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Goal Directed Transfusion

Transfusion in trauma

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Annual meeting of KTAS, 2021 10 02


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Conflict of interest
NO COI to declare

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Contents


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01
Benefits of GDT

- n = 839
- Trauma pt

- INR > 1.4
- PTT > 35 s

- ACT > 128 s
- MA < 55

Contents lists available at ScienceDirect

The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com

Discrepancies between conventional and viscoelastic assays in identifying trauma-induced coagulopathy

Joshua J. Sumislawski [a, *], S. Ariane Christie [b], Lucy Z. Kornblith [b], Gregory R. Stettler [a], Geoffrey R. Nunns [a], Hunter B. Moore [a], Ernest E. Moore [a], Christopher C. Silliman [c], Angela Sauaia [a], Rachael A. Callcut [b], Mitchell Jay Cohen [a]

	Conventional	TEG	P
Abnormality	20%	**49%**	
Transfusion	high	**low**	< 0.017
Mortality	40%	**6%**	< 0.017

Sumislawski et al, Am J Surg, 2019

Mortality of MTP guided by Conventional vs Viscoelastic

		n	Conventional	Viscoelastic
Baksaas et al	ICM, 2021	396	17%	14%
Sumislawski et al	AJS, 2019	839	40%	**6%**
Gonzalez et al	Ann Sur, 2016	117	36.4%	**19.6%**

Rotational thromboelastometry

- 목적
  1. 응고 인자 수혈 가이드
  2. 어떤 종류의 응고인자를 줘야 하나 판단
  3. 수혈을 안해도 될 상황 구분
     - Medical vs Surgical
  4. 예측 인자로써는 아직 부족

Gorlinger et al, KJA, 2019

PT, INR, aPTT, fibrinogen	Viscoelastic
Can not Dx coagulopathy	Fibrino**Lysis**, **Hyper**coagulability
	Whole clot cascade Initial thrombin – maximum clot – lysis
Slow (> 30 min) Prolonged turn around	**Fast** (5 – 10 min) Short turn around

Napolitano et al, Expert Rev Hematol, 2021

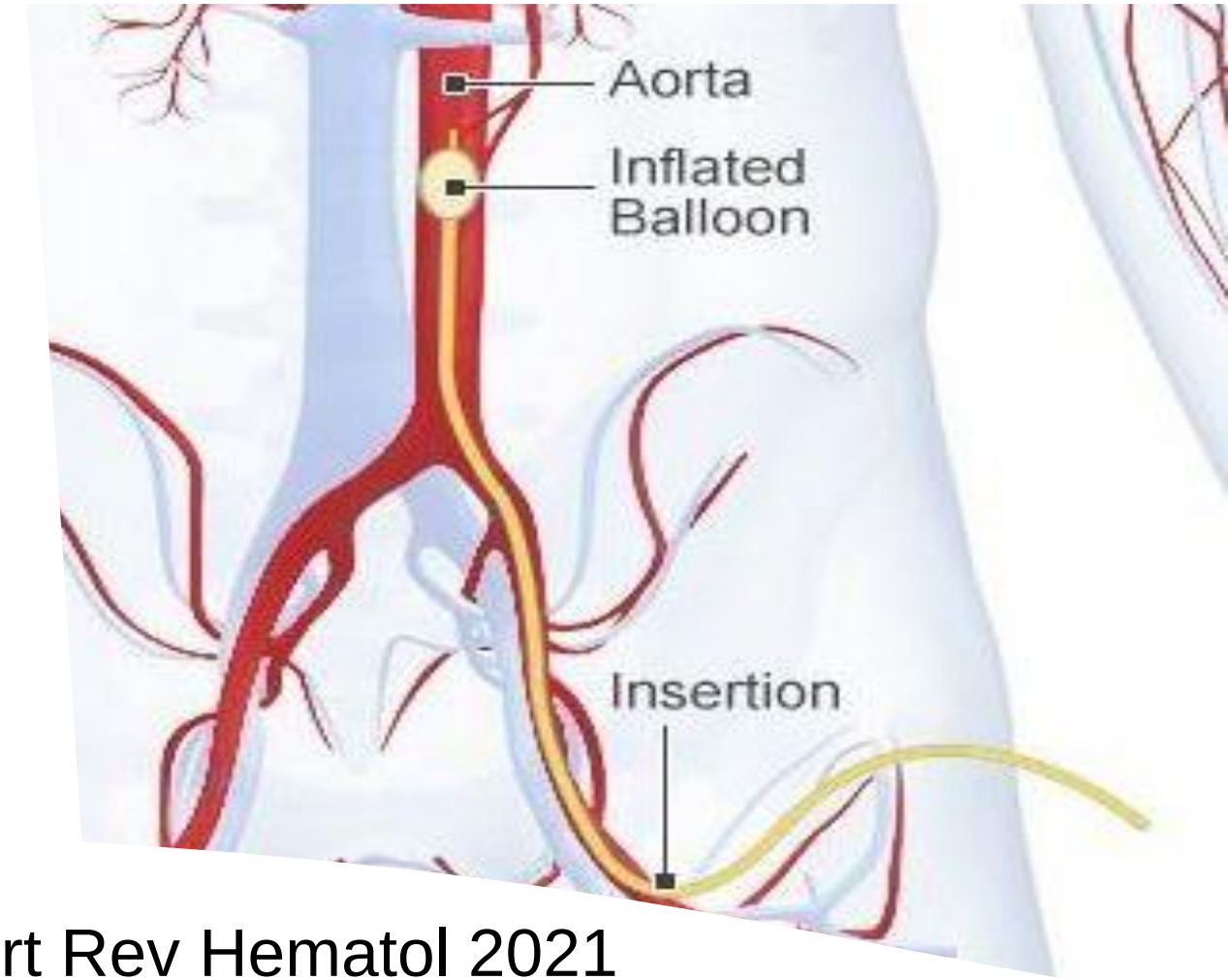
More Rapid, Simple pipette, Cartridge based

ROTEM sigma

TEG 6S

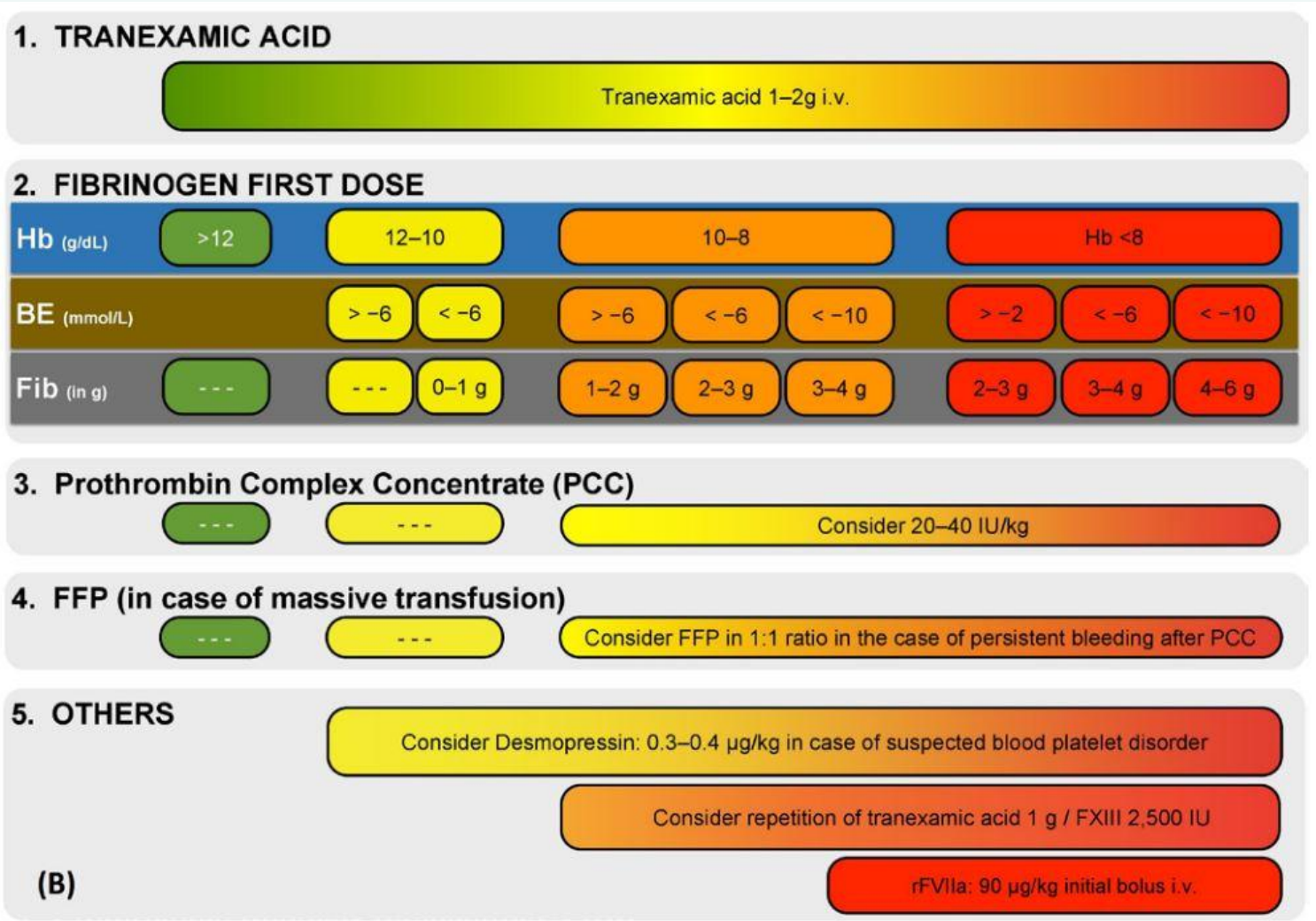
Early hemorrhage control

- **Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA)**

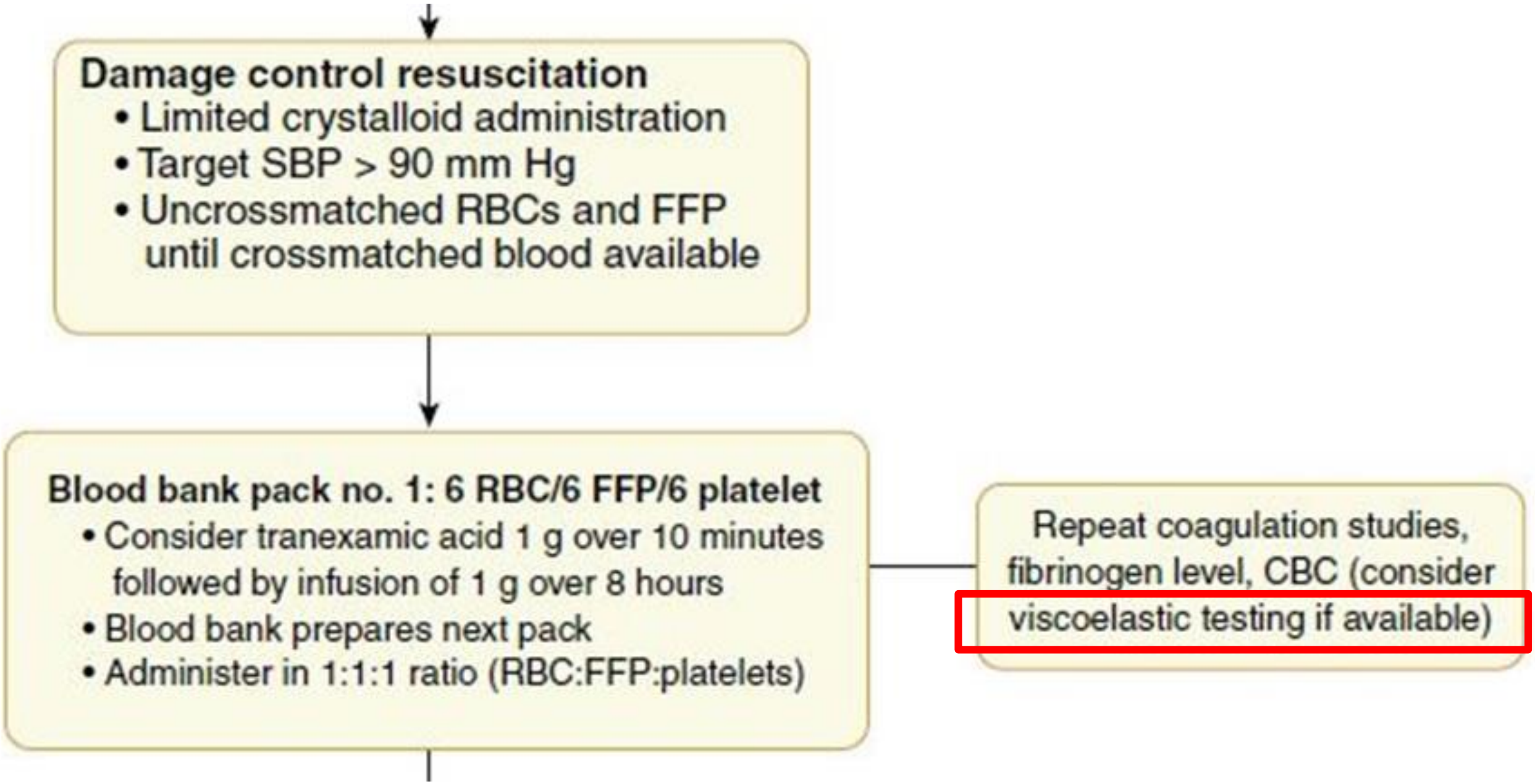


Napolitano et al, Expert Rev Hematol 2021

Algorithm without viscoelastic test in trauma



Casu, Trauma Surg ACO, 2021

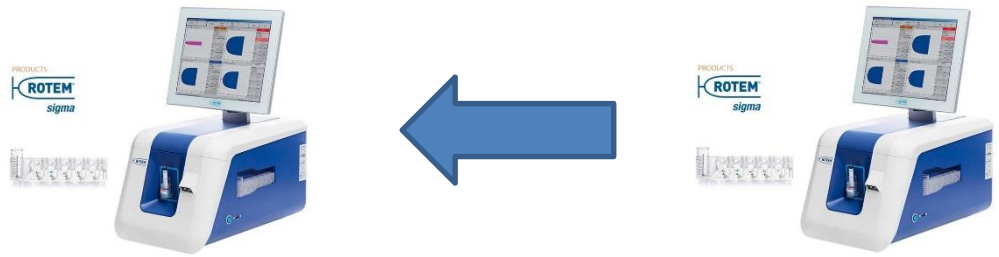


Miller's Anesthesia 9ed, pp 2133

	Phase 1	Phase 2	Phase 3
Clinical status	■ Life-threatening uncontrolled hemorrhage	■ Ongoing hemorrhage—not immediately life-threatening—partial surgical control	■ Hemorrhage controlled

Clinical priorities	■ STOP THE BLEEDING
	■ Call for HELP
	■ Control airway, FiO2 1.0
	■ Damage control resuscitation
	  ■ SBP <100 mm Hg
	  ■ MAP 50-60 mm Hg
	  ■ Consider modifications if TBI, carotid stenosis, CAD
		■ TAILORED RESUSCITATION
		■ Place supportive lines (arterial/CVC)
		■ Prevent hypothermia
		  ■ Esophageal temperature probe
		  ■ Warmed fluids
		  ■ Warming blankets (upper/lower)
		  ■ Increase room temperature
			■ RESTORE PHYSIOLOGY
			■ Rapid intravascular filling
			■ Stepwise deepening of anesthesia
			  ■ Fentanyl boluses
			  ■ Increased volatile anesthetics
			■ Additional lines (urinary catheter, nasogastric tube)
			■ Communicate with all team members and ICU

Blood products	■ Activate MTP ■ Consider emergency (uncrossmatched blood products ■ Early use ■ Empiric 1:1:1 ratio (PRBC:FFP:platelets)	■ Viscoelastic monitoring to guide coagulation products ■ Hb to guide red blood cell transfusion	■ Only as required on testing ■ Deactivate MTP when appropriate



Miller's Anesthesia, 9ed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02
Red blood cells

Meta analysis

	Setting	RR (95% CI) 30d mortality	Restrictive (7 – 8 g/dL)	Liberal (10 g/dL)
Carson Cochrane, 2016	Trauma	0.97 [0.81, 1.16]		
Zhu Medicine, 2019	Hip Fx	1.11 [0.81, 1.52]	**high MI**	**high stroke**
Hirano Crit Care, 2019	Sepsis	0.99 [0.67, 1.46]		
Kheiri et al J T Throm, 2019	Cardiac Surgery	1.03 [0.74, 1.45]		

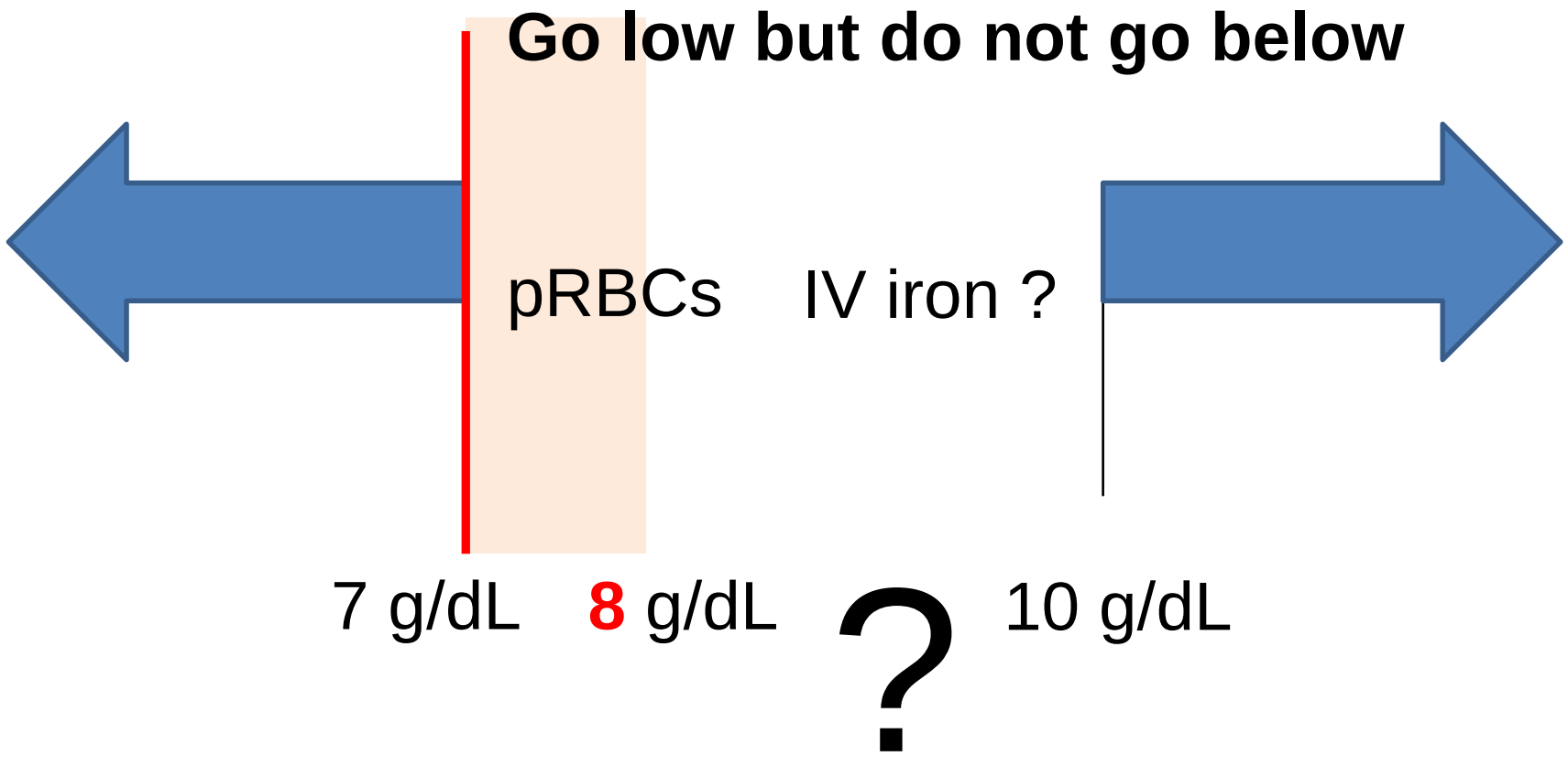
Shander et al, Curr Opin Anaes , 2020

RCTs showing various conditions

	Setting	Threshold	Benefits of restrictive
Palmieri Mil Med, 2019	**Burn**	7 vs 10	**Shorter ventilator day** Similar mortality
Voigt JTACS, 2018	**Burn** **Pediatric**	7 vs 10	**Lower mortality**
Zerah J Am Geri, 2018	**Elderly** **> 70 yrs**	**8** vs 10	**Lower coronary event** Similar mortality
Gobatto Crit Care, 2019	**TBI**	**7** vs 9	**Worse neurologic status** **High mortality**

Shander et al, Curr Opin Anaesh, 2020

Threshold of Hgb in trauma



Carson et al, Uptodate, 2018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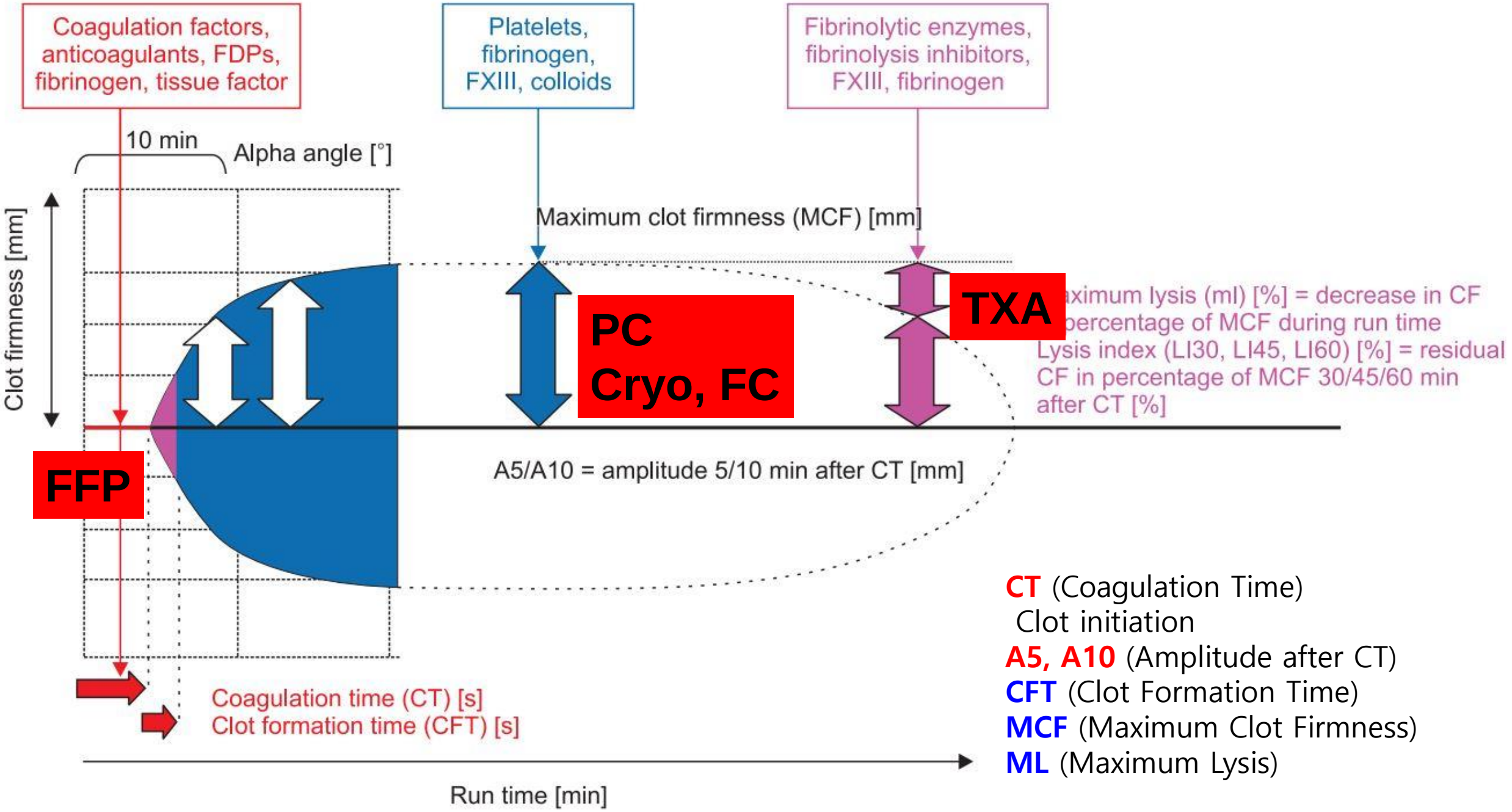
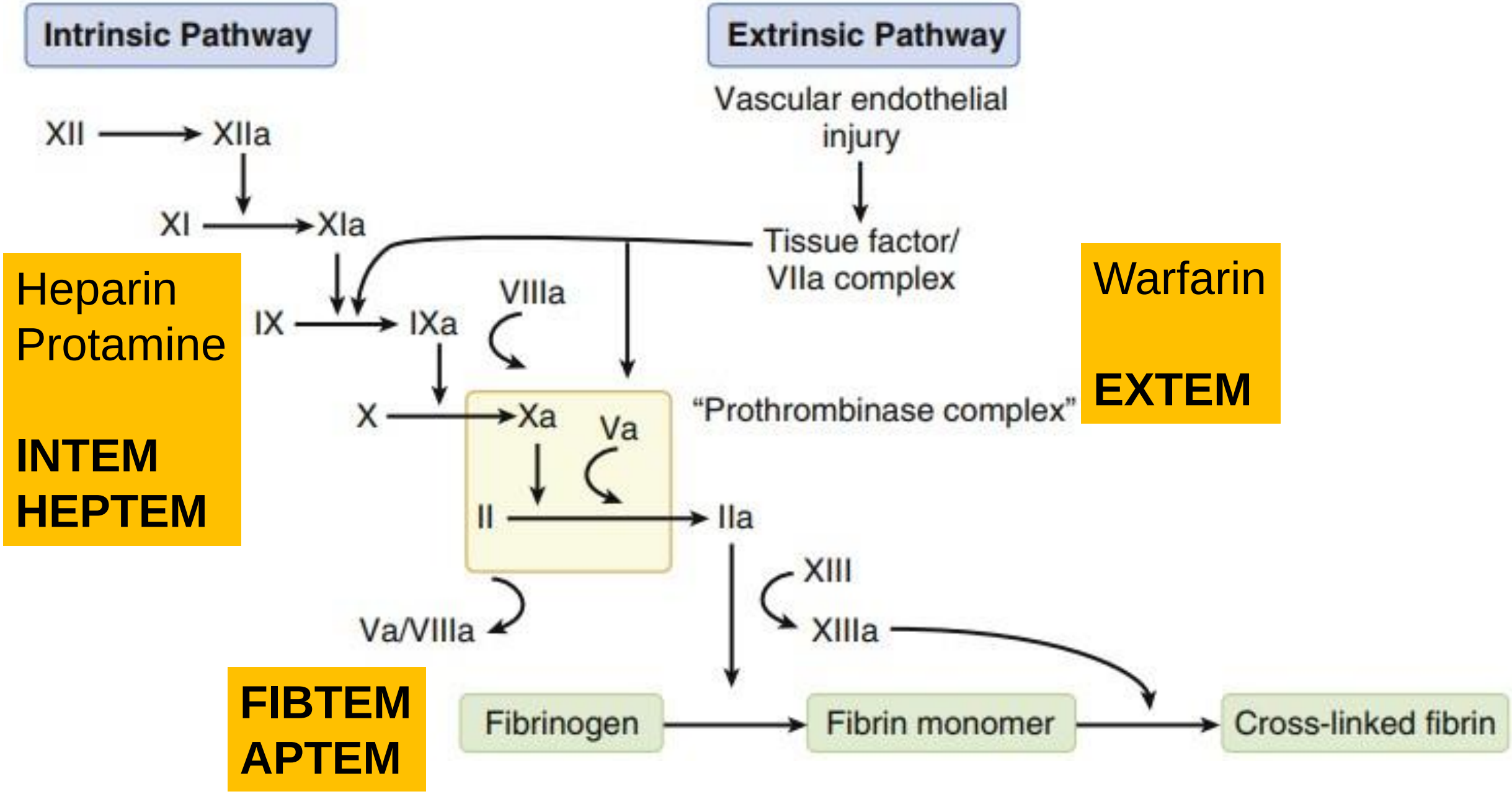
03
ROTEM



CT (Coagulation Time)
Clot initiation
A5, A10 (Amplitude after CT)
CFT (Clot Formation Time)
MCF (Maximum Clot Firmness)
ML (Maximum Lysis)

Gorlinger et al, KJA, 2019



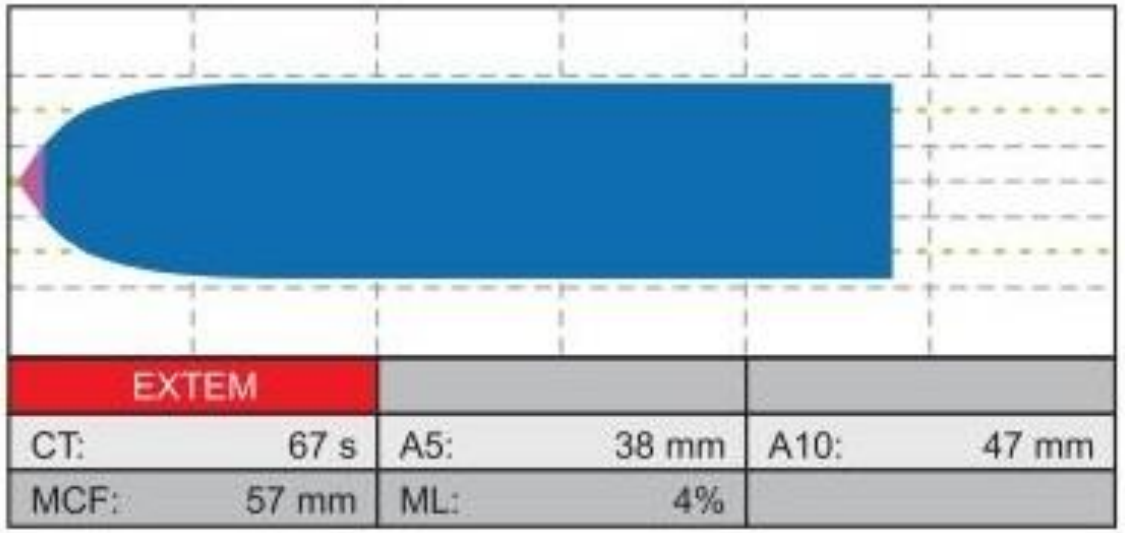
Miller's Anesthesia. 9ed. pp 1581.

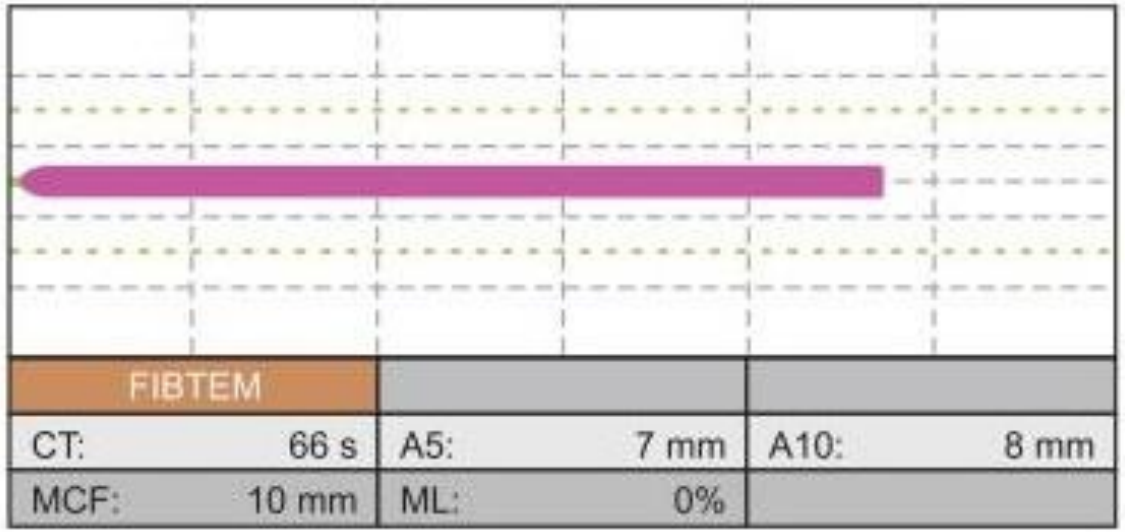
Assay	activator	
INTEM	CaCl2 + ellagic acid	**Intrinsic** **FFP, Plt**
HEPTEM	CaCl2 + ellagic acid + **Heparinase**	**Protamine**
EXTEM	CaCl2 + TF + polybrene	**Extrinsic** **FFP, Plt, Vit K**
FIBTEM	CaCl2 + TF + polybrene + cytochalasin D	**Fibrinogen** **Cryo, FC**
APTEM	CaCl2 + TF + polybrene + **Aprotinin** / TXA	fibrino**lysis** **TXA**

Gorlinger et al, KJA, 2019

Normal clot

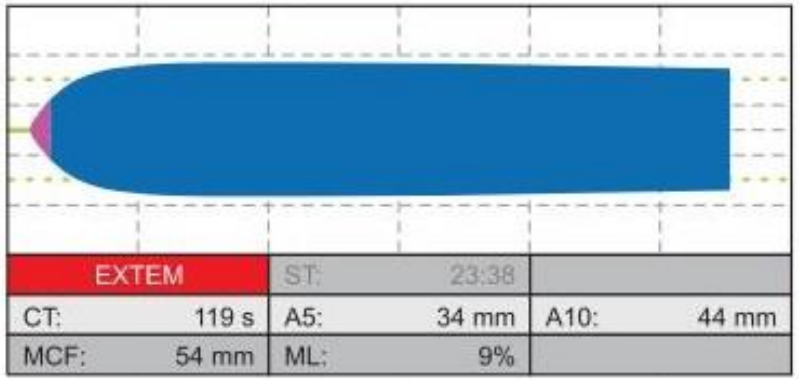
CT_{EX}	43 – 82 mm
$A5_{EX}$	33 – 52 mm
MCF_{EX}	52 – 70 mm
ML_{EX} or ML_{FIB}	< 15%
$LI60_{EX}$ or $LI60_{FIB}$	> 85%
$A5_{FIB}$	5 – 20 mm
MCF_{FIB}	7 – 24 m

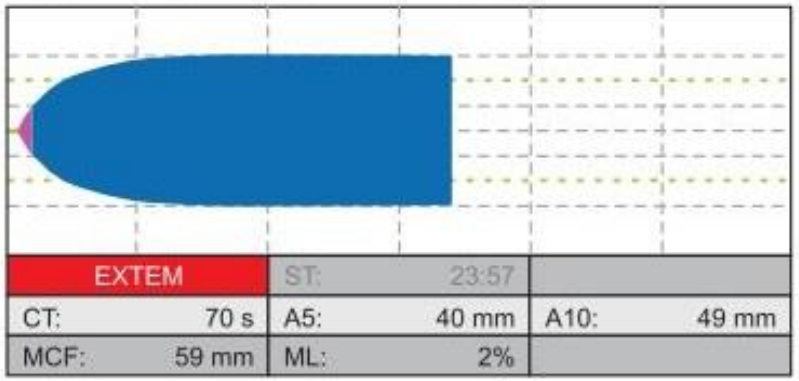




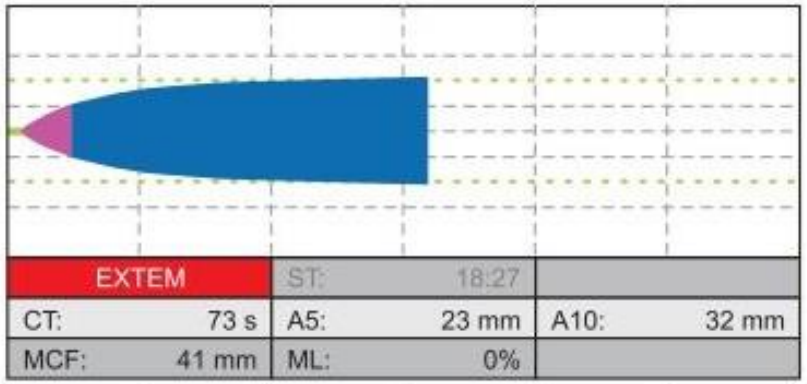
Gorlinger et al, KJA, 2019, A5 based

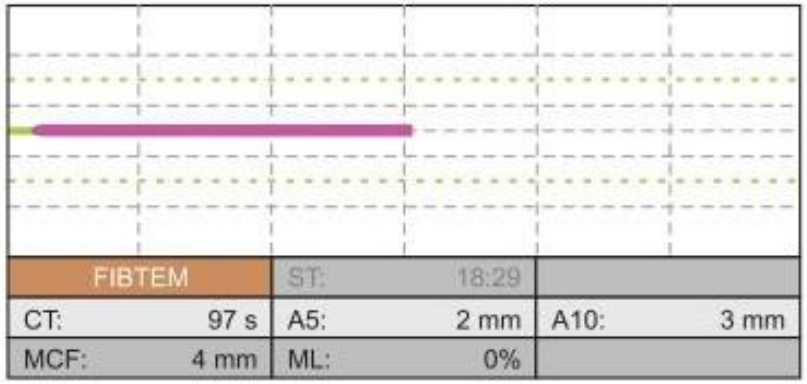
Deficiency of vitamin K-dependent factors (cirrhosis or warfarin):
CT_{EX} > 80 s (in this case, CT_{EX} decreased to 70 s after 4F-PCC administration; right graph)



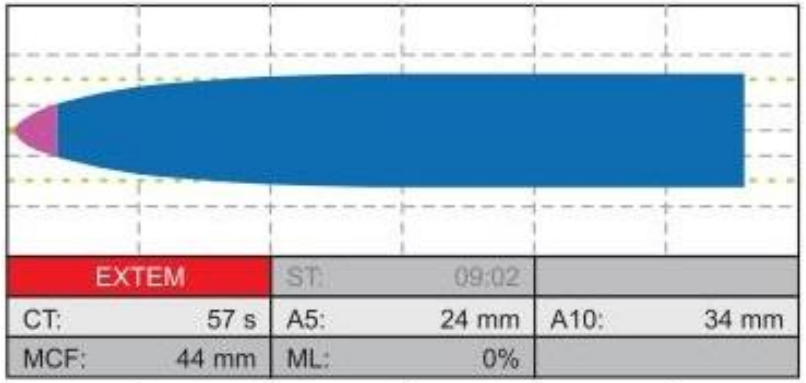


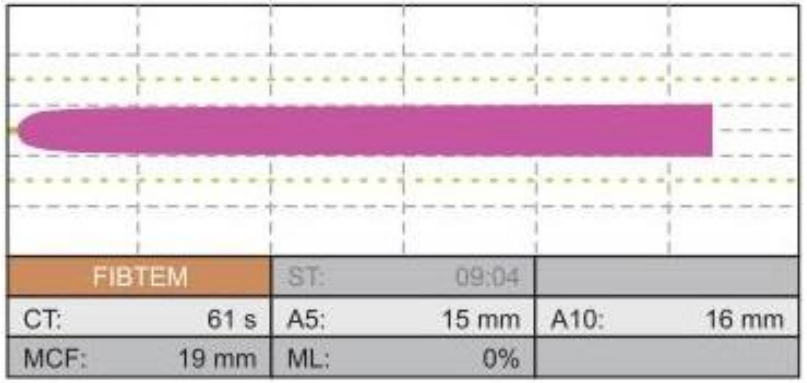
Fibrin polymerization disorder (e.g., low fibrinogen or low FXIII or colloid infusion):
$A5_{EX}$ < 35 mm
and
$A5_{FIB}$ < 9 mm





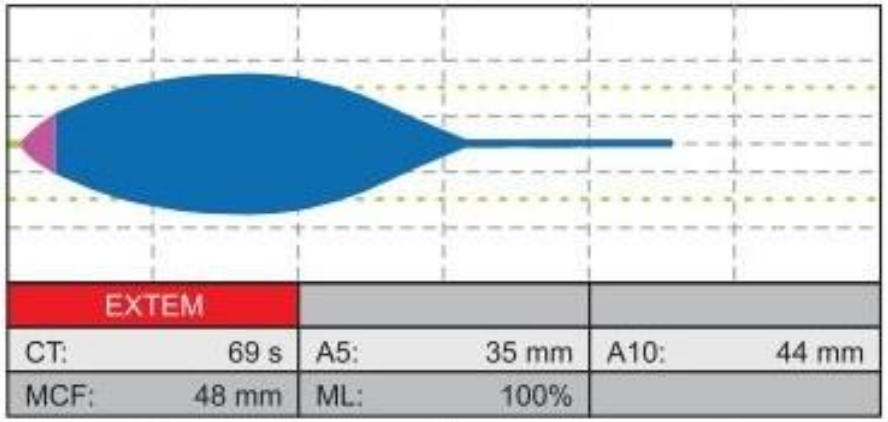
Thrombocytopenia or severe platelet dys-function (thrombin pathway or GPIIbIIIa-R):
$A5_{EX}$ < 35 mm
and
$A5_{FIB}$ ≥ 9 mm

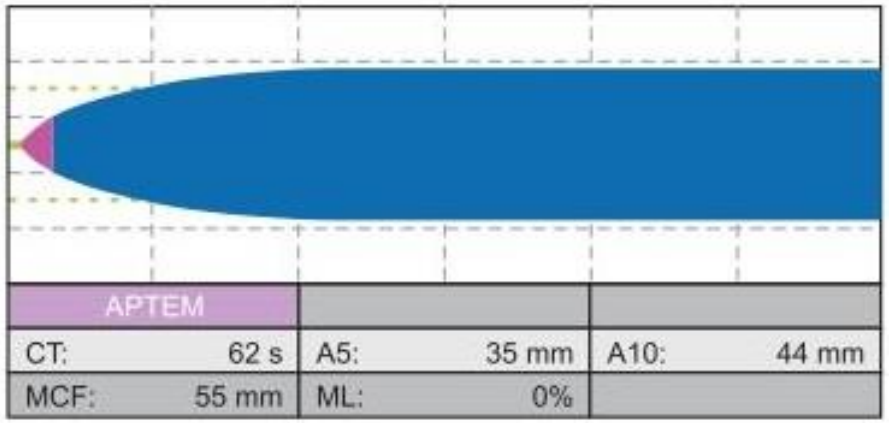




Gorlinger et al, KJA, 2019, A5 based

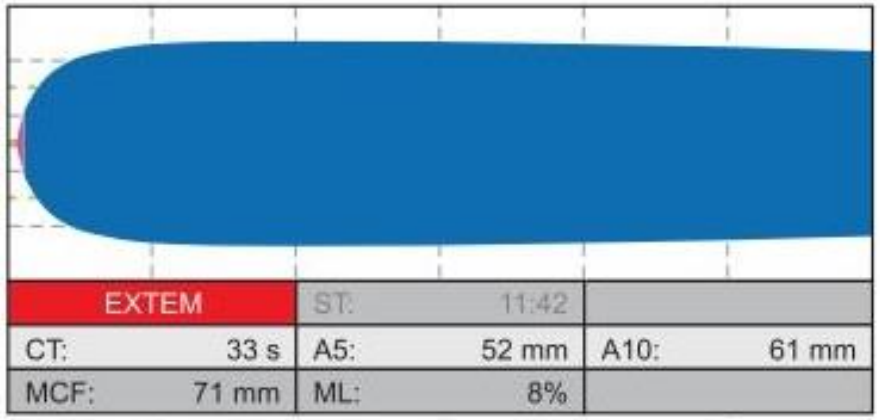
Hyperfibrinolysis:
ML_{EX} ≥ 15% or ML_{FIB} ≥ 10% within 60 min (LI60 ≤ 85%);
APTEM confirms TXA effect;
Note: FIBTEM is most sensitive and specific to hyperfibrinolysis!

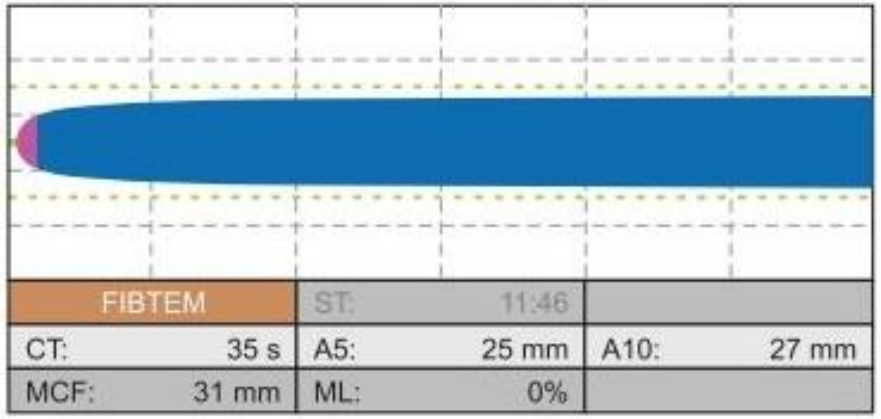




Hypercoagulability (high thrombotic risk):

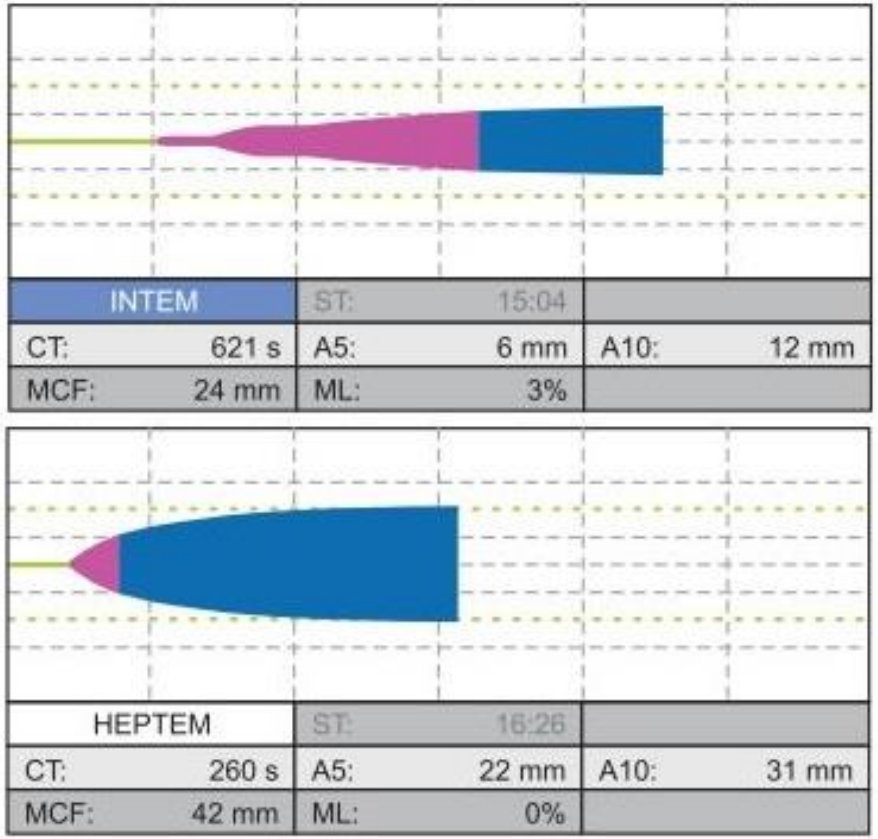
CT_{EX}	< 45 s
CFT_{EX}	< 45 s
MCF_{EX}	> 68 mm
MCF_{FIB}	> 22 mm
$LI60_{EX}$	≤ 3%



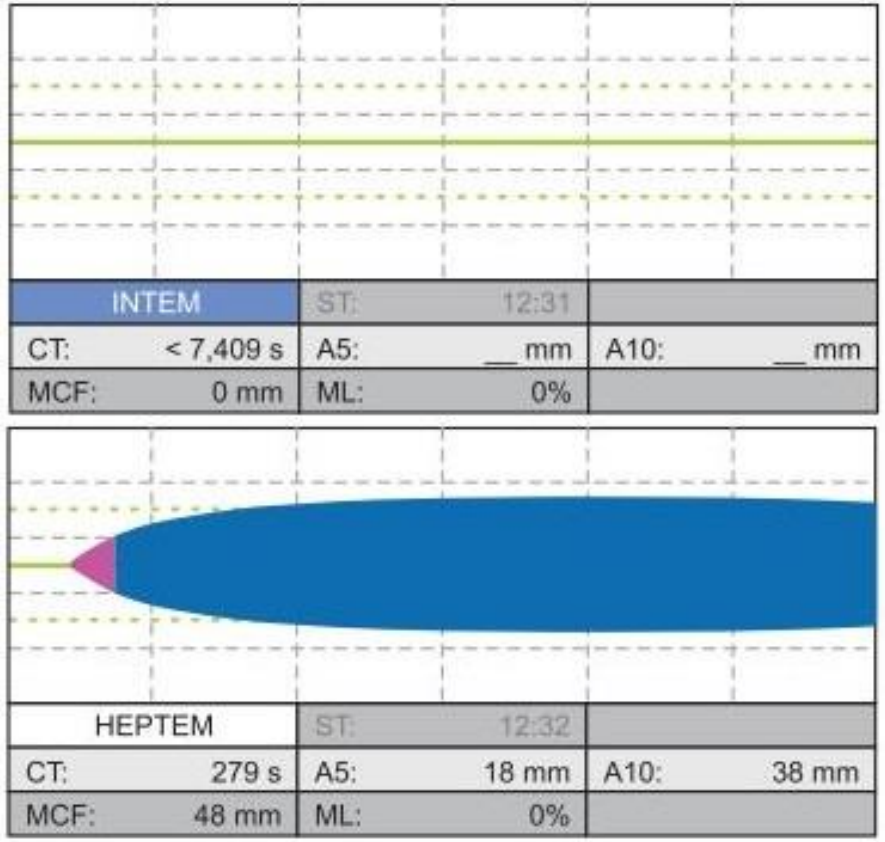


Gorlinger et al, KJA, 2019, A5 based

Heparin, low dose (endogenous HLE, e.g., during OLT, sepsis or severe shock):
CT_{IN}/CT_{HEP}-ratio 1.1−2.5
(significant ≥ 1.25)



Heparin, high dose (e.g., during CPB):
INTEM flat-line (CT_{IN} > 1200 s)
and
CT_{HEP} < 280 s



Gorlinger et al, KJA, 2019, A5 based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04
Coagulopathy

Europe guideline in trauma, 5ed, 2019

FFP
INR > 1.5 or **Viscoelastic guide**
Only major bleeding

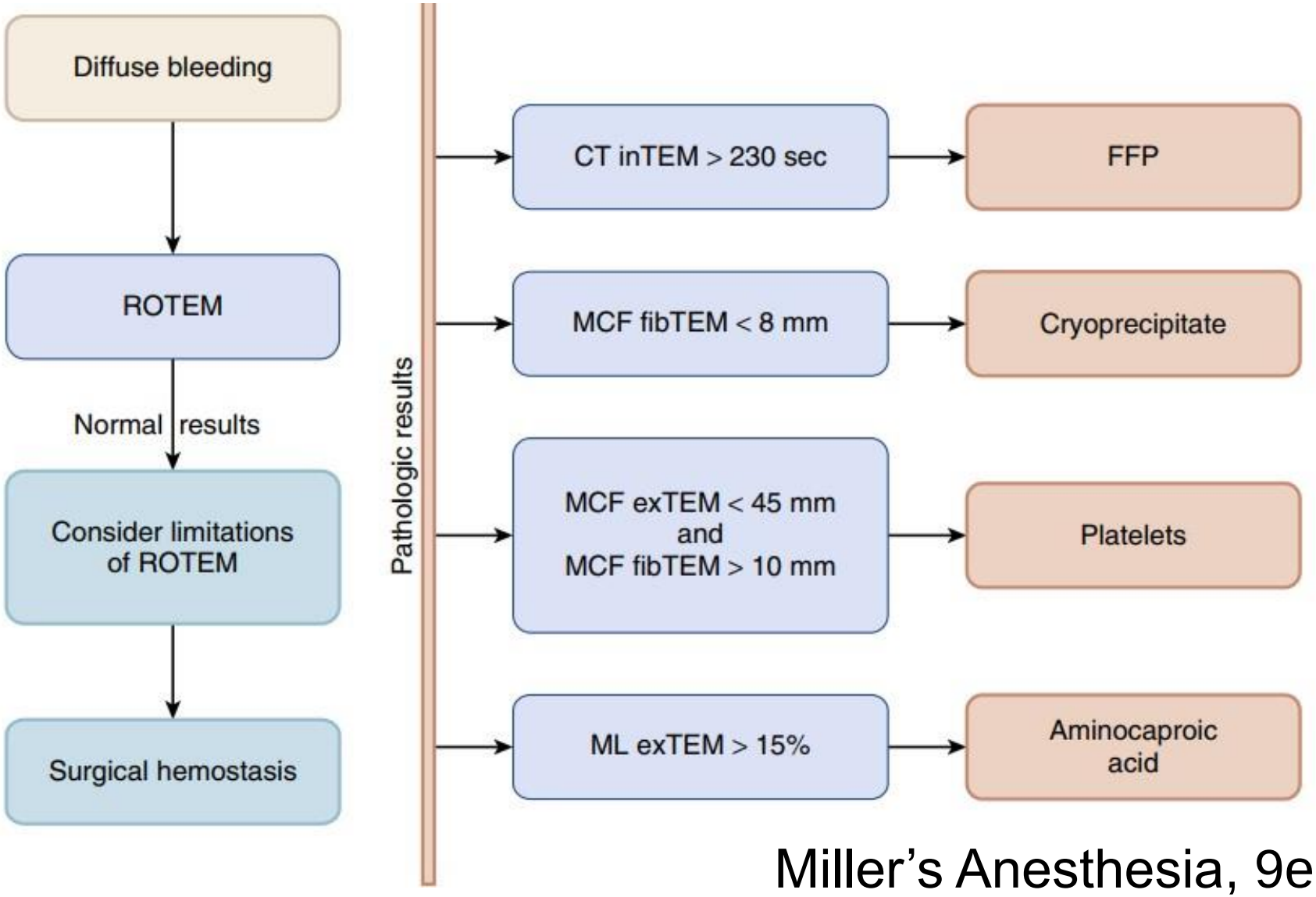
Fibrinogen (FC or Cryo)
Fib < 1.5 g/L or **Viscoelastic guide**
Initial 3-4g, repeat

Coagulation Factor (PCC)
Viscoelastic guide, F8 monitor
Also as reversal of DOAC

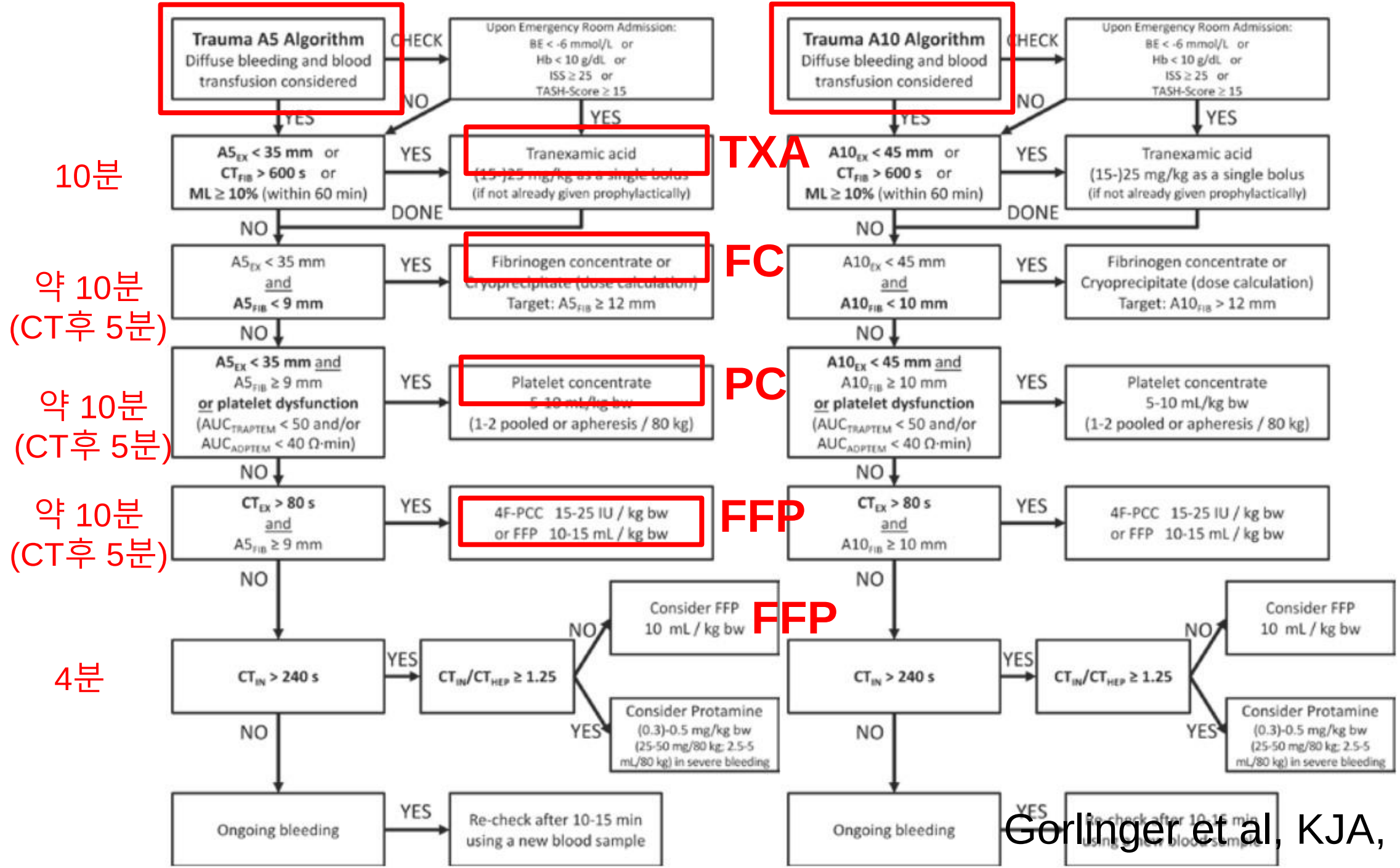
Platelet
Viscoelastic guide
Target plt > 50,000 (100,000 in ongoing bleeding)
4-8 units

Spahn et al, Crit Care, 2019

Algorithm in Trauma (CT, MCF based)

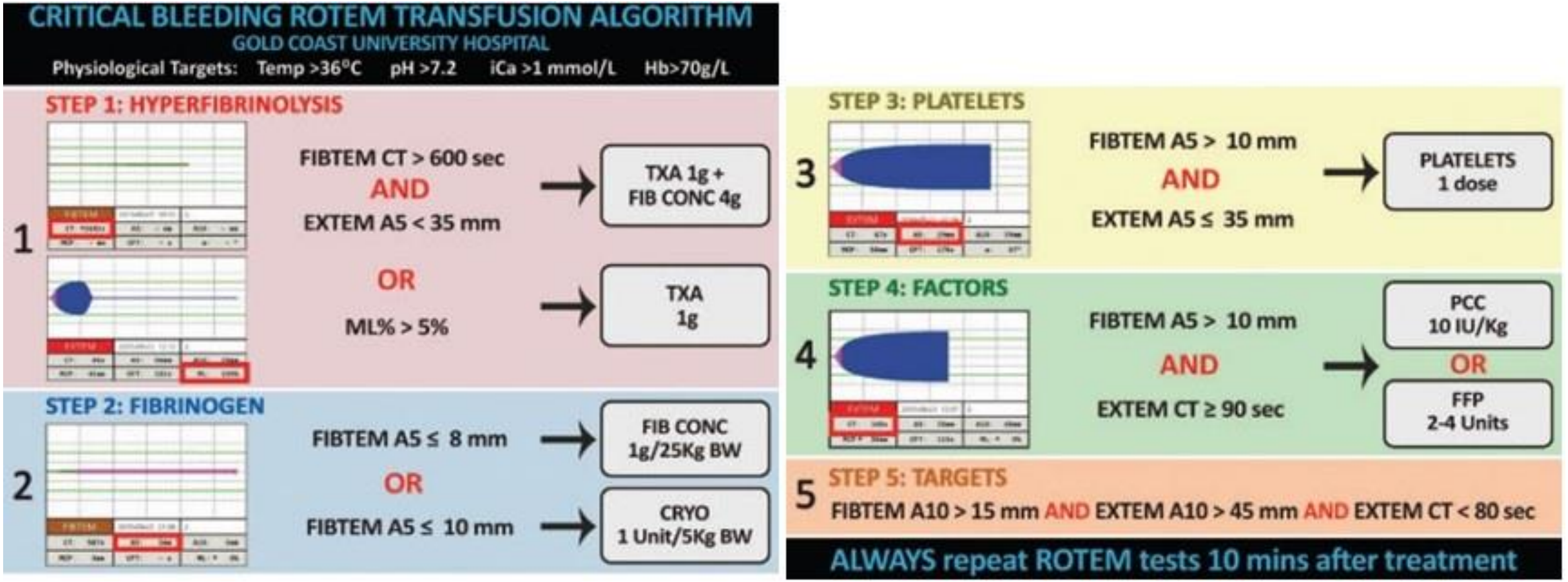


Miller's Anesthesia, 9ed, pp2134



Gorlinger et al, KJA, 2019

Easy Algorithm in Trauma (A5 based, EXTEM, FIBTEM)



Winearls, A&A, 2016

Early coagulation factor administration

Reversal of trauma-induced coagulopathy using first-lin coagulation factor concentrates or fresh frozen plas (RETIC): a single-centre, parallel-group, open-lab randomised trial

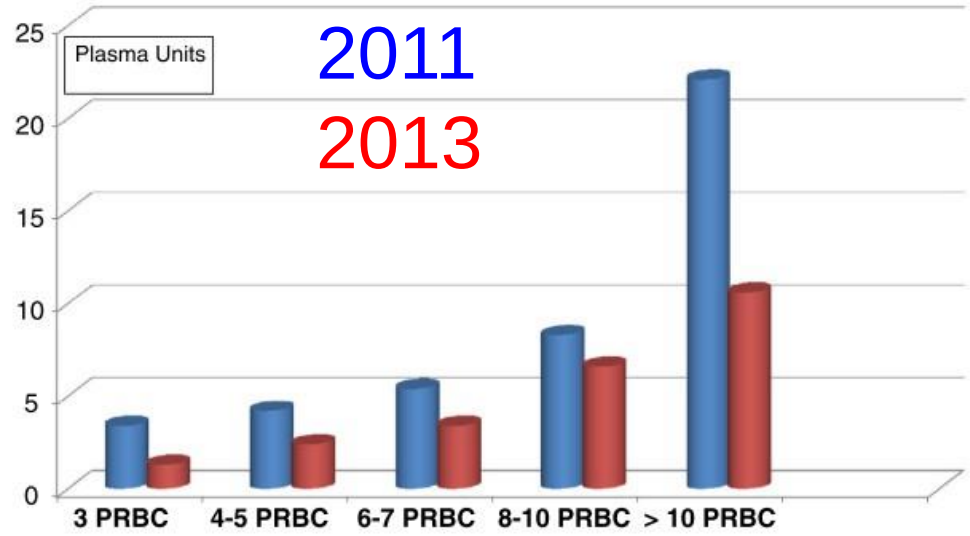
Petra Innerhofer, Dietmar Fries, Markus Mittermayr, Nicole Innerhofer, Daniel von Barbara Friesenecker, Ingo H Lorenz, Mathias Ströhle, Verena Raste Benjamin Treichl, Agnes Meur

	CFC	FFP	P
MOF	50%	66%	0.15
Rescue therapy	**4%**	52%	< 0.001
Massive Transfusion	**12%**	30%	0.042

- ROTEM based
  - **$A10_{FIB}$ < 9mm**
  - CT_{EX} > 90 s
- 44 pt (FFP 15 mL/kg)
- 52 pt (FC 50 mg/kg, 4F PCC 20 IU/kg, FX8 20 IU/kg)

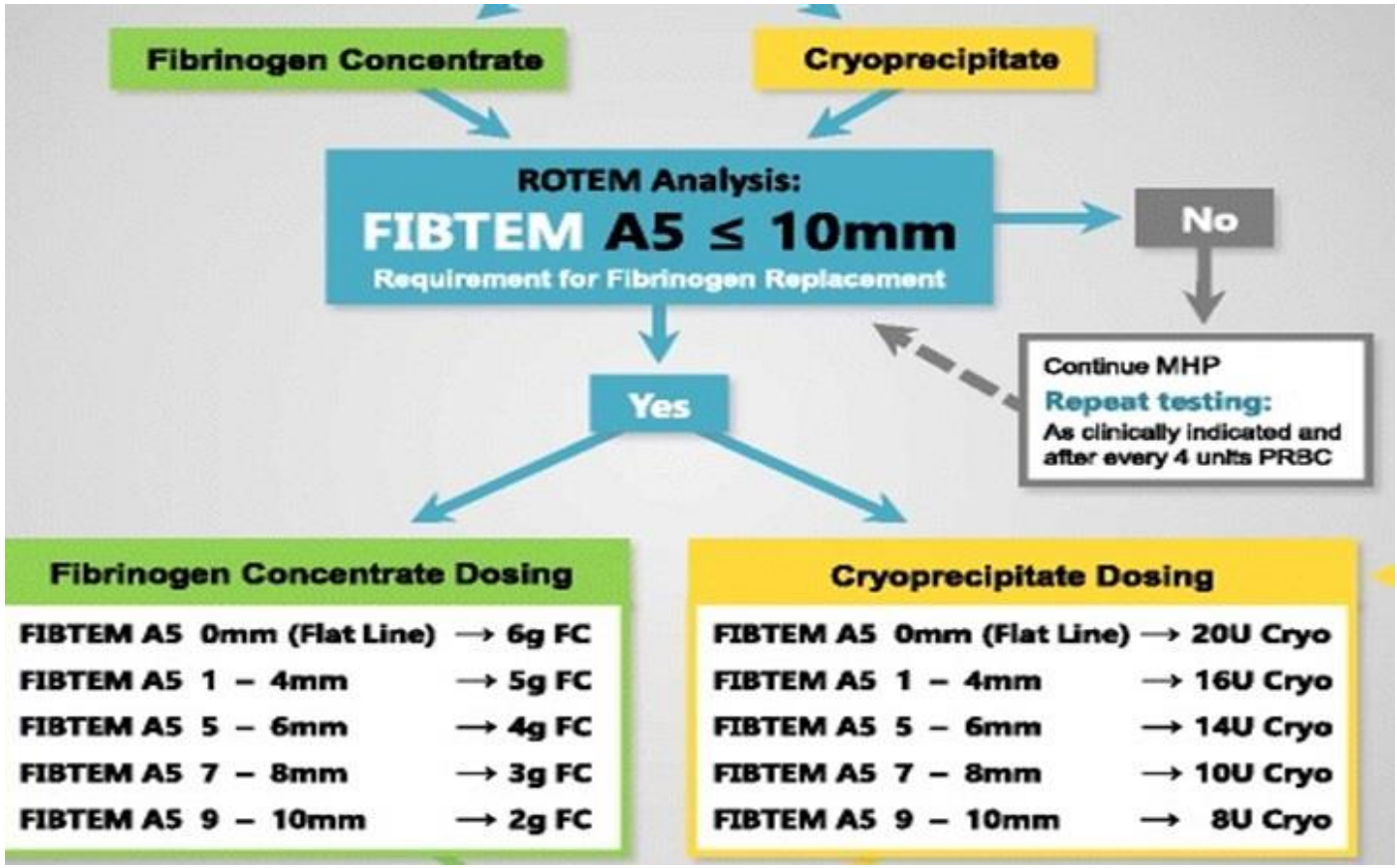
Innerhofer et al, Lancet Haematol, 2017

Early Fibrinogen administration by $A5_{FIB}$



Nardi et al, Crit Care, 2015

Winearls et al, Trials, 2017



Early Fibrinogen administration

Trials	Setting	Percent, Time
CRYOSTAT-1	Early Cryo vs. standard	85% pt, **60 min**
E-FIT-1	FC vs Placebo	69% pt, < **45 min**
FEISTY-Pilot	FC vs Cryo	FC (**29 min**) Cryo (60 min)
FlinTIC	FC vs Placebo prehospital	good FIBTEM (FC) poor FIBTEM (placebo)
FiiRST-1	FC vs Placebo	95% pt, < **60 min**
PRooF-iTH	FC vs Placebo	

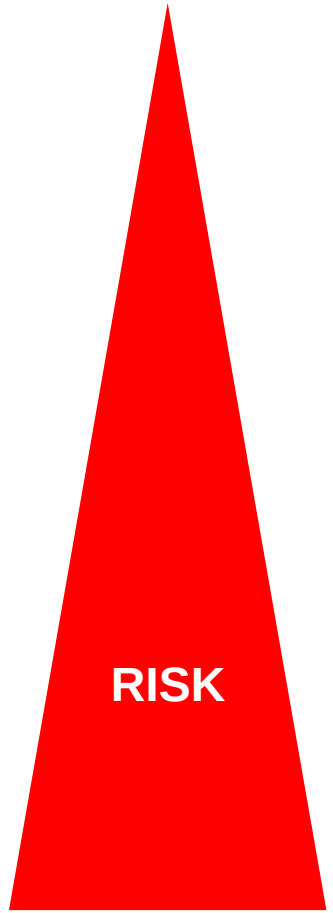
Winearls et al, Curr Opin Anaesthesiol, 2021

Fibrinogen

Fibrinogen concentrate (**3 g** / 3 bt / **150 mL**)

Cryoprecipitate (**3.3 g** / 10 u / **380 mL**)

FFP (**2.8 g** / 4 u / **1070 mL**)



TRALI

TACO

ARDS

Thrombosis

Napolitano et al, Expert Rev Hematol, 2021

Cryoprecipitate vs Fibrinogen concentrate

Cryoprecipitate	Fibrinogen concentrate
15 – 20 u (3.3g / 10 u)	3 – 4 g (1 g / 1 bt)
Viral	**No viral**
Inaccurate dosing	**Accurate** dosing
High volume	**Low volume**
Long thaw time	Short thaw time
Cross-matching	No cross-matching

Napolitano et al, Expert Rev Hematol, 2021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Consideration

Doubt positive findings, trust negative finding,

Positive predictive value	Negative predictive value
Standard test (14%–24%)	
Viscoelastic (15%–24%)	Viscoelastic (90%–97%)
Platelet function test (27%–50%)	Platelet function test (80%–95%)

Gorlinger et al, KJA, 2019

Lethal diamond (Phase I control)

Hypothermia
(Temp > 35°C)

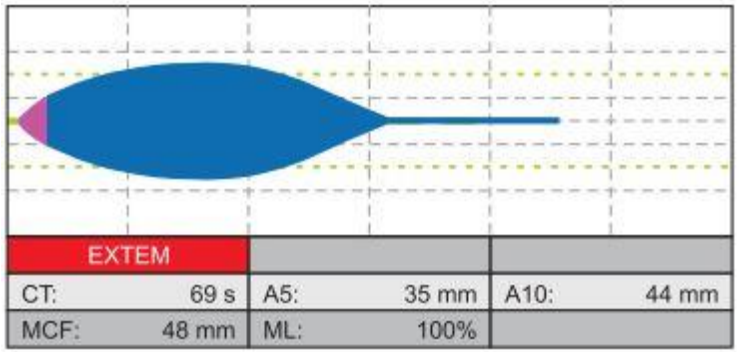
Hypocalcemia
(Ca^{2+} > 1 mmol/L)

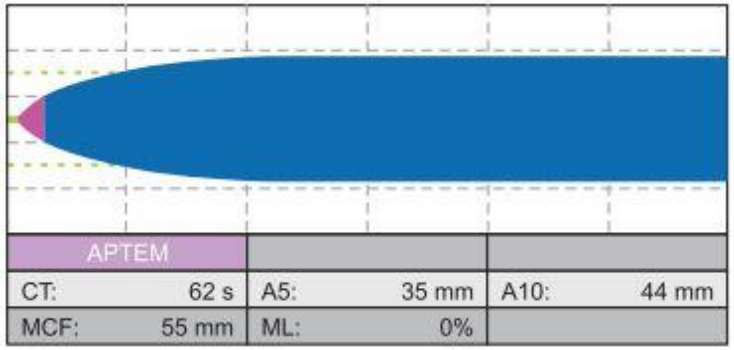
Acidosis
(pH > 7.3)

Coagulopathy

Napolitano et al, Expert Rev Hematol, 2021

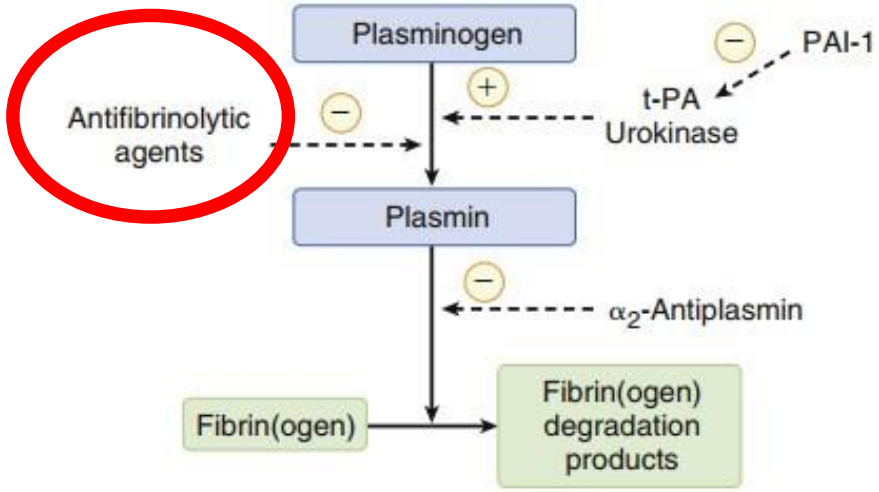
Tranexamic acid and hyperfibrinolysis





ML_{EX} > 15%

CTfib > 600s
$A5_{EX}$ < 35 mm
$CT_{EX} > CT_{AP}$
$CT_{AP}/CT_{EX} < 0.75$



Gorlinger et al, KJA, 2019

Miller's Anesthesia, 9ed

Empirical use of TXA in trauma

Trials	Year	Dose	Criteria	Benefit
CRASH-2	2010	1 g (bolus) – 1 g (8 h)	< 8 h	**< 3 h**
TAMPITI	2016 - now	2 g - 4 g (bolus)	< 2 h	
STAAMP	2020	1 g (bolus)	< 2 h prehospital	**< 1 h**
PATCH	2014 - now	1 g (bolus) – 1 g (8 h)	< 3 h prehospital	

TXA **3 – 6 h** after injury in CRASH-2 trial

Mortality (**4.4%** vs 3.1%; **RR, 1.44**; 95% CI, 1.12, 1.84; P = 0.004)

Napolitano et al, Expert Rev Hematol, 2021

2 Faces of Trauma Induced Coagulopathy (TIC)

Tissue hypoperfusion

Bleeding

Protein C activation

Factor 5, 8, thrombin inhibition

Thrombotic

Fibrinolysis shutdown

	Incidence	Mortality	OR	P
Hyperfibrinolysis	18%	34%	3.3 (2.4 – 4.6%)	< 0.001
Thrombosis	**46%**	**23%**	**1.6** (1.3 – 2.1%)	< 0.001

Duque et al, Anesth Analg, 2020

Moore et al, J Am Coll Surg, 2016

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06

Case

Summary

TRAUMA

- Red blood cells — **Go low (7 - 8) but do not go below**
- Viscoelastic test — **As soon as you can**
- Coagulation factors — **As early as possible with viscoelastic test**
- Tranexamic acid — **As early as possible with viscoelastic test**

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Thank You