	EPL	A	CI	TEG ACT	LY30
min	min	deg	mm	d/sc	%	mm			%
10,1	2,0	63,3	71,5	12,5K	1,0	65,2	-1,6		1,0
4 — 8	0 — 4	47 — 74	54 — 72	6,0K — 13,2K	0 — 15		-3 — 3		0 — 8

Application to clinical setting is ***to be determined***

A VISCOELASTIC TESTS-BASED ALGORITHM (TEG-ROTEM)

Rule-out surgical sources

Yes

GO-ON WITH HEMOSTASIS RE-EXPLORATION

No

Other causes