

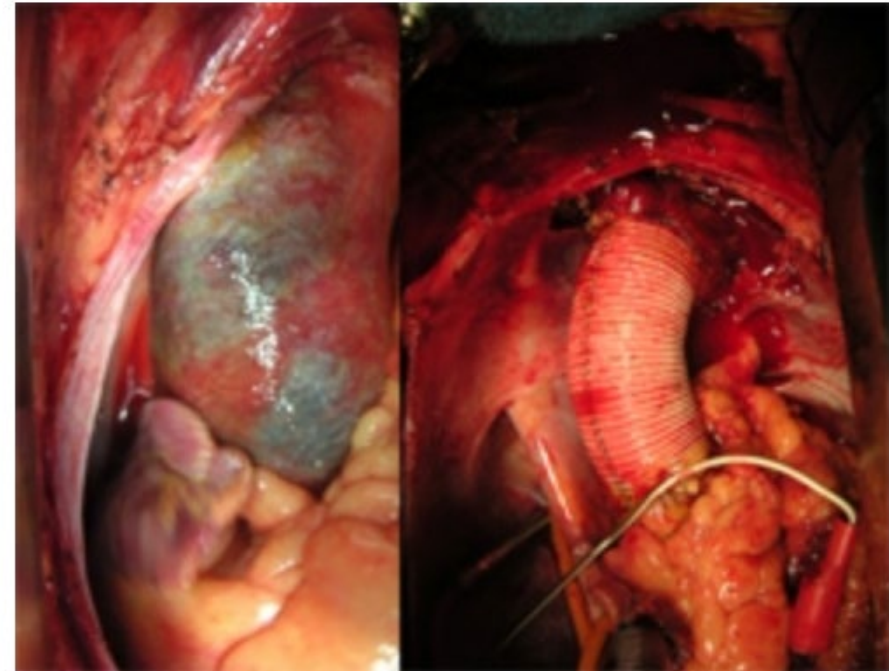
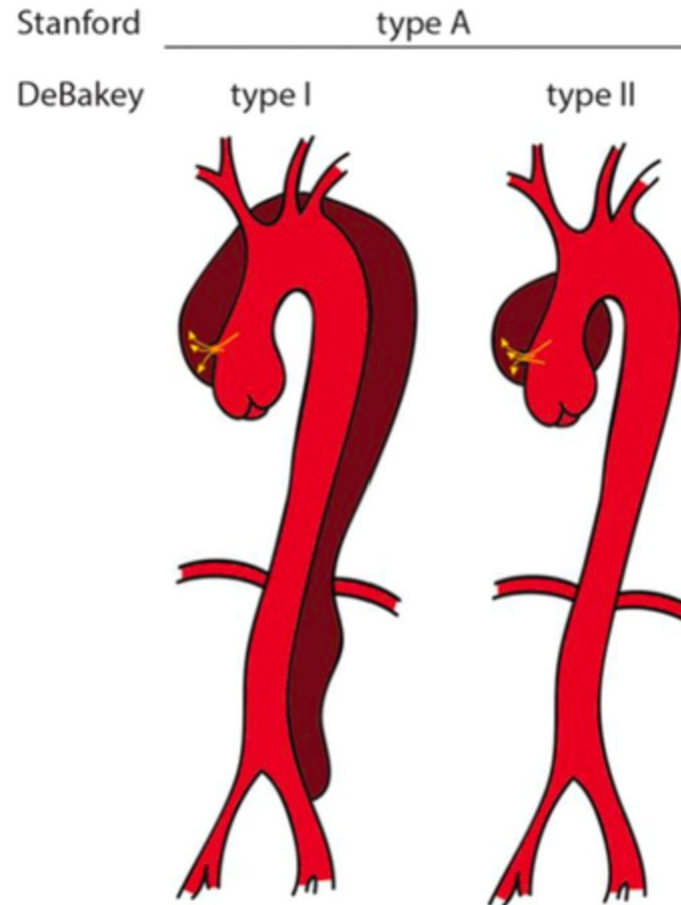


VFN PRAHA

Disekce po pumpě teče, kolik dám čeho a proč?

Petr Kopecký
5.10.2023

Disekce aorty A – 2,53/100000 ob./rok





Disekce po pumpě teče

- Co dám? – VŠECHNO CO MÁM
- Proč? – UŽ TO CHCI MÍT ZA SEBOU 😊

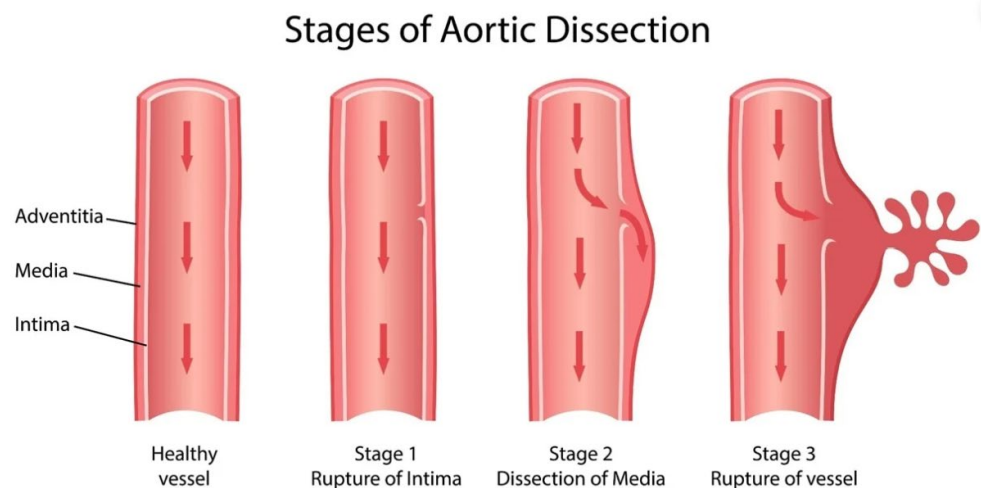


Krvácející pacient – identifikace příčiny

- Chirurgický zdroj (koagulační faktor XIV)
- Tvorba thrombinu - fibrinu
- Stabilita a pevnost koagula (fibrinolýza)
- Funkce krevních destiček
- Antiagregační/antikoagulační terapie
- *Dg. per se (disekce aorty)*



Disekce aorty – koagulopatie



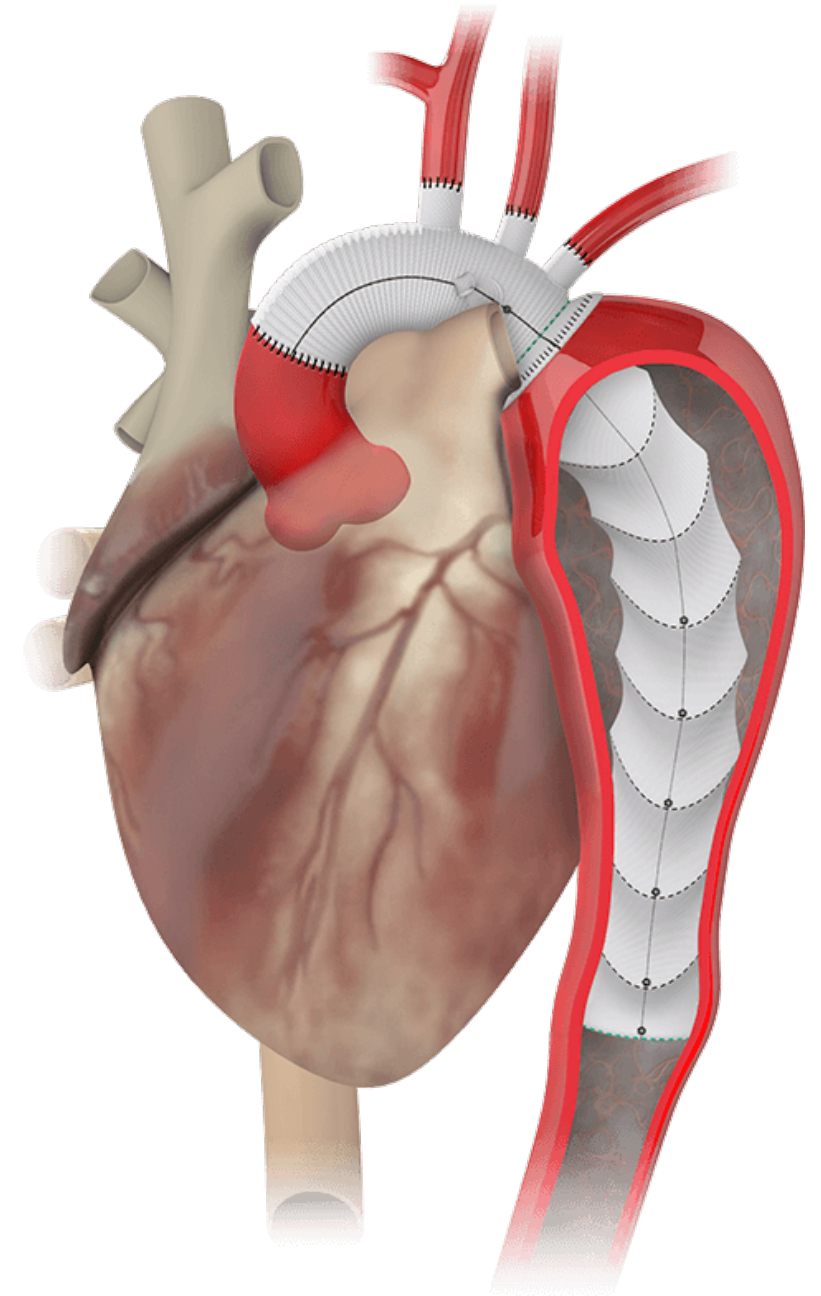
- Subendoteliální povrch – konsumpční koagulopatie
- Deplece f. II, V, VII, X, XII, elevace FDP
- Trombocytopenie i trombocytopatie
- CPB – zhoršení stávajícího stavu
- Hypotermie, vnitřní prostředí



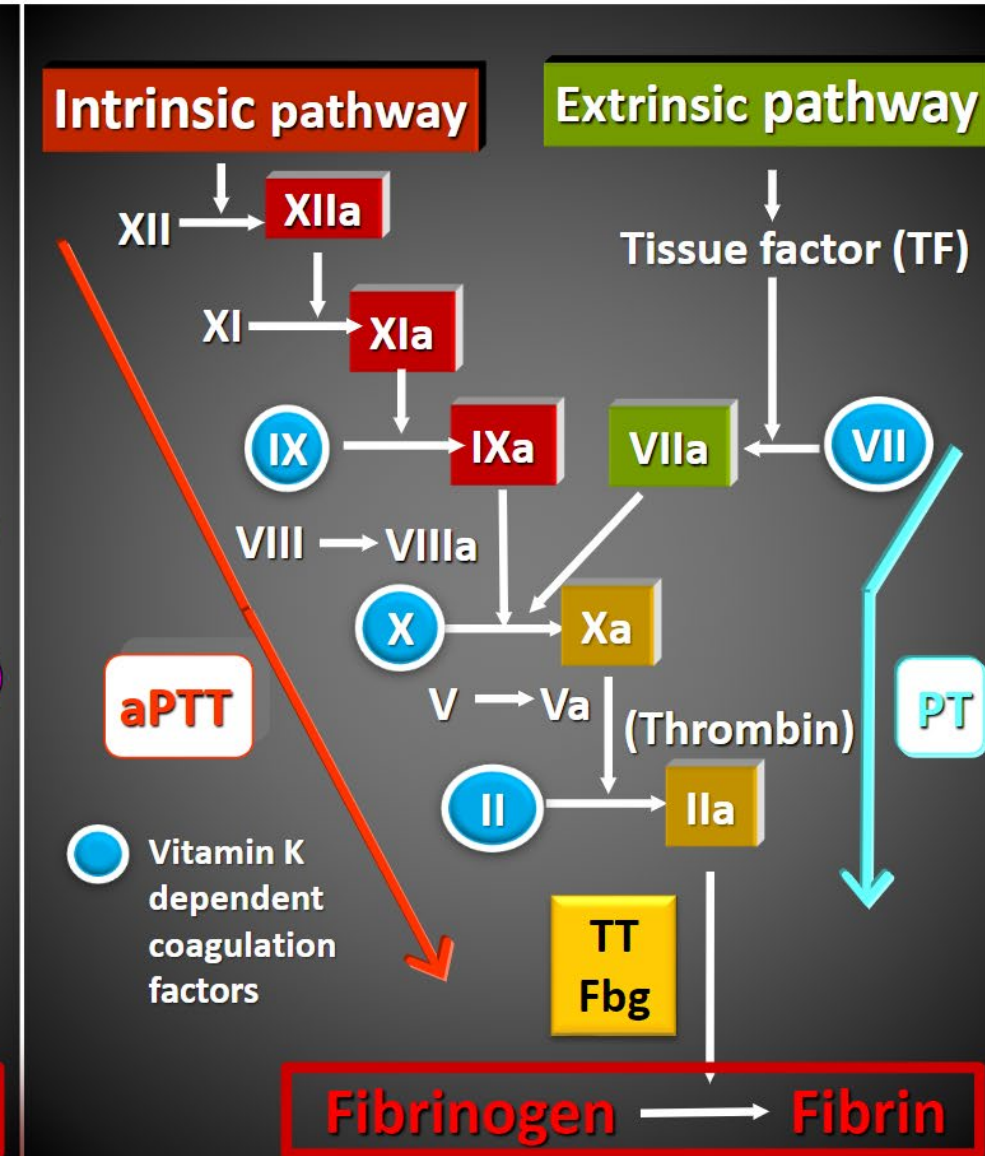
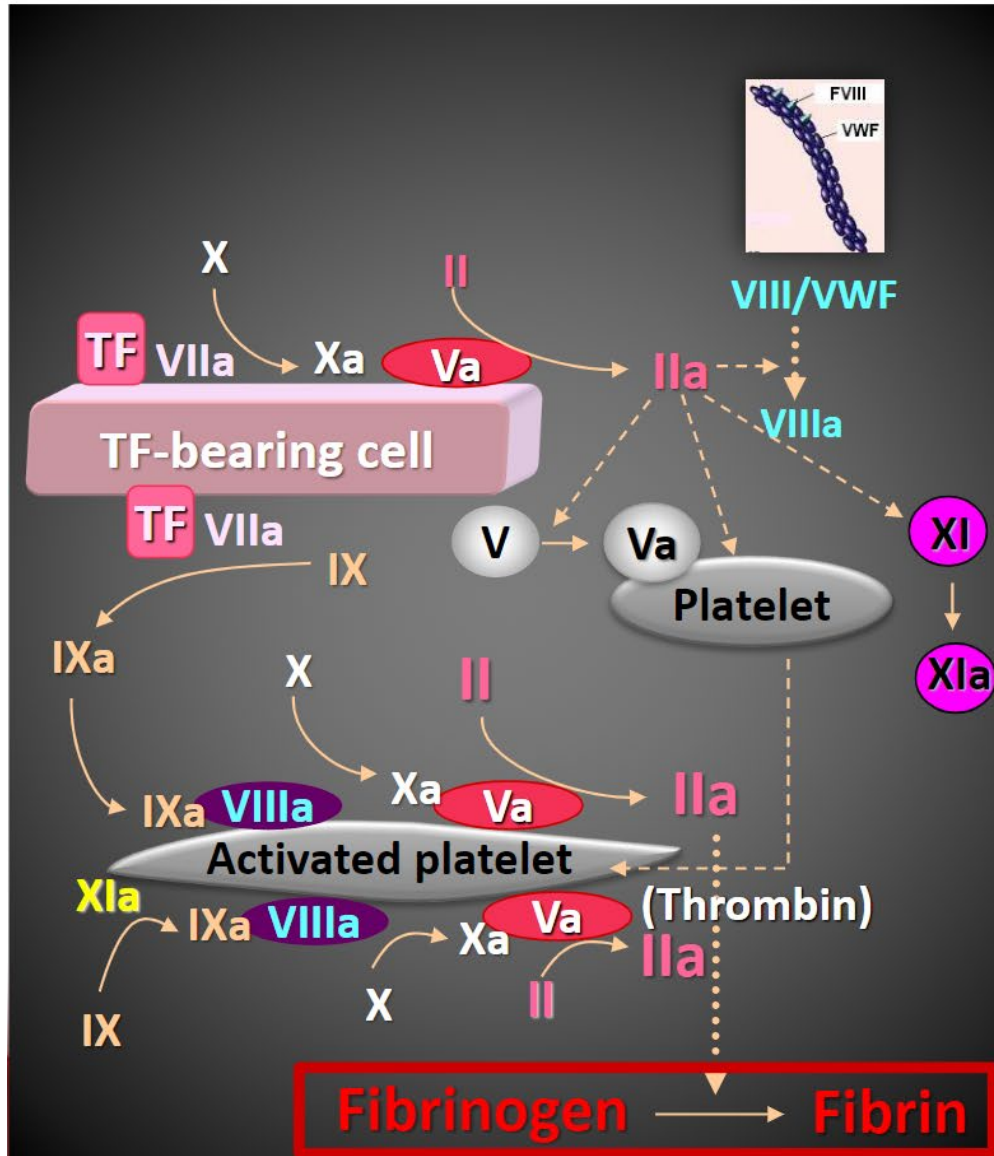
Thoraflex



- disekce aorty typu A šíříce se distálně



Koagulace in vivo vs. in vitro





Bedside vyšetření

WHOLE BLOOD CLOTTING TIME first coagulation assay - Lee White method (1913.)

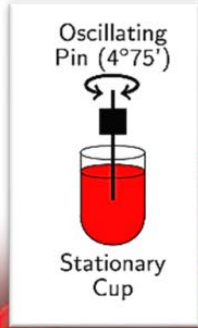
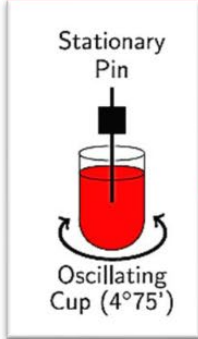
Portable coagulometers



Addis instrument for the determination of clotting time in whole blood (1908.)

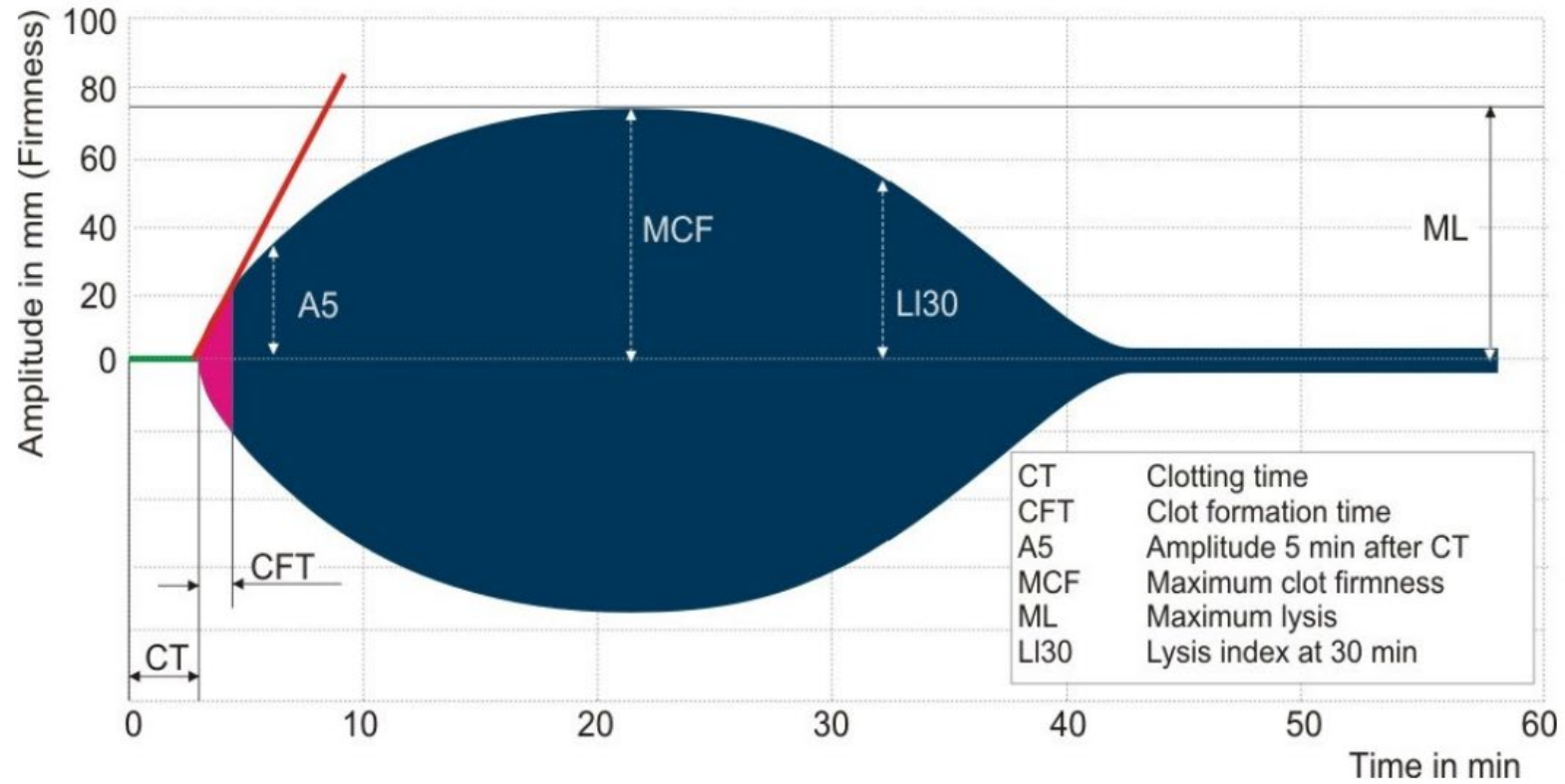


Viscoelastic global hemostasis assays



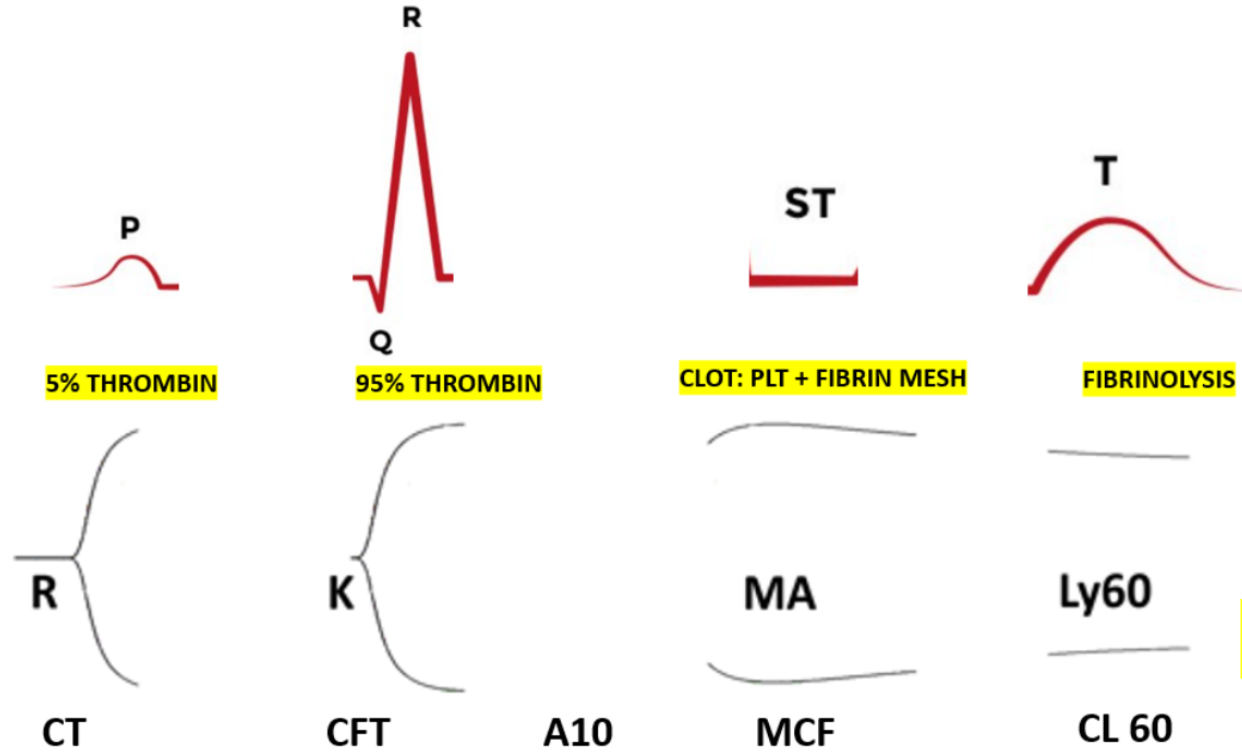


ROTEM - křivka





Viscoelastická křivka - EKG



Balance number 1

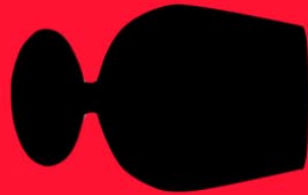
Thrombin balance

Balance number 2

Lysis balance



Pro milovníky vína



brandy snifter
normal



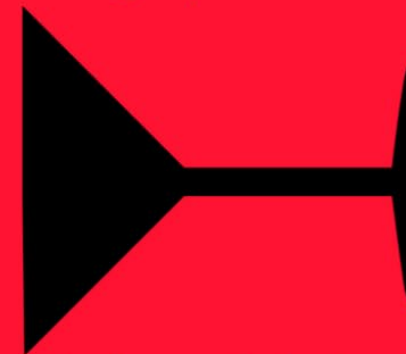
red wine glass
factor deficiency
↑ R, ↑ K,
give FFP



champagne flute
fibrinogen deficiency
↑ R, ↑ K, ↓ MA, ↓ α angle
give cryoprecipitate



test tube
thrombocytopenia/thrombocytopathy
↓ mA, normal R, ↑ K
give platelets



inverted martini glass
fibrinolysis
↑ Ly30, continuous ↓ MA
give TXA

*bases of glasses not actually part of TEG
@FOAMpodcast



ROTEM má svoje limity

ROTEM

STRENGTH	LIMITATIONS
Analyze all 3 phases of coagulation	Preoperative ROTEM results are poor predictors of postoperative bleeding.
Provide a rapid assessment of the overall coagulation status of the patient	Cannot reflect the contribution of endothelium to coagulation – disorders of primary haemostasis (VWD) cannot be determined
To be of benefit in detecting a hypercoagulable state in postoperative patients	Tracings insensitive to ASPIRIN and CLOPIDOGREL
ROTEM-based transfusion algorithms reduce rates of transfusion of blood components and reduce rates of surgical re-exploration	Not reflect the effects of hypothermia as the measurement is undertaken at 37 °C.
INTEM cartridges – very sensitive to residual heparin (0.005 IU/mL), may be useful in detection of Inadequate heparin reversal or heparin rebound	Not yet standardized: sample collection and processing (native or citrated, time delay), activators used and other modifications, difficult to compare results between institutions. Concerns about adequate maintenance, quality control, and supervision of personnel running the tests



Stavební kameny terapie koagulační poruchy



- Fibrinogen
- Prothrombin Complex Concentrate
- Kyselina tranexamová
- Krevní deriváty (ERY, FFP, trombocyty)
- Homeostáza vnitřního prostředí (pH, teplota, calcium)



V PŘÍPADĚ MASIVNÍHO KRVÁCENÍ POTŘEBUJEME VŠE

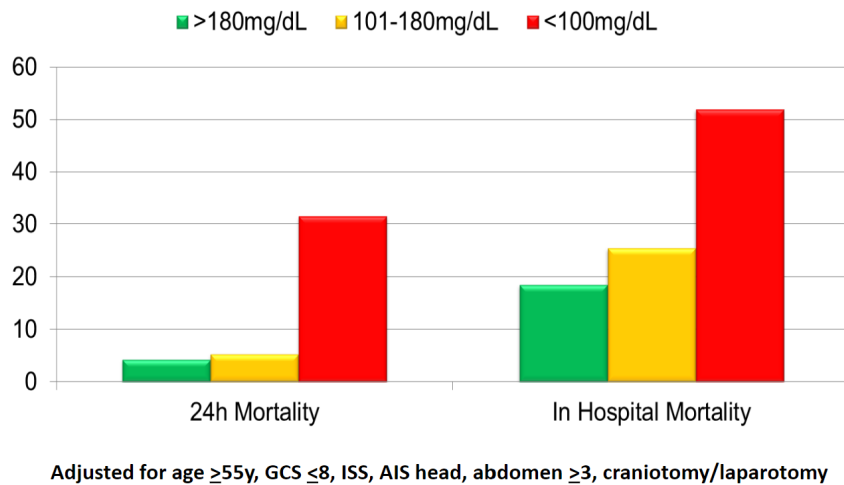
- Goal Directed Therapy podle VET co nejdříve!





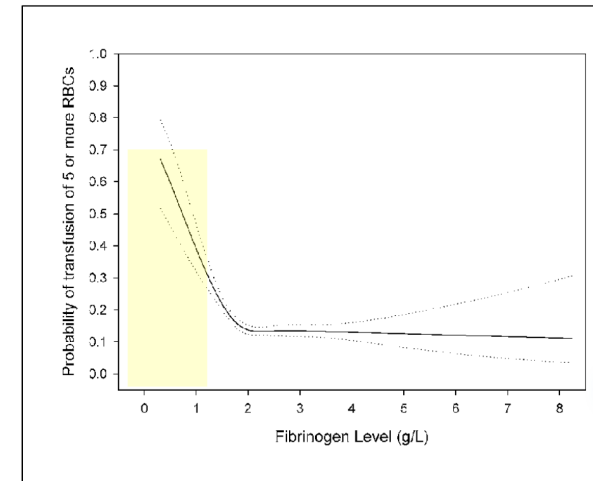
Fibrinogen

- Role v primární i sekundární hemostáze
- Kriticky nízká hladina dříve než ostatní koagulační faktory
- Deficit považován za hlavní příčinu koagulopatie



Inaba et al. J Am Coll Surg, 2013;216:290-297

- **Observational study n=4606**
- Correlation Post-CABG Fibrinogen and RBC transfusion
- Category „low Fib.“ (< 2g/l): N=1918
 - 363 (18.9%) > 5 RBCs
- Category „high Fib.“ (> 2g/l): N=2688
 - 164 (13.5%) > 5 RBCs

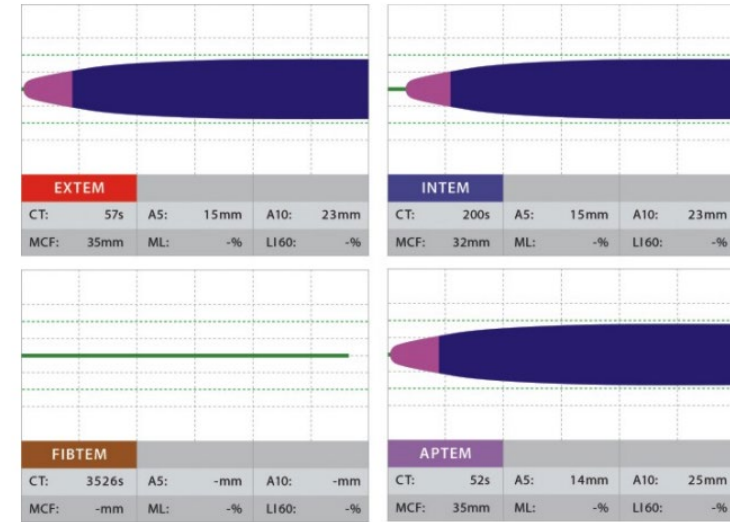


Karkouti et al, Anesth Analg. 2013;117:14-



Fibrinogen – možnosti substituce

- FFP (fresh frozen plasma)
- Kryoprecipitát
- Koncentrát fibrinogenu



Cryoprecipitate
~ 15 g/L



Fibrinogen concentrate
20 - 30 g/L



Fresh frozen plasma/ Freeze dried plasma
~ 2.0 - 2.5 g/L

	Fibrinogen concentrate	Cryo-precipitate	SD Plasma	Fresh frozen plasma
Constituents	Concentrated fibrinogen	Contains factors VIII, XIII, VWF, fibrinogen	Standardized content of all clotting factors	all clotting factors and other proteins in changing concentrations
Pathogen transmission and safety	<u>Viral inactivation</u> , minimal risk of pathogen transmission	Potential risk of pathogen transmission, Thrombosis risk	<u>Pathogen inactivated</u> , no known cases of TRALI, maximized safety	risk of pathogen transmission, TRALI/TACO, Allergic reactions
Dosing	<u>Well defined quantity</u> of fibrinogen	<u>Variable</u> fibrinogen levels	<u>Standardized high</u> level of Fibrinogen	<u>Variable</u> fibrinogen level (1-3g/l)
Volume	<u>Low</u>	medium	High	High – Very high
Preparation	<u>Minimal delay</u>	Pooling and thawing required	Thawing required	Thawing required
Cross matching	<u>None required</u>	Centre dependent	AB compatibility	AB compatibility



Fibrinogen - EBM

EJA

Eur J Anaesthesiol 2023; **40**:226–304

GUIDELINES

Management of severe peri-operative bleeding: Guidelines from the European Society of Anaesthesiology and Intensive Care

Second update 2022

Sibylle Kietzbl, Aamer Ahmed, Arash Afshari, Pierre Albaladejo, Cesar Aldecoa, Giedrius Barauskas, Edoardo De Robertis, David Faraoni, Daniela C. Filipescu, Dietmar Fries, Anne Godier, Thorsten Haas, Matthias Jacob, Marcus D. Lancé, Juan V. Llau, Jens Meier, Zsolt Molnar, Lidia Mora, Niels Rahe-Meyer, Charles M. Samama, Ecaterina Scarlatescu, Christoph Schlimp, Anne J. Wikkelsø and Kai Zacharowski

We recommend treatment with fibrinogen concentrate or cryoprecipitate, if bleeding is accompanied by hypofibrinogenaemia (viscoelastic signs of a functional fibrinogen deficit or a plasma Clauss fibrinogen level $\leq 1.5 \text{ g l}^{-1}$). 1B

GUIDELINES

Open Access



The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition

Rolf Rossaint^{1*}, Arash Afshari², Bertil Bouillon³, Vladimir Cerny^{4,5}, Diana Cimpoesu⁶, Nicola Curry^{7,8}, Jacques Duranteau⁹, Daniela Filipescu¹⁰, Oliver Grottke¹, Lars Grønlykke¹¹, Anatole Harrois⁹, Beverley J. Hunt¹², Alexander Kaserer¹³, Radko Komadina¹⁴, Mikkel Herold Madsen², Marc Maegele¹⁵, Lidia Mora¹⁶, Louis Riddez¹⁷, Carolina S. Romero¹⁸, Charles-Marc Samama¹⁹, Jean-Louis Vincent²⁰, Sebastian Wiberg¹¹ and Donat R. Spahn¹³

We recommend treatment with **fibrinogen concentrate** or cryoprecipitate if major bleeding is accompanied by **hypofibrinogenaemia (viscoelastic signs of a functional fibrinogen deficit or a plasma Clauss fibrinogen level $\leq 1.5 \text{ g/L}$)**. (Grade 1C)*

We suggest an **initial fibrinogen supplementation of 3–4 g**. This is equivalent to 15–20 single donor units of cryoprecipitate or 3–4 g fibrinogen concentrate. **Repeat doses should be guided by VEM and laboratory assessment of fibrinogen levels**. (Grade 2C)



Fibrinogen vs. FFP - EBM

GUIDELINES

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Rolf Rossaint^{1*}, Arash Afshari², Bertil Bouillon³, Vladimir Cerny^{4,5}, Diana Cimpoesu⁶, Nicola Curry^{7,8}, Jacques Duranteau⁹, Daniela Filipescu¹⁰, Oliver Grottko¹, Lars Grønlykke¹¹, Anatole Harrois⁹, Beverley J. Hunt¹², Alexander Kaserer¹³, Radko Komadina¹⁴, Mikkel Herold Madsen², Marc Maegele¹⁵, Lidia Mora¹⁶, Louis Riddez¹⁷, Carolina S. Romero¹⁸, Charles-Marc Samama¹⁹, Jean-Louis Vincent²⁰, Sebastian Wiberg¹¹ and Donat R. Spahn¹³

We recommend that the use of **FFP be avoided** for the correction of **hypofibrinogenaemia** if **fibrinogen concentrate** and/or cryoprecipitate are available. (Grade 1C)

Fibrinogen – kolik a kdy?

- FIBTEM A10 0-3mm 6g
- FIBTEM A10 4-6mm 3-4g
- Cíl A10 > 9mm, MCF > 40mm

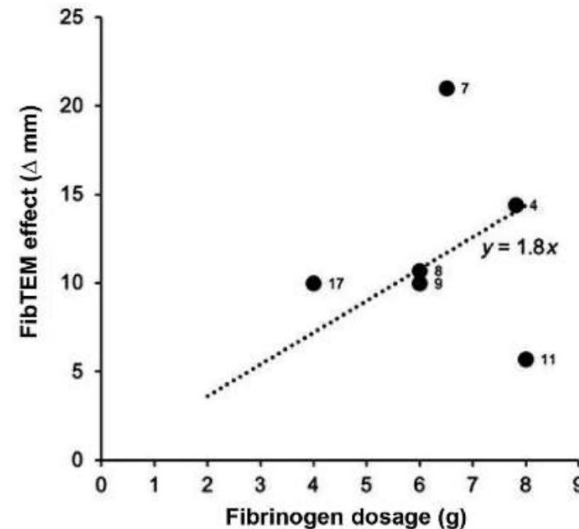
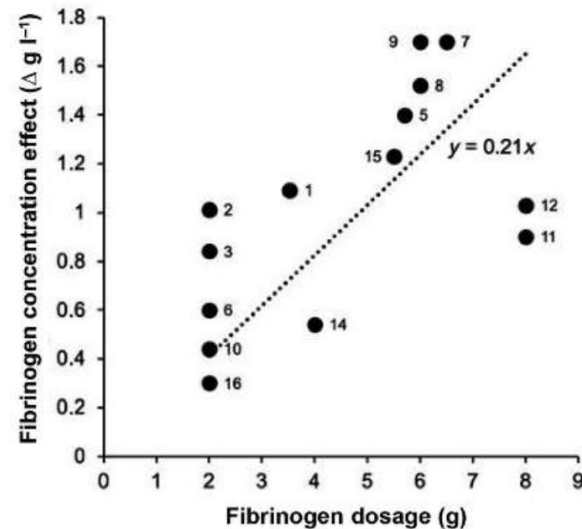
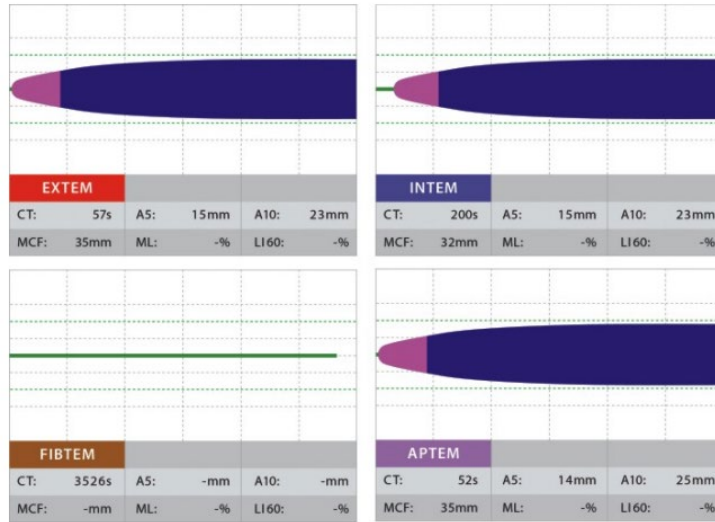
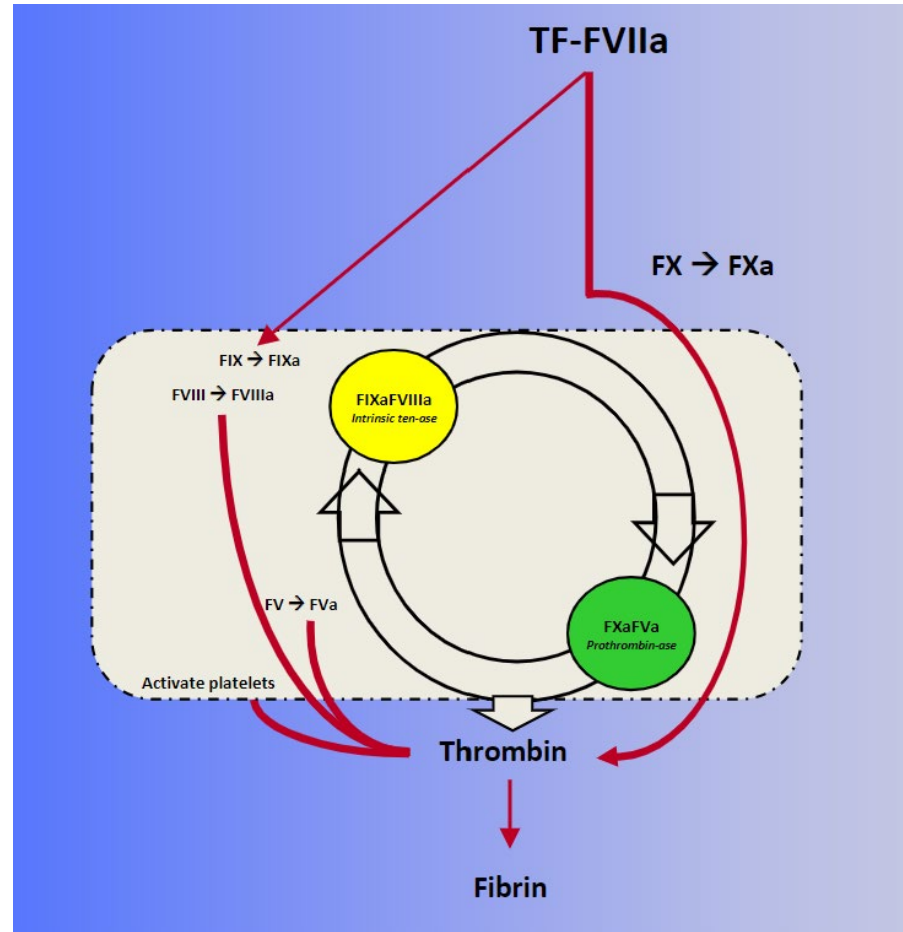


Figure 2 The effect of fibrinogen concentrate on the fibrinogen level in cardiac surgery patients. The left panel shows the effect on Clauss fibrinogen assay, right panel shows the effect on the fibrin-based thromboelastometry assay. The numbers represent the individual studies found in Data S1 (Studies evaluating the effect of fibrinogen concentrate on the plasma fibrinogen level).





4F-Prothrombin Complex Concentrate



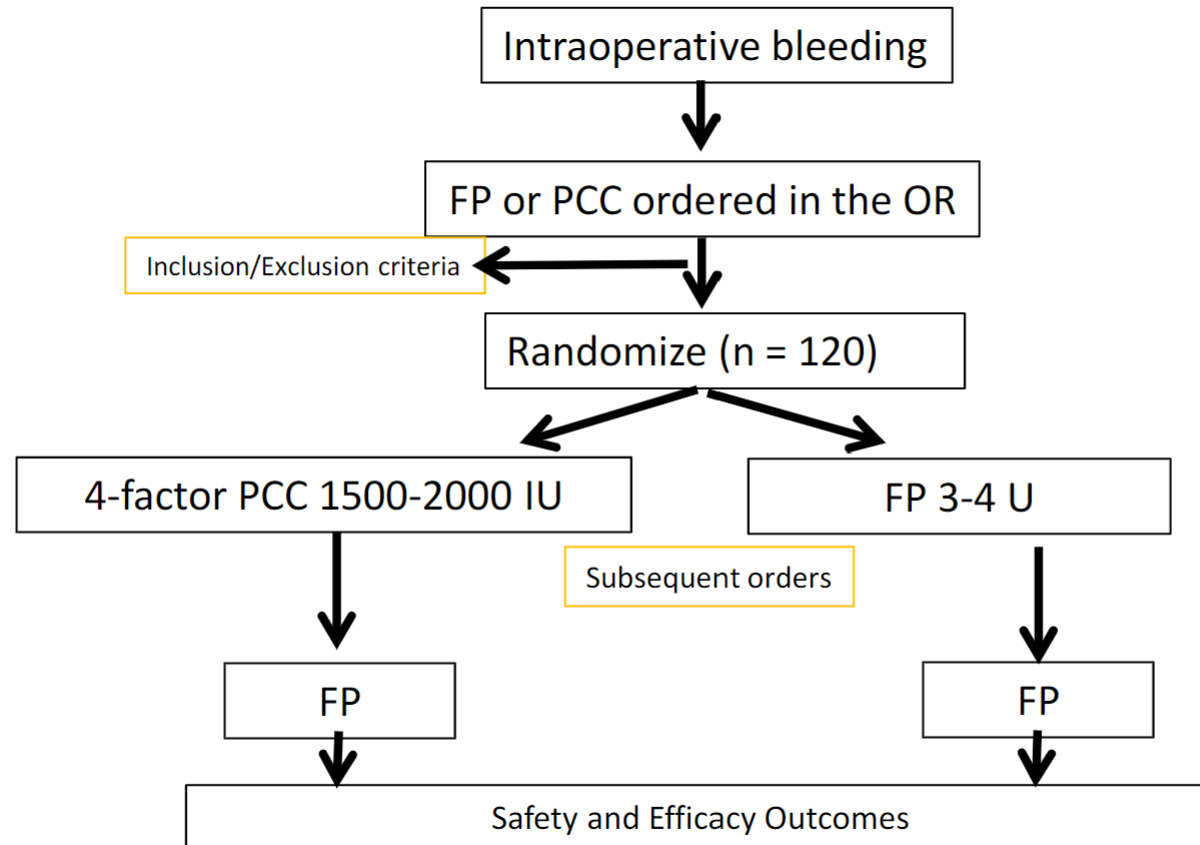


Kardiochirurgie – 4F-PCC

Outcomes	Matched FP group (n=117) (%)	Matched PCC group (n=117) (%)	P-value	Relative risk
Primary transfusion outcomes				
Avoidance of perioperative red cell transfusions	13 (11.1)	27 (23.1)	0.01	2.4 (1.2–4.8)
Massive transfusion (10 or more perioperative red cell transfusions)	28 (23.9)	18 (15.4)	0.05	0.58 (0.33–1.0)
Refractory bleeding (perioperative rFVIIa used)	22 (18.8)	12 (10.3)	0.06	0.49 (0.24–1.03)
Other transfusion outcomes				
Surgical re-exploration	30 (25.6)	27 (23.1)	0.65	1.14 (0.65–2.05)
Avoidance of perioperative platelet transfusions	13 (11.1)	18 (15.4)	0.35	1.42 (0.68–2.97)
Avoidance of perioperative fibrinogen replenishment	59 (50.4)	55 (47.0)	0.58	0.86 (0.50–1.48)
Clinical outcomes				
Acute kidney injury (excluding seven patients on renal replacement therapy before surgery; three in FP and four in PCC groups)				
Class 0	75 (65.8)	67 (59.3)	0.44*	0.82 (0.49–1.36)*
Class I	25 (21.9)	31 (27.4)		
Class II	4 (3.5)	3 (2.6)		
Class III	10 (8.8)	12 (10.6)		
Death (in-hospital)	15 (12.8)	15 (12.8)	1.0	1.0 (0.44–2.31)
Stroke (in-hospital)	8 (6.8)	7 (6.0)	0.78	1.17 (0.39–3.47)
Deep vein thrombosis or pulmonary embolism (in-hospital)	1 (0.8)	1 (0.8)	1.0	1.0 (0.06–15.99)



Kardiochirurgie – 4F-PCC





Kardiochirurgie – 4F-PCC

	4F-PCC Group (N=54)	FP Group (N=47)	P-value
Further hemostatic therapy needed (to 4 hrs)	11 (20%)	15 (32%)	0.25
Severe / Massive hemorrhage	11 (21%)	18 (38%)	0.08
24-hr chest tube drainage (median; IQR)	450 (370-630)	700 (470-950)	<0.001
24-hr allogeneic blood component transfusions			
RBC + Platelet + FP (including IMP)	8.7 (7.2-10.5)	14.8 (12.3-17.9)	<0.001
PCC:FP Ratio (95% CI)			0.58 (0.45-0.77)
RBC + Platelet + FP (excluding IMP)	8.6 (7.0-10.6)	10.8 (8.6-13.4)	0.15
PCC:FP Ratio (95% CI)			0.80 (0.59-1.08)
RBC	2.2 (1.7-2.9)	3.2 (2.5-4.2)	0.05
Platelet	6.2 (5.1-7.6)	7.2 (5.9-8.9)	0.3
FP	0.3 (0.2-0.4)	4.4 (3.6-5.3)	<0.001



4F-PCC

EJA

Eur J Anaesthesiol 2023; 40:226–304

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We recommend treatment with PCC if available instead of FFP if bleeding is accompanied by signs of coagulation factor deficiency (viscoelastic signs of a functional coagulation factor deficiency or a high PT ratio). 1B

GUIDELINES

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The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition

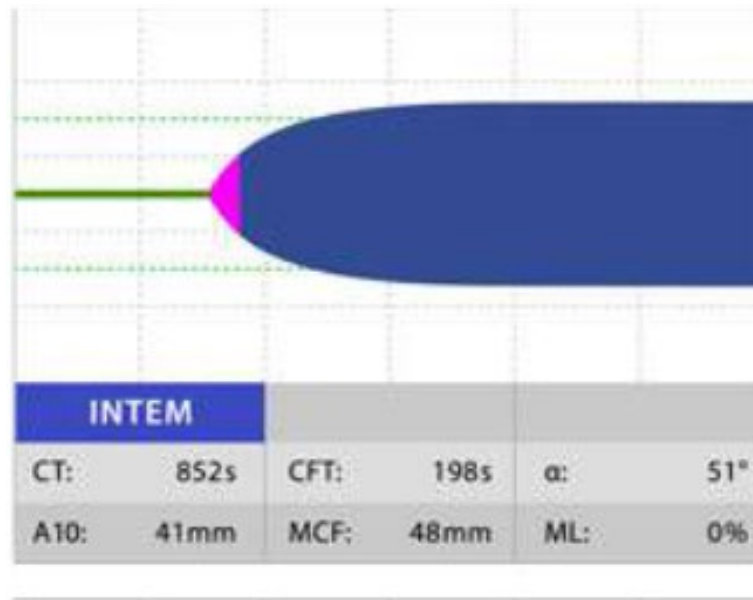
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Provided that **fibrinogen levels are normal**, we suggest that **prothrombin complex concentrate (PCC)** is administered to the bleeding patient based on **evidence of delayed coagulation initiation using VEM**. (Grade 2C)



4F-PCC – kolik a kdy?

- Dávka: 1500-2000IU (15-25 IU/kg)
- Cíl CT < 80, 240s



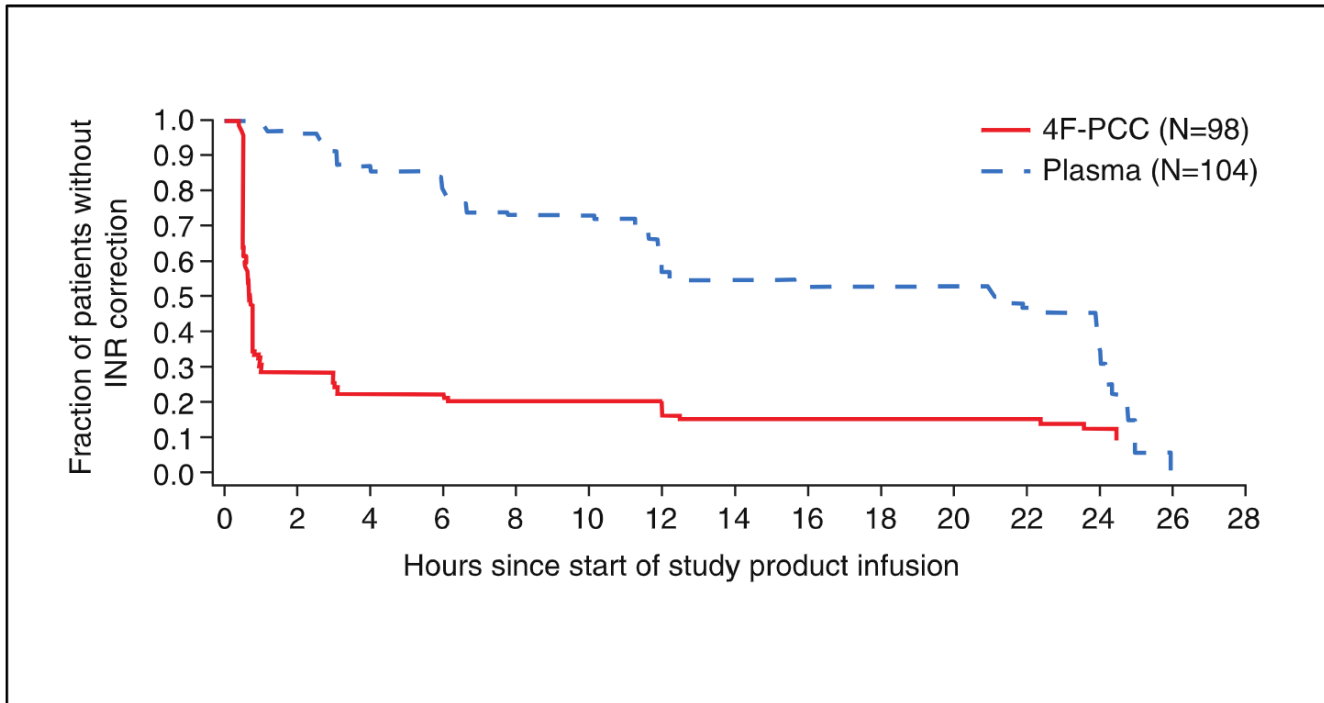


4F-PCC a antikoagulancia

Jahr	Anticoagulant
1940er	UFH Heparin
1950er	Warfarin (Coumarin®) Phenprocoumon (Marcumar®)
1980er	LMWH Heparin
1990er	parenterale direkte Thrombininhibitoren (Lepirudin (Refludan®) 1998, 2013 abgelaufen; Bivalirudin (Angiox®) 2000; Argatroban (Agatra®) 2000)
2002	Fondaparinux (Arixtra®)
2008	Dabigatran (Pradaxa®)
2008	Rivaroxaban (Xarelto®)
2011	Apixaban (Eliquis®)
2014	Edoxaban (Lixiana®)
2016	Antidote for Dabigatran: Idarucizumab (Praxbind®)
2019	Antidot for F.Xa-Inhibitors: Andexanet alfa (Ondexxya®)



4F-PCC a VKA



Baseline INR	4F-PCC Dose, IU of Factor IX per kg Body Weight*	Plasma Dose, mL per kg Body Weight*
2 to <4	25	10
4-6	35	12
>6	50	15

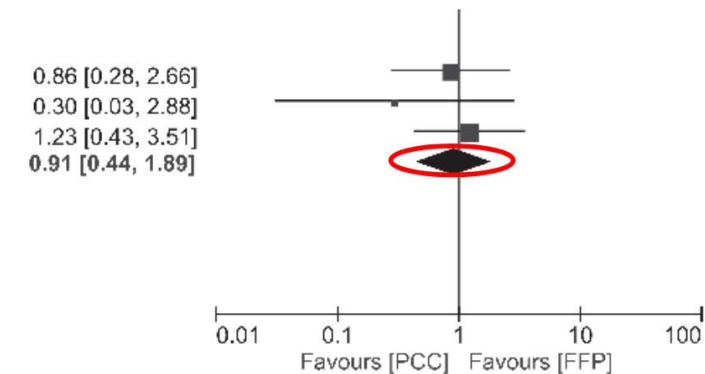
Sarode et al, Circulation. 2013;128:1234-1243

3.2.2 Thromboembolic diseases

Goldstein 2015	6	90	7	91	41.6%
Hickey 2013	1	165	3	149	10.3%
Sarode 2013	8	103	7	109	48.1%
Subtotal (95% CI)		358		349	100.0%

Total events 15 17
 Heterogeneity: Tau² = 0.00; Chi² = 1.26, df = 2 (P = 0.53); I² = 0%
 Test for overall effect: Z = 0.24 (P = 0.81)

Chai-Adisaksopha et al, TH 2016





4F-PCC a DOAC

Anaesthesia 2018, 73, 1535-1545

Erdoes et al. | Direct oral anticoagulants in cardiac surgery

Table 1 Characteristics of DOACs with their specific and non-specific sensitive and (less sensitive) monitoring possibilities, cut-off values for anti-IIa or anti-Xa levels (where appropriate) and time interval for discontinuation before surgery (T_s), specific antidotes and non-specific measures to reduce peri-operative bleeding. Values are plasma concentrations ($\text{ng}\cdot\text{ml}^{-1}$) or hours (h).

DOAC	Monitoring		Cut-off; ($\text{ng}\cdot\text{ml}^{-1}$) High-risk surgery (urgent surgery) ^a	T_s ; (h) Low bleeding risk (high bleeding risk) ^b	Measures to reduce bleeding		
	Specific	Non-specific			Antidote	Non-specific	
					1st choice	2nd choice	
Dabigatran Pradaxa [®]	Anti-IIa	TT/dTT ECT aPTT (PT)	< 30 (< 50)	> 24 (> 48)	Idarucizumab Ciraparantag ^c	Ultrafiltration on CPB Haemodialysis	TXA FVII Fibrinogen
Rivaroxaban Xarelto [®]	Anti-Xa	PT (aPTT)	< 30 (< 50)	> 24 (> 48)	Andexanet alpha ^c Ciraparantag ^c	Four-factor PCC	TXA FVII Fibrinogen
Apixaban Eliquis [®]	Anti-Xa	PT (aPTT)	< 30 (< 50)	> 24 (> 48)	Andexanet alpha ^c Ciraparantag ^c	Four-factor PCC	TXA FVII Fibrinogen
Edoxaban Lixiana [®]	Anti-Xa	PT (aPTT)	< 30 (< 50)	> 24 (> 48)	Andexanet alpha ^c Ciraparantag ^c	Four-factor PCC	TXA FVII Fibrinogen

DOAC, direct oral anticoagulant; TT, thrombin time; dTT, diluted thrombin time; ECT, ecarin clotting time; aPTT, activated prothrombin time; PT, prothrombin time; CPB, cardiopulmonary bypass; PCC, prothrombin complex concentrate; TXA, tranexamic acid.

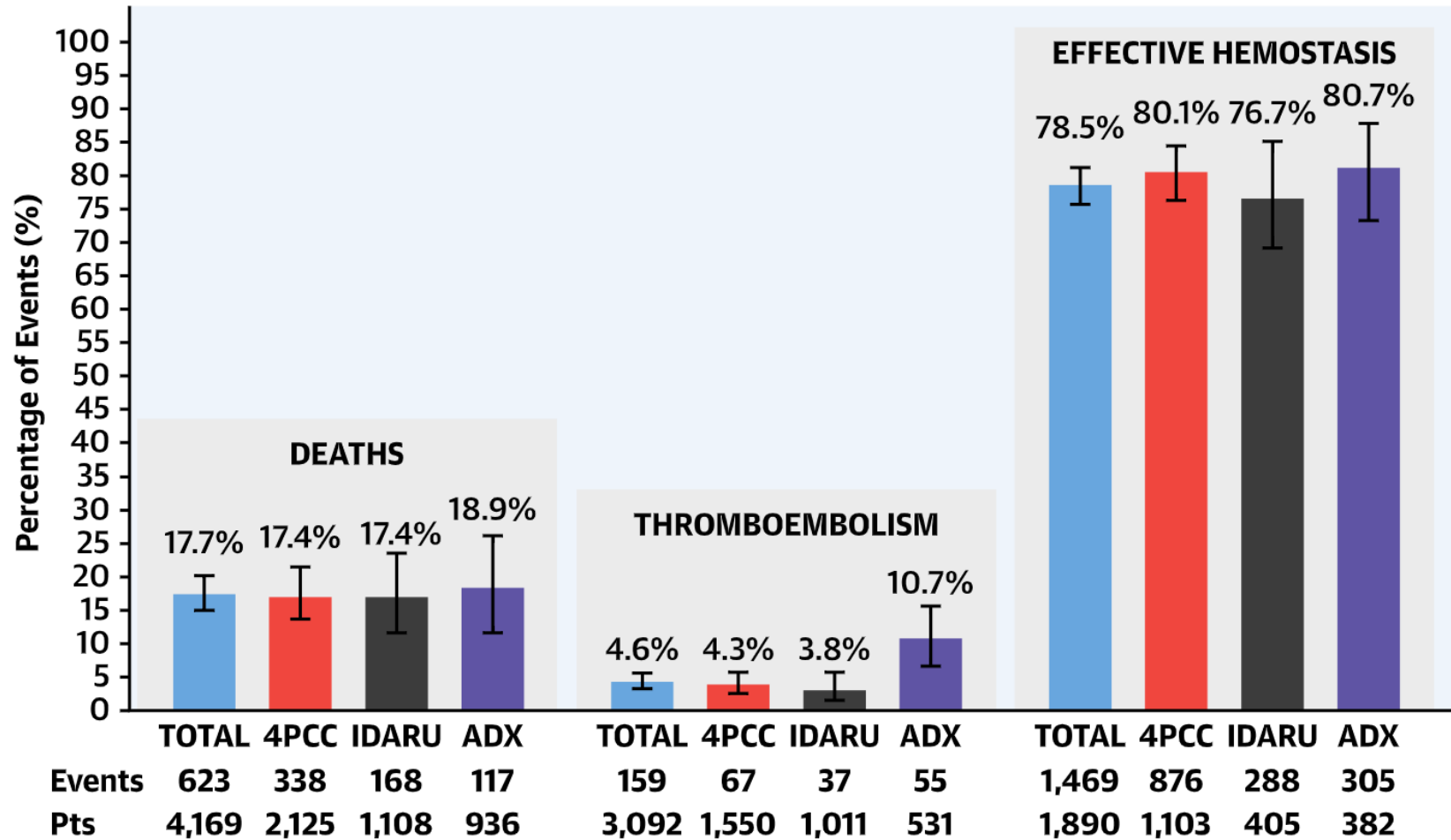
^aUrgent surgery with low bleeding risk.

^bFurther risk factors: elderly patients (> 75 years), renal impairment or failure, low body mass index.

^cRecently approved or under development, not yet licensed or commercially available.



4F-PCC a DOAC





Kyselina tranexamová

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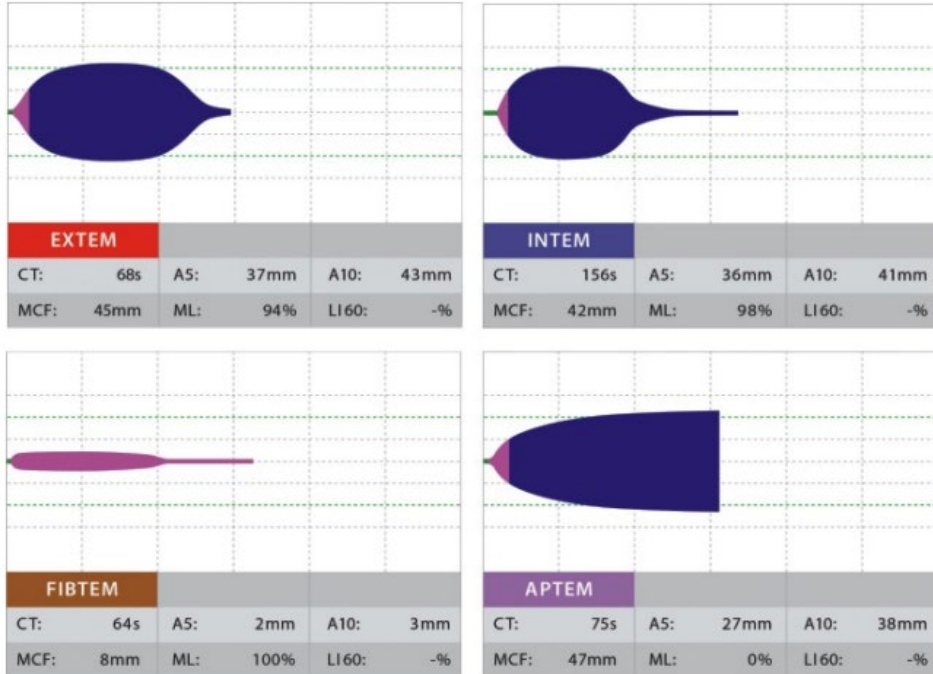
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We recommend that tranexamic acid (TXA) be administered to the trauma patient who is bleeding or at risk of significant bleeding as soon as possible, if feasible en route to the hospital, and within 3 h after injury at a loading dose of 1 g infused over 10 min, followed by an i.v. infusion of 1 g over 8 h **Grade 1A**

We recommend that the administration of TXA not await results from a viscoelastic assessment **Grade 1B**



Kyselina tranexamová – kolik a kdy?

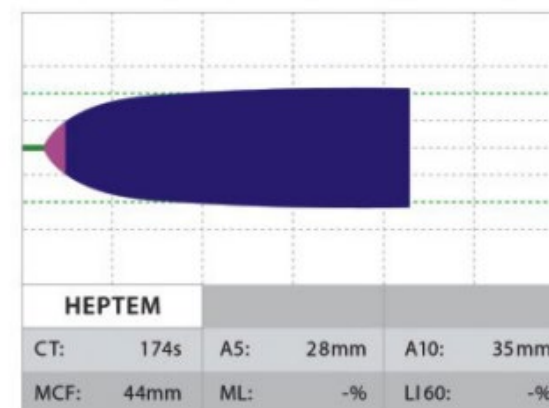
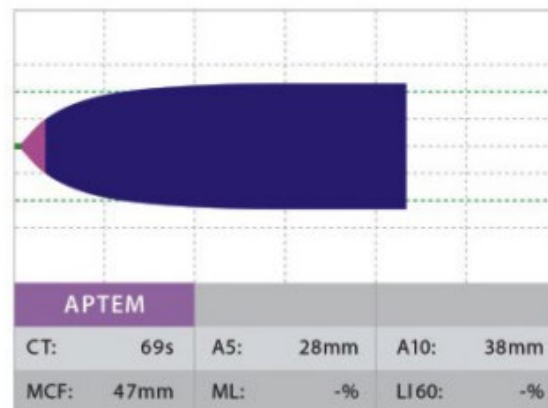
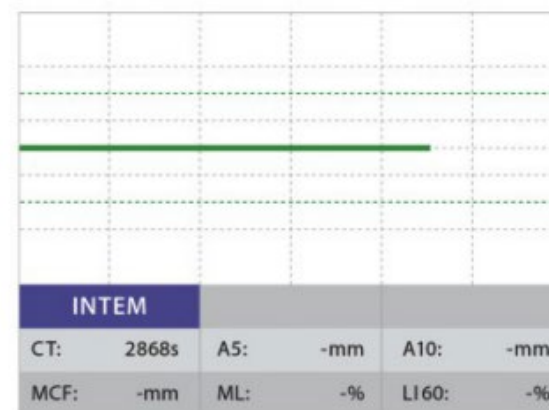
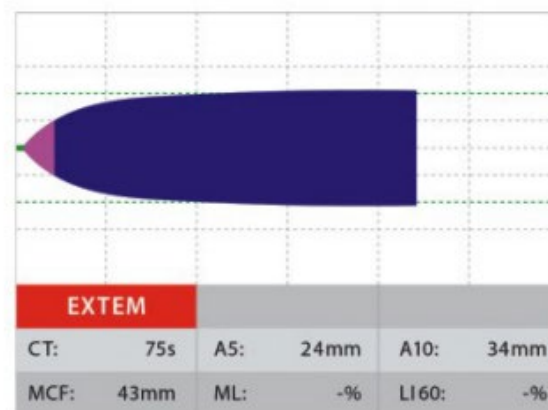


- 15-20mg/kg – vždy co nejdříve





Nezapomínat na heparin



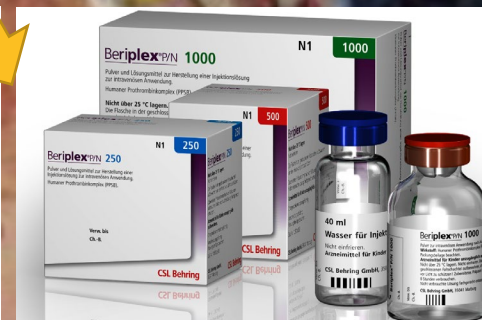
Masivní krvácení – co podám?

krystaloidy + koloidy

ERY + FFP + FBG + 4F-PCC + PLT + TXA



Hemodynamická stabilita



Hemostatická stabilita

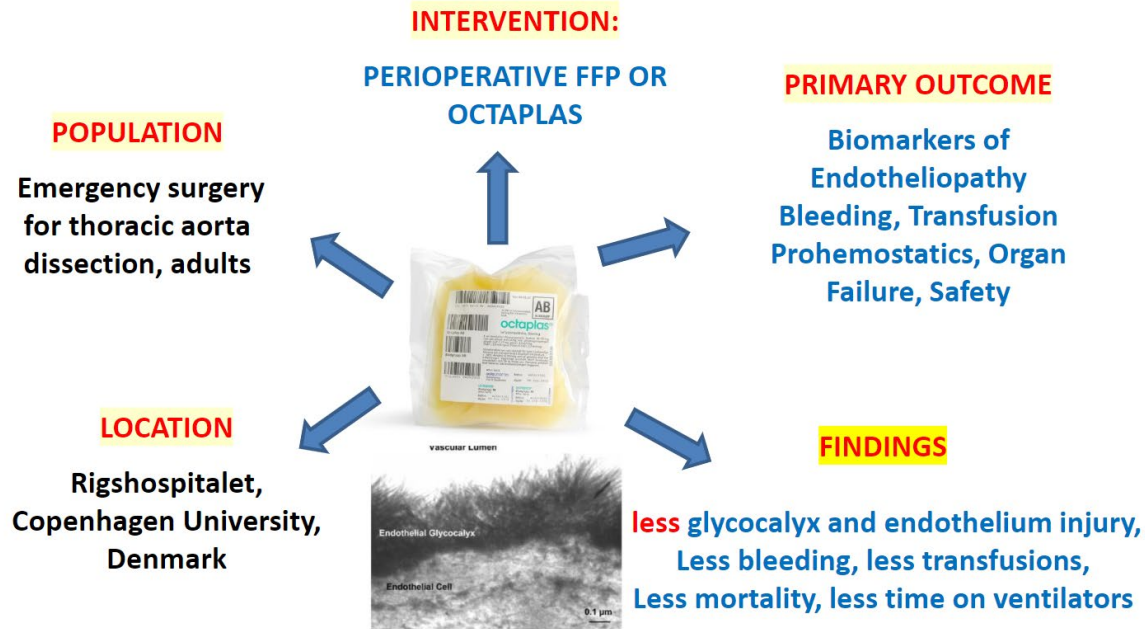
Potřebujeme vše!



FFP vs. SD plazma

Resuscitation of Endotheliopathy and Bleeding in Thoracic Aortic Dissections: The VIPER-OCTA Randomized Clinical Pilot Trial

Anesth Analg 2018;127:920-7



- ↓ less damage to *endothelial glycocalyx* (syndecan-1) *
- ↓ less *endothelial tight junction injury* (sVE-cadherin) *
- ↓ less *microthrombotic adhesion* (sE selectin)
- ↑ better anticoagulation regulation in glycocalyx (TM)
- ↓ less *days on ventilator* (1 day vs 2 days) *
- ↓ less *bleeding* during surgery (2150ml vs 2750ml; 21%) *
- ↓ less *RBC* transfusion (3975ml vs 6220ml, 35%) *
- ↓ less *platelets* transfusion (1400ml vs 2450ml) *
- ↓ fibrinogen, PCC, rFVIIa (7 vs 13 pts) ...fewer fixes
- ↓ less *30-day mortality* (20.7% vs 25%)

Solvent/detergent plazma:

- Virová inaktivace
- Definované množství koagulačních faktorů
- Snížená incidence TRALI



Spolupráce s chirurgem

Management of severe peri-operative bleeding: Guidelines from the European Society of Anaesthesiology and Intensive Care: Second update 2022

“talk to surgeon” is better than “wait till relevant shock index” to start MTP

- Vessel injury
- Surgeon reported that injured vessel is hidden in connective tissue. His opinion that it may take unpredictable time to fix the vessel!

Immediate intervention with MTP (plasma or factors – what’s available sooner)!

- Periodic assessment and addition of concentrates
- Hemodynamic stabilisation and **RBC/FFP/PLT** + goal-directed therapy with concentrates

- Vessel injury
- Visually, blood loss about 1 Litre in few minutes
- The surgeon was able to fix the injured vessel

- Crystalloids and factor concentrates would be enough!
- You will have some time to access coagulation



„time”



and /or



„volume”



Recommendation 16

In the early treatment phase of **uncontrolled massive elective surgery bleeding**, we suggest massive transfusion (≥ 6 to 10 units) with a high ratio ($\geq 1 : 1$) of **plasma to RBCs**. **2C**

We recommend switching to a goal-directed transfusion strategy (based on Hb and/or physiological RBC transfusion triggers, **coagulation factor substitution** and **platelet transfusion triggers**) **as soon as possible**. **1C**



VFN PRAHA

Děkuji za pozornost...