KARDİYAK CERRAHİDE ANTİFİBRİNOLİTİK KULLANIMI

-RUTİN KULLANILMAMALI-

Dr.Zeliha Özer
Maltepe Üniversitesi Tıp Fakültesi
Anesteziyoloji ve Reanimasyon AD

Nothing has been more controversial

in recent times

than the aprotinin controversy.

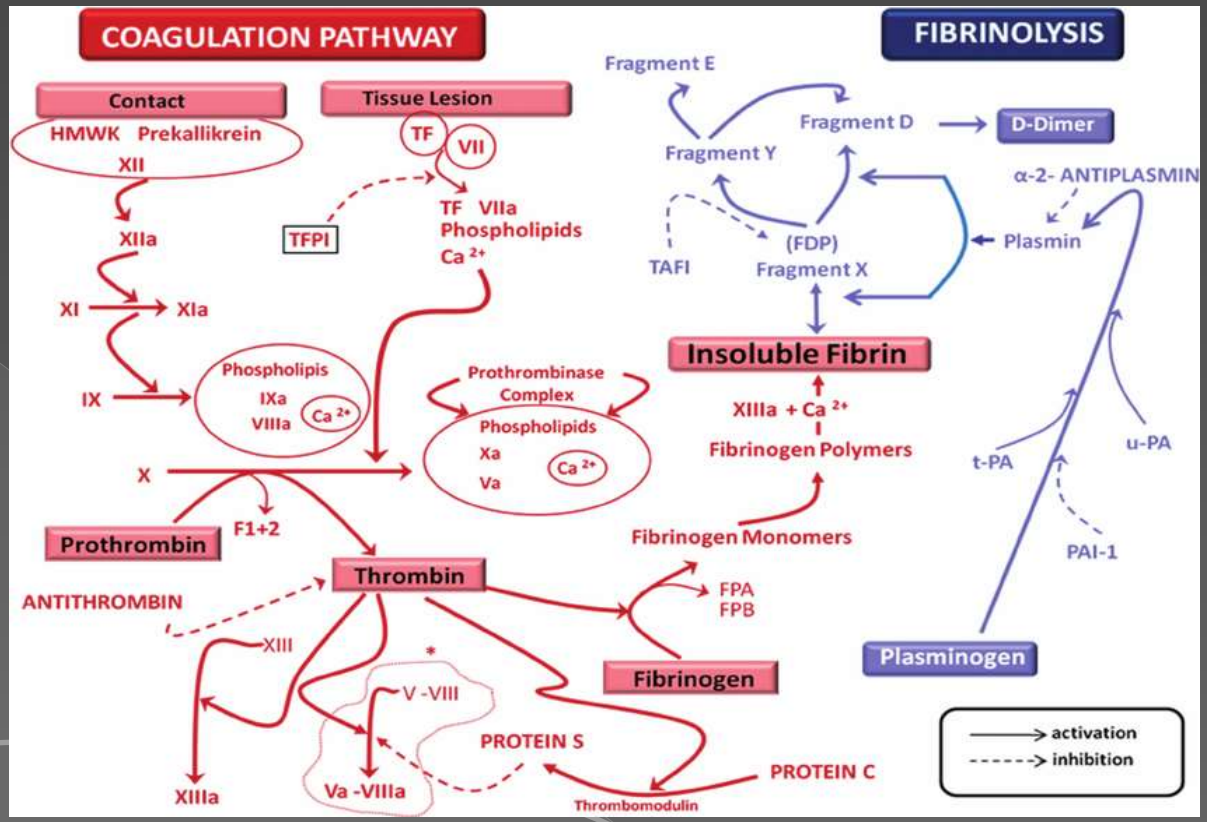
RUTİN OLARAK KULLANMAYALIM

KPB, İNFLAMATUVAR YANIT,KOAGÜLASYON

ANTİFİBRİNOLİTİK İLAÇLARIN YAN ETKİLERİ

HEDEFE YÖNELİK TEDAVİ GEREKLİLİĞİ

KPB



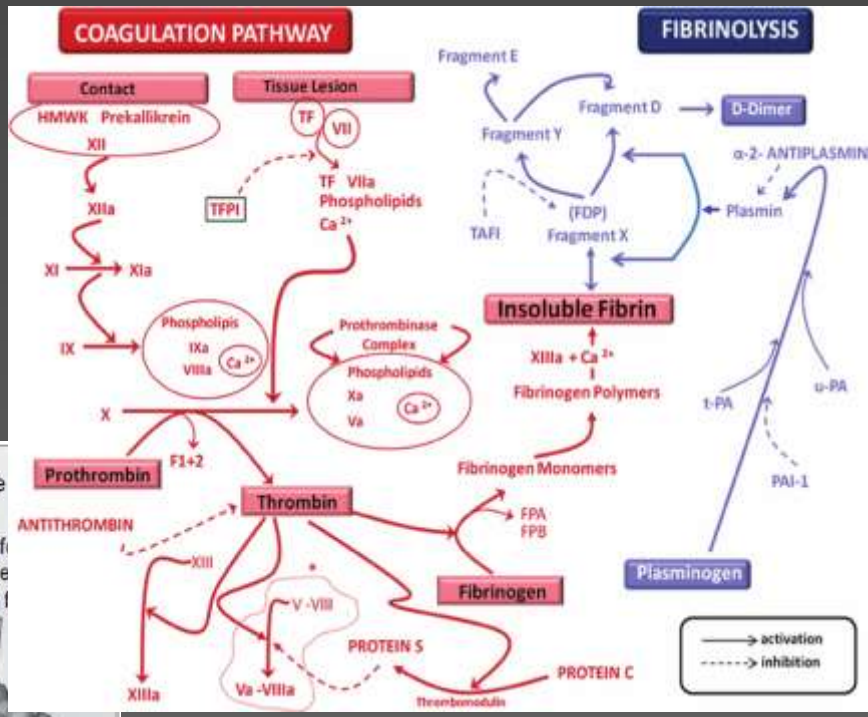
KONTAKT AKTİVASYON
CERRAHİ TRAVMA-DOKU FAKTÖRÜ SALINIMI

İNFLAMASYON
KOAGÜLASYON SİSTEMİNİN AKTİVASYONU

KALP CERRAHİSİNDE KOAGÜLOPATİ MULTİFAKTÖRİYELDİR!!

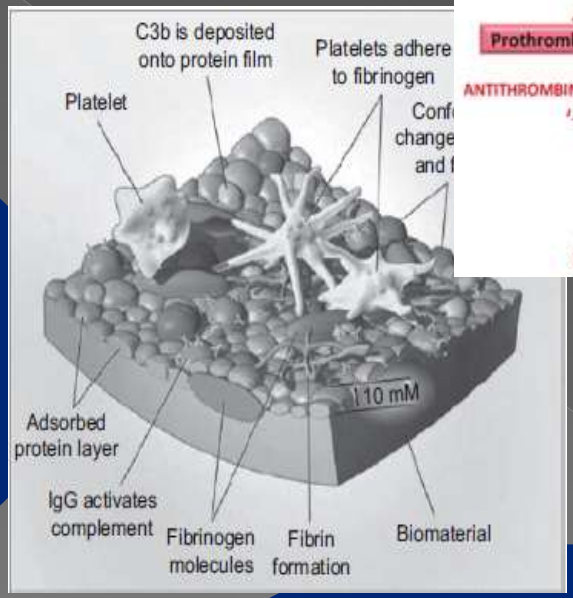
Hemodilüsyon
Tüketim artışı

Koagülasyon faktörlerinde azalma



Hemodilüsyon
Sekestrasyon
Destrüksiyon
Tüketim

Trombosit sayısında azalma



HİPOTERMİ

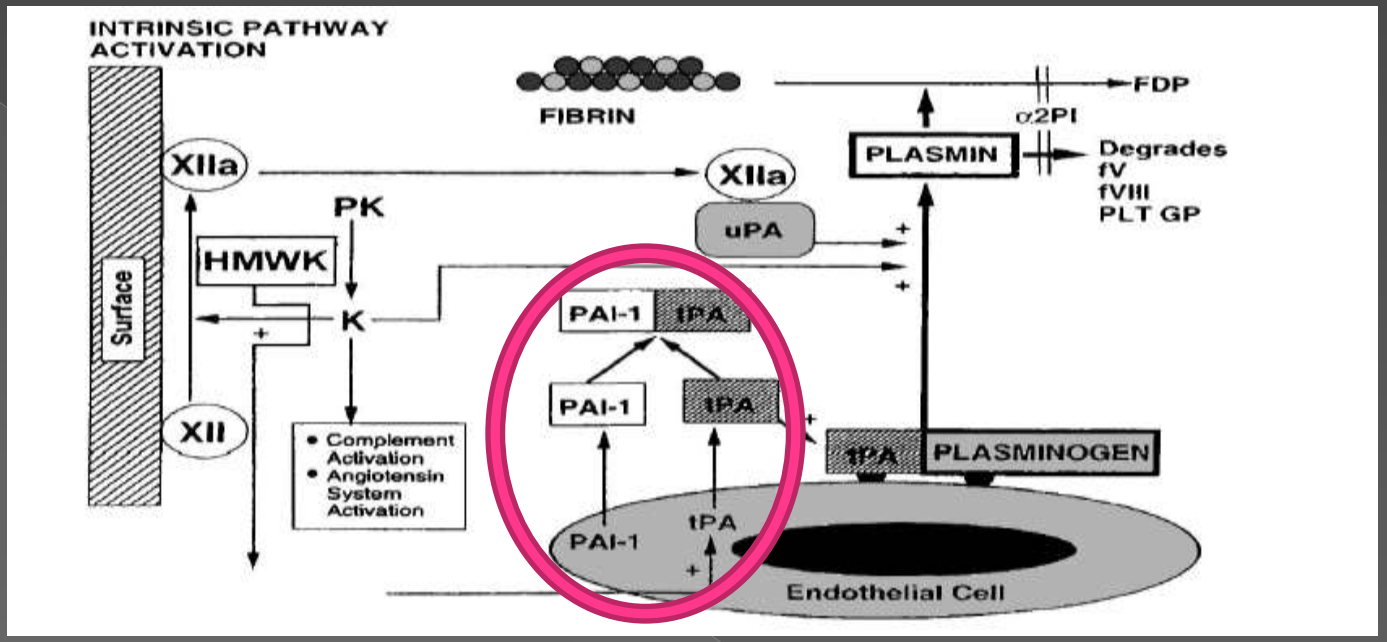
Kompleks cerrahi operasyon
KPB süresi

Hastalara ait ko-morbid nedenler
İlaçlar

KPB'IN NEDEN OLDUĞU FİBRİNOLİTİK YANIT MULTİFAKTÖRİYELDİR VE BİREYSEL FARKLILIKLAR GÖSTERİR!!

Endotelyal hücre aktivasyonu ve doku plazminojen aktivatörü salınımı

Thromb Haemost. 1995 Nov;74(5):1293-7
İndividual variations in the fibrinolytic response during and after cardiopulmonary bypass.
Chandler WL[1], Fitch JC, Wall MH, Verrier ED, Cochran RP, Soltow LO, Spiess D.



KPB

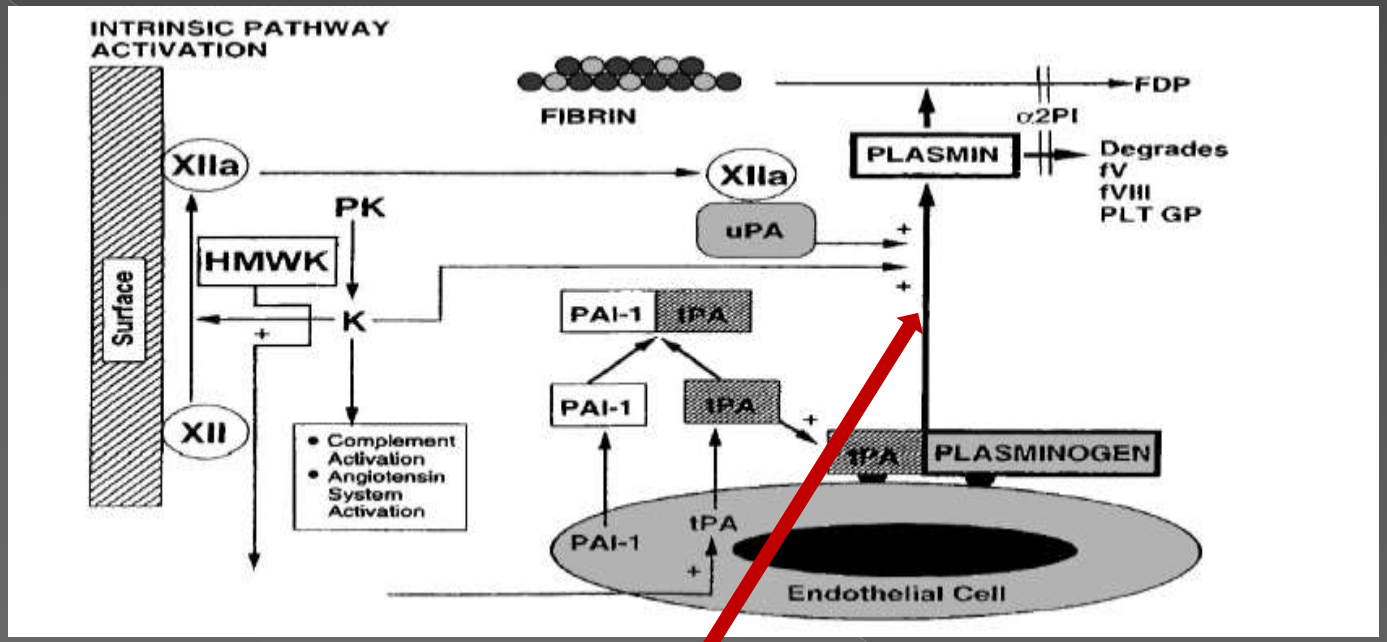
Doku plazminojen aktivatörü (tPA) ↑

Doku plazminojen aktivatör inhibitörü (tPAI) ↓

KPB SONRASI

(tPAI) HIZLA YÜKSELİR

Arteryel tromboz
Vasküler graft oklüzyonu
Derin ven trombozu
İnme
Miyokardiyal iskemi-enfarkt



ANTİFİBRİNOLİTİKLER

Hemostasis

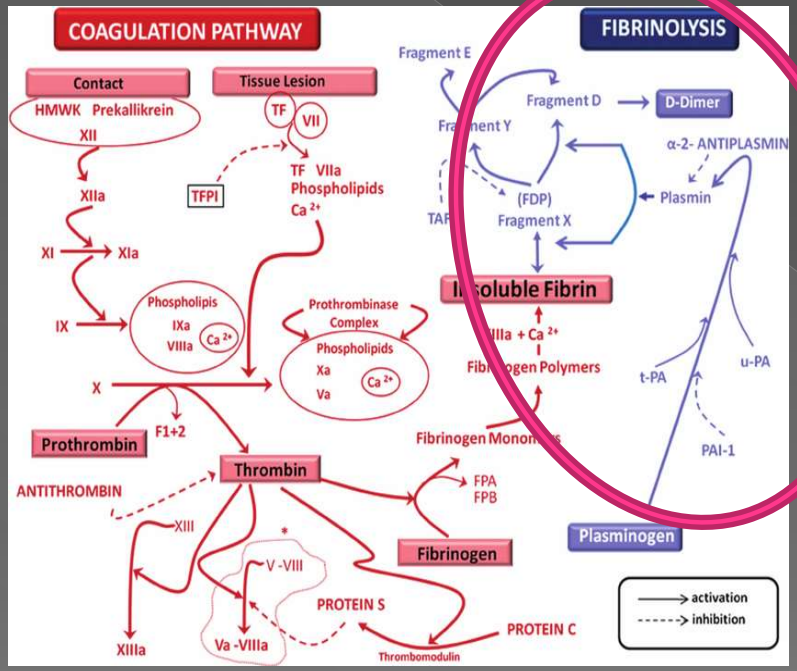
Antifibrinolitikler

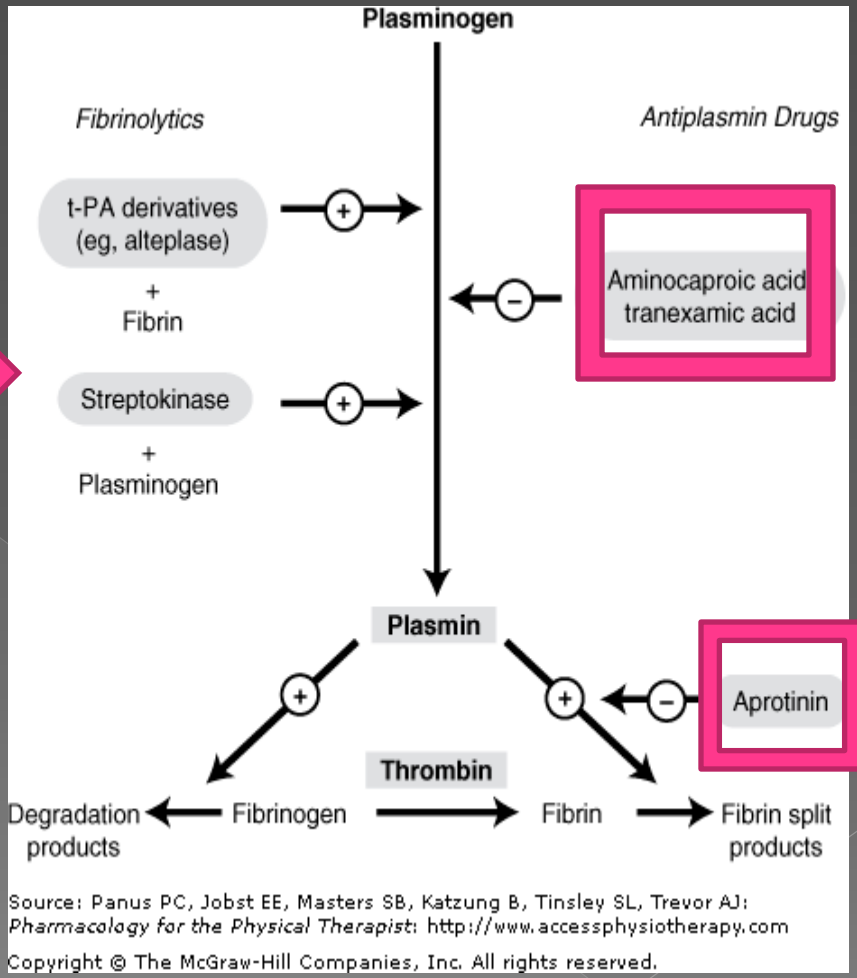
Süregelen intravasküler koagülasyon ve sekonder fibrinoliz varlığında hastalar için potansiyel olarak zararlı olabilirler

Stroke, MI,
Thrombosis,
DVT, PE

Major surgery
Trauma
Hemophilia

BioNep, Inc.


COAGULATION PATHWAY
FIBRINOLYSIS
Contact
Tissue Lesion
HMWK Prekallikrein
XII
XIIa
TF
VII
TF VIIa
Phospholipids
Ca 2+
TFPI
XI
XIa
IX
Phospholipis
IXa
VIIIa
Ca 2+
Prothrombinase Complex
Phospholipids
Xa
Va
X
Prothrombin
F1+2
Thrombin
ANTITHROMBIN
XIII
XIIIa
V -VIII
Va -VIIIa
PROTEIN S
PROTEIN C
Thrombomodulin
FPA
FPB
Fibrinogen
Fragment E
Fragment D
D-Dimer
Fragment Y
α-2- ANTIPLASMIN
Plasmin
(FDP)
Fragment X
Soluble Fibrin
Fibrinogen Polymers
t-PA
u-PA
PAI-1
Plasminogen
activation
inhibition


Plasminogen
Fibrinolytics
Antiplasmin Drugs
t-PA derivatives (eg, alteplase)
+
Fibrin
Streptokinase
+
Plasminogen
Aminocaproic acid
tranexamic acid
Plasmin
Aprotinin
Thrombin
Degradation products
Fibrinogen
Fibrin
Fibrin split products
Source: Panus PC, Jobst EE, Masters SB, Katzung B, Tinsley SL, Trevor AJ: Pharmacology for the Physical Therapist: http://www.accessphysiotherapy.com
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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 29, 2008 VOL. 358 NO. 22

A Comparison of Aprotinin and Lysine Analogues in High-Risk Cardiac Surgery

Dean A. Fergusson, M.H.A., Ph.D., Paul C. Hébert, M.D., M.H.Sc., C. David Mazer, M.D., Stephen Fremes, M.D., Charles MacAdams, M.D., John M. Murkin, M.D., Kevin Teoh, M.D., M.Sc., Peter C. Duke, M.D., Ramiro Arellano, M.D., M.Sc., Morris A. Blajchman, M.D., Jean S. Bussières, M.D., Dany Côté, M.D., Jacek Karski, M.D., Raymond Martineau, M.D.,* James A. Robblee, M.D., M.B.A., Marc Rodger, M.D., M.Sc., George Wells, Ph.D., Jennifer Clinch, M.A., and Roanda Pretorius, M.Sc., for the BART Investigators†

DISCUSSION

Among patients undergoing high-risk cardiac surgery, we documented an increase of 2 percentage points in the rate of death (from approximately 4% to 6%) among patients receiving aprotinin, as compared with those receiving either tranexamic acid or aminocaproic acid. The observed increase in mortality translates into a number needed to harm of 50 patients. When we compared the combined mortality rates in the lysine-analogue groups with the rate in the aprotinin group, we noted a significant absolute increase of 2.1%, or a relative increase of 54%, in the number of deaths in the aprotinin group.

J Anesth (2010) 24:96–106
DOI 10.1007/s00540-009-0866-9

REVIEW ARTICLE

Lessons from the aprotinin saga: current perspective on antifibrinolytic therapy in cardiac surgery

Masahiro Ide · Daniel Bolliger · Taro Taketomi · Kenichi A. Tanaka

Re-evaluation of the role of antifibrinolytic therapy with lysine analogs during cardiac surgery in the post aprotinin era

Andreas Koster and Uwe Schirmer

Institute of Anesthesiology, Heart and Diabetes Center Nordrheinwestfalen, Bad Oeynhausen, Ruhr University of Bochum, Bochum, Germany

Purpose of review

Hemorrhage, transfusions and the need for re-exploration can have a detrimental effect

Yarar/risk profilini yükseltmek için, yetkililer bu güçlü ilaçların kullanımını daha iyi kontrol etmek zorundadır!
Gereken önlemler en kısa süre içinde alınmalıdır!

Lizin analoglarının güvenlik ve etkinlikleri ile ile ilgili yeterli düzeyde araştırma yapılmış mıdır

Kanamayı azaltıyor!!
Kan transfüzyonunu azaltıyor???

RE-EKSPLORASYONU azaltıyor mu?
MORTALİTE üzerine olumlu etkileri var mı?
KAR-ZARAR araştırması yapılmış mıdır?

Seizure 36 (2016) 70–73

Contents lists available at ScienceDirect

Seizure

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

Review

Tranexamic acid-associated seizures: A meta-analysis

Zhang Lin, Zou Xiaoyi *

Department of Neurology, West China Hospital, Sichuan University, Chengdu, China

-Traneksamik asit kan-beyin bariyerini geçebilir.

-Nöronlar ve glial hücreleri etkileyerek serebral fonksiyonlarda bozulmalara yol açabilir.

-Postoperatif konvülzyon insidansında artışa neden olduğunu gösteren bir çok çalışma vardır.

.10

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European Journal of Cardio-thoracic Surgery 39 (2011) e114–e121

EUROPEAN JOURNAL OF
CARDIO-THORACIC
SURGERY

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High-dose tranexamic acid is related to increased risk of generalized seizures after aortic valve replacement

Cornelius Keyl [a,*], Reiner Uhl [b], Friedhelm Beyersdorf [c], Susanne Stampf [d], Cornelius Lehane [b], Christoph Wiesenack [e], Dietmar Trenk [f]

[a] Department of Anesthesiology, Heart Center Bad Krozingen, Bad Krozingen, Germany

ures and by translating scientific findings into therapeutic interventions for patients.

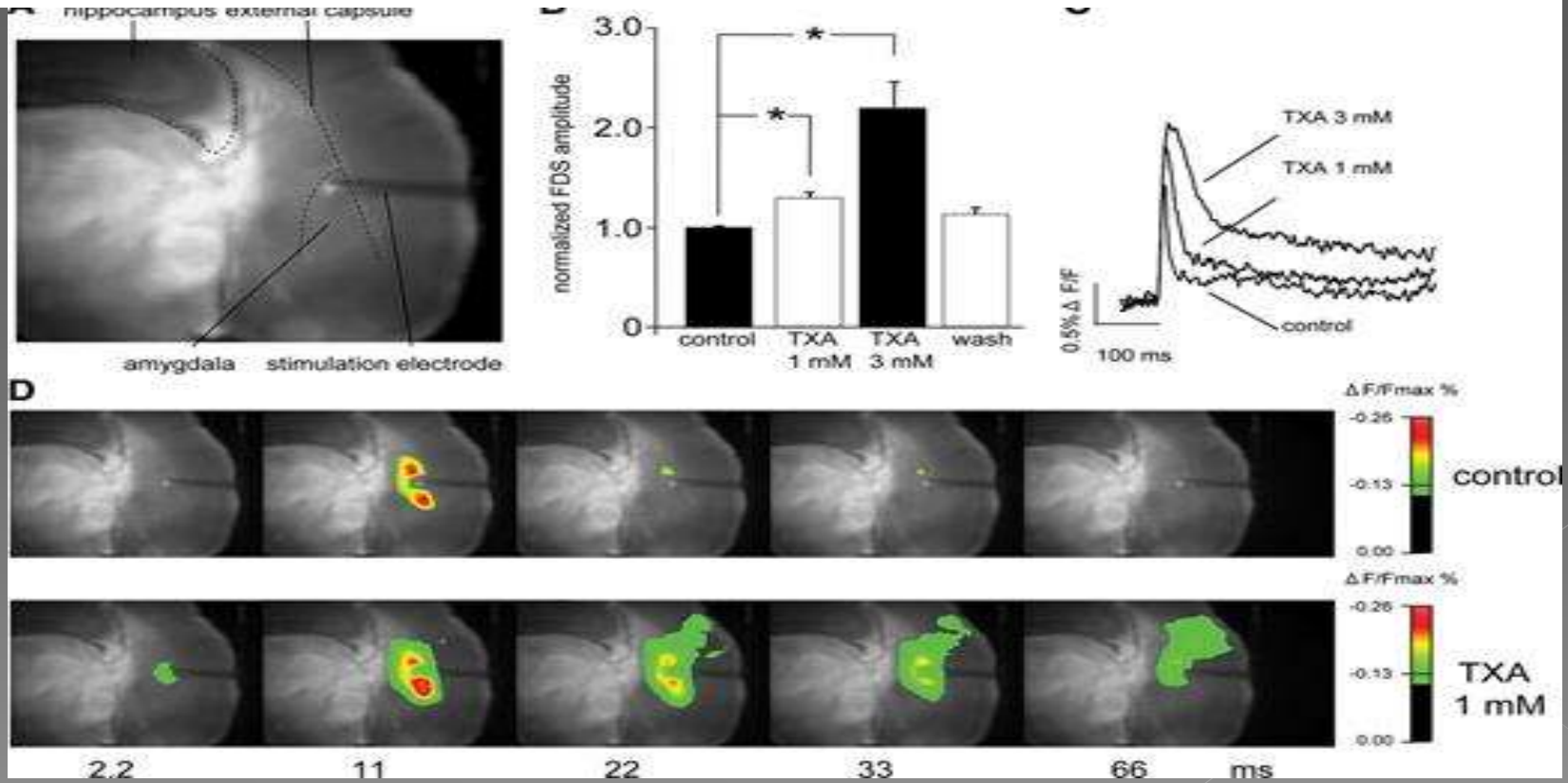
ANN NEUROL 2016;79:18–26

Traneksamik asit GABA ve glisin'i antagonize ederek nöronal eksitasyonu arttırmaktadır!

Tranexamic Acid Impairs γ-Aminobutyric Acid Receptor Type A–mediated Synaptic Transmission in the Murine Amygdala

A Potential Mechanism for Drug-induced Seizures?

Stephan Kratzer, M.D., Hedwig Irl, M.S., Corinna Mattusch, Ph.D., Martina Bürge, M.D., Jörg Kurz, M.D., Eberhard Kochs, M.D., Matthias Eder, Ph.D., Gerhard Rammes, Ph.D., Rainer Haseneder, M.D.



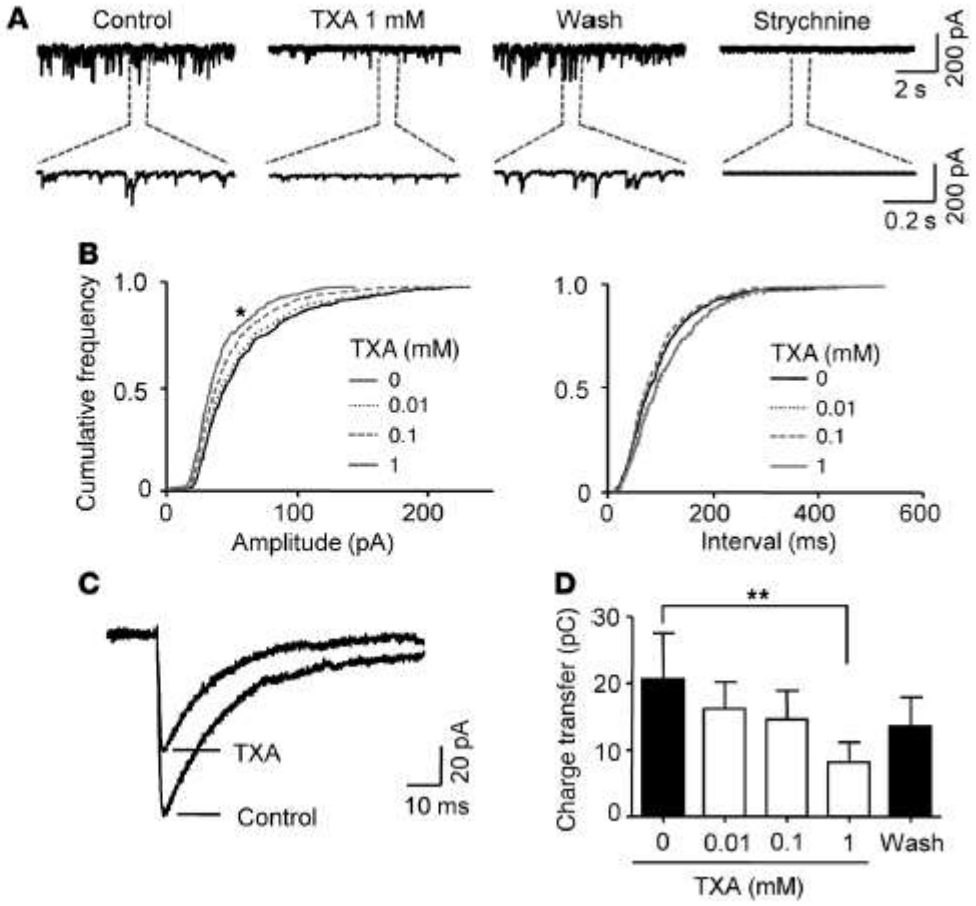


Figure 5

TXA inhibits glycinergic mIPSCs at higher concentrations. (**A**) Glycinergic mIPSCs recorded from a spinal cord neuron, in the absence and presence of TXA. Application of strychnine abolished all glycinergic mIPSCs. pC stands for picocoloumbs. (**B**) Cumulative frequency plots for mIPSCs show the effect of TXA on the amplitude and inter-event interval. TXA (1 mM) significantly decreased the amplitude of the mIPSCs (left panel) without affecting the inter-event interval (right panel). (**C**) Average traces from 100 individual mIPSCs before and after application of TXA (1 mM). Data for **A**–**C** were obtained from the same spinal cord neuron. (**D**) TXA (1 mM) significantly decreased charge transfer of glycinergic mIPSCs, whereas lower concentrations had no significant effect ($n = 5$). $^{*}P < 0.05$, $^{**}P < 0.01$ versus 0 TXA. Data are mean ± SEM.

ELSEVIER

European Journal of Cardio-thoracic Surgery 37 (2010) 1375–1383

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

Review

Lessons from aprotinin: is the routine use and inconsistent dosing of tranexamic acid prudent? Meta-analysis of randomised and large matched observational studies☆

Dumbor L. Ngaage[a,*], John Martin Bland[b]

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[b] *Department of Health Sciences, University of York, United Kingdom*

Received 30 September 2009; received in revised form 15 November 2009; accepted 18 November 2009; Available online 1 February 2010

Traneksamik asit yan etkileri doz bağımlıdır!

DOZ???

Jerrold H. Levy, M.D., F.A.H.A., F.C.C.M., Editor

Antifibrinolytic Therapy for Cardiac Surgery

An Update

Andreas Koster, M.D., David Faraoni, M.D., F.C.C.P., Jerrold H. Levy, M.D., F.A.H.A., F.C.C.M.

Table 1. Antifibrinolytic Agents: Drugs Description, Doses, and Mechanisms of Action

Drugs	Composition	Mechanism of Action	Elimination	Pharmacodynamics	Suggested Dosing in Adults	Approval
Aprotinin	Protein, isolated from bovine lung tissue	Protease inhibitor; reversibly complexes with the active sites of plasmin, kallikrein, and trypsin; inhibition of fibrinolysis, activated factor XIIa, thrombin-induced platelet activation, and inflammatory response	Predominantly proteolysis, <10% renal	Initial plasma half-life 150 min and terminal half-life 10 h	1. "Full dose": 2×10^6 KIU bolus patient, 2×10^6 KIU bolus CPB, continuous infusion of 5×10^5 KIU. 2. "Half dose": 1×10^6 KIU bolus patient, 1×10^6 KIU bolus CPB, continuous infusion of [illegible] KIU	Suspended since 2008; suspension lifted in Canada in 2011 and Europe in 2012; In the United States still suspended
Tranexamic acid	Synthetic lysine analog	Antifibrinolytic; competitive inhibition of the activation of plasminogen to plasmin	Renal	Plasma half-[illegible] 3 h	1. "High dose": 30 mg/kg bolus patient, 2 mg/kg CPB, and continuous infusion of 16 mg/kg; 2. "Low dose": 10 mg/kg bolus patient, 1–2 mg CPB, and continuous infusion of 1 mg/kg	[illegible]ited States, Canada, E[illegible]ope
ε-Aminocaproic acid	Synthetic lysine analog	Antifibrinolytic: competitive inhibition of the activation of plasminogen to plasmin	Renal	Plasma half-life 2 h	100 [illegible] mg/kg bolus patient, [illegible] mg/kg CPB, and continuous infusion of 30 mg/kg	United States, Canada

CPB = cardiopulmonary bypass; KIU = Kallikrein International Unit.

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European Journal of Cardio-thoracic Surgery 39 (2011) e114–e121

www.elsevier.com/locate/ejcts

High-dose tranexamic acid is related to increased risk of generalized seizures after aortic valve replacement

Cornelius Keyl [a,*], Reiner Uhl [b], Friedhelm Beyersdorf [c], Susanne Stampf [d], Cornelius Lehane [b], Christoph Wiesenack [e], Dietmar Trenk [f]

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[c] Department of Cardiovascular Surgery, University Medical Center Freiburg, Freiburg, Germany
[d] Institute of Medical Biometry and Medical Informatics, University Medical Center Freiburg, Freiburg, Germany
[e] Department of Anesthesiology, Marienhospital Gelsenkirchen, Gelsenkirchen, Germany
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Received 21 September 2010; received in revised form 20 December 2010; accepted 21 December 2010; Available online 4 February 2011

Abstract

Objective: To investigate the incidence of postoperative generalized seizures in patients undergoing aortic valve replacement (AVR) under extracorporeal circulation, who received either high-dose tranexamic acid (TXA) or epsilon aminocaproic acid (EACA) as an antifibrinolytic agent. **Methods:** This retrospective analysis comprised 682 consecutive patients undergoing AVR with or without simultaneous coronary artery bypass surgery. Patients operated on before March 2008 were treated intra-operatively with TXA (100 mg kg^{-1}; $n = 341$), patients operated on after March 2008 received EACA (50 mg kg^{-1} loading dose, followed by 25 mg kg^{-1} h^{-1}, and an additional 5 g in the extracorporeal circuit; $n = 341$).

100mg/kg

50mg/kg, yükleme dozu, 25mg/kg/h infüzyon

British Journal of Anaesthesia **110** (1): 34–40 (2013)
Advance Access publication 17 September 2012 · doi:10.1093/bja/aes310

BJA

Moderate dosage of tranexamic acid during cardiac surgery with cardiopulmonary bypass and convulsive seizures: incidence and clinical outcome

A. Koster[1]*, J. Börgermann[2], A. Zittermann[2], J. U. Lueth[1], T. Gillis-Januszewski[2] and U. Schirmer[1]

[1] Institute for Anaesthesiology and [2] Department of Cardiac and Thoracic Surgery, Heart and Diabetes Centre North Rhine-Westphalia, Bad Oeynhausen, Ruhr-University Bochum, Georgstr. 11, D-32545 Bad Oeynhausen, Germany

* Corresponding author. E-mail: akoster@hdz-nrw.de

Editor's key points

- This is a retrospective data analysis of 4883 patients who underwent cardiac surgery.

Background. Convulsive seizures (CS) occur in ~1% of the patients after cardiac surgery with cardiopulmonary bypass. Recent investigations indicate an up to seven-fold increase in CS in cardiac surgical patients receiving high doses (>60 mg kg^{-1} body weight) of tranexamic acid (TA).

Methods. In a retrospective data analysis of 4883 cardiac surgical patients, we investigated the incidence of CS in patients receiving a moderate dose of TA (24 mg kg^{-1} body weight)

Table 4 Primary and secondary endpoints according to surgical procedure in the tranexamic acid and reference group. Continuous data are presented as mean (SD). CABG, coronary artery bypass grafting; TA, tranexamic acid

Parameter	Reference group, CABG (n=1707)	TA group, CABG (n=397)	P-value
Primary endpoint			
Convulsive seizures (%)	1.2	1.8	0.322
Secondary endpoints			
Duration of mechanical ventilation support (h)	18.7 (82.3)	21.9 (71.1)	0.024
Intensive care unit stay (h)	60.4 (133.7)	77.2 (186.6)	0.039
In-hospital mortality (%)	1.1	1.5	0.446
	Reference group, open heart (n=2143)	**TA group, open heart (n=636)**	**P-value**
Primary endpoint			
Convulsive seizures (%)	1.3	3.0	0.004
Secondary endpoints			
Duration of mechanical ventilation support (h)	25.1 (99.2)	47.0 (144.9)	<0.001
Intensive care unit stay (h)	71.4 (137.6)	122.5 (205.1)	<0.001
In-hospital mortality (%)	1.7	5.7	<0.001

Seizures After Open Heart Surgery: Comparison of ε-Aminocaproic Acid and Tranexamic Acid

Klaus Martin, MD,* Jürgen Knorr, MD,* Tamás Breuer, MD,* Ralph Gertler, MD,* Martin MacGuill, MD,* Rüdiger Lange, PhD,† Peter Tassani, PhD,* and Gunther Wiesner, PhD*

Objective: Although the lysine analogs tranexamic acid (TXA) and aminocaproic acid (EACA) are used widely for antifibrinolytic therapy in cardiac surgery, relatively little research has been performed on their safety profiles, especially in the setting of cardiac surgery. Two antifibrinolytic protocols using either TXA or aminocaproic acid were compared according to postoperative outcome.

Design: A retrospective analysis.

Setting: A university-affiliated hospital.

Participants: Six hundred four patients undergoing cardiac surgery.

Interventions: One cohort of 275 consecutive patients received TXA; a second cohort of 329 consecutive patients was treated with EACA. Except for antifibrinolytic therapy, the anesthetic and surgical teams and their protocols remained unchanged.

Measurements and Main Results: Besides major outcome criteria, namely postoperative bleeding, the need for allogeneic transfusions, operative revision because of bleeding, postoperative renal dysfunction, neurologic events, heart failure, and in-hospital mortality, the authors specifically sought differences between the groups concerning seizures. The 2 cohorts were comparable over a range of perioperative factors. Postoperative seizures occurred significantly more frequently in TXA patients (7.6% *v* 3.3%, $p = 0.019$), whereas EACA patients had a higher incidence of postoperative renal dysfunction (20.0% *v* 30.1%, $p = 0.005$). There were no differences in all other measured major outcome factors.

Conclusion: Both lysine analogs are associated with significant side effects, which must be taken into account when performing risk-benefit analyses of their use. Their use should be restricted to patients at high risk for bleeding; routine use on low-risk patients undergoing standard surgeries should face renewed critical reappraisal.

KEY WORDS: cardiac surgery, tranexamic acid, aminocaproic acid, clinical outcome, bleeding, seizure

Table 4. Postoperative Outcome

	EACA (n = 329)	TXA (n = 275)	*p* Value	Relative Risk (95%-CI)
Seizure	11 (3.3)	21 (7.6)	0.019	0.44 (0.89-0.22)
Stroke/TIA	5 (1.5)	4 (1.5)	1.00*	1.04 (3.85-0.28)
Revision because of bleeding	24 (7.3)	10 (3.6)	0.052	2.00 (4.17-0.98)
Renal dysfunction	99 (30.1)	55 (20.0)	0.005	1.49 (2.00-1.12)
Renal failure	32 (9.7)	23 (8.4)	0.562	1.16 (1.92-0.70)
Heart failure	11 (3.3)	5 (1.8)	0.313*	1.85 (5.26-0.65)
In-hospital mortality	16 (5.0)	13 (4.7)	0.899	1.03 (2.08-0.50)

NOTE. Data are presented as patient numbers (percentages) with *p* values for chi-square tests.

Abbreviation: TIA, transient ischemic attack.

Orta doz traneksamik asit bile konvülzyon oranını 2 katına çıkarmaktadır.

Özellikle açık kalp cerrahisi uygulanan hastalar risk altındadır.

Traneksamik asit'in güvenlik profilini belirlemek için prospektif klinik çalışmalara gereksinim vardır.

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Advance Access publication 23 July 2013 · doi:10.1093/bja/aet255

BJA

Population pharmacokinetics of tranexamic acid in adults undergoing cardiac surgery with cardiopulmonary bypass

S. Grassin-Delyle[1,3*], B. Tremey[2], E. Abe[3], M. Fischler[2,4], J. C. Alvarez[3,4], P. Devillier[1,4] and S. Urien[5,6]

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E-mail: s.grassindelyle@hopital-foch.org

DÜŞÜK DOZ 10 mg/kg bolus, 1mg/kg/st inf., 1mg/kg KPB
Konsantrasyon 28-55 µg/mL

YÜKSEK DOZ 30 mg/kg bolus, 16mg/kg/st inf., 2mg/kg KPB
Konsantrasyon 114-209 µg/mL

Society of Cardiovascular Anesthesiologists

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Hemostasis and Transfusion Medicine Section Editor: Jerrold H. Levy

SPECIAL ARTICLE

The Effective Concentration of Tranexamic Acid for Inhibition of Fibrinolysis in Neonatal Plasma In Vitro

Branden E. Yee, MD, MPH,* Richard N. Wissler, MD, PhD,* Christine N. Zanghi, MD, PhD,* Changyong Feng, PhD,*† and Michael P. Eaton, MD*

October 2013 • Volume 117 • Number 4

www.anesthesia-analgesia.org

Fibrinolizisi tamamen önlemek için traneksamik asit minimum konsantrasyonu **bebeklerde 6.54µg/mL, erişkinlerde 17.5µg/mL.dir.**

ELSEVIER

European Journal of Cardio-thoracic Surgery 35 (2009) 167–171

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

The blood sparing effect and the safety of aprotinin compared to tranexamic acid in paediatric cardiac surgery☆

Tamás Breuer [a,d], Klaus Martin [a,*], Markus Wilhelm [a], Gunther Wiesner [a], Christian Schreiber [b], John Hess [c], Rüdiger Lange [b], Peter Tassani [a]

Table 3
Postoperative outcome.

	Tranexamic acid ($n = 114$)	Aprotinin ($n = 85$)	p value
Mechanical ventilation (h)	23 (10–81)	38 (14–92)	0.13
ICU stay (day)	7 (4–13)	8 (5–12)	0.44
Rethoracotomy	11 (9.6%)	2 (2.4%)	**0.039**
Low cardiac output syndrome	14 (12.3%)	11 (12.9%)	0.89
Renal injury	11 (9.6%)	9 (10.6%)	0.83
Renal failure	2 (1.8%)	0	0.51
Seizure	4 (3.5%)	0	0.14
Other neurological events	3 (2.6%)	4 (4.7%)	0.46
In-hospital mortality	3 (2.6%)	3 (3.5%)	0.70

Data are presented as median (25–75th percentile) or incidence (percent). ICU, intensive care unit. Bold indicates significant value.

TX 50mg/kg bolus, pre-post KPB
100mg/100mL pompa

Traneksamik asit grubunda , erişkin hastalara benzer oranda konvulzyon (+)

İnfantlarda postoperatif konvülzyon nörolojik gelişimi olumsuz etkileyeceğinden çok ciddi bir durumdur!!

Endikasyonu tam olarak belirlemeden herhangi bir ilacın rutin olarak kullanımından vazgeçilmelidir!

Perioperatif monitorizasyon ile **hiperfibrinolizis belirlenerek** antifibrinolitik ajanların kullanımı daha akılcı olacaktır!!

Management of Hemorrhage in Cardiothoracic Surgery

Klaus Görlinger, MD,[*] Linda Shore-Lesserson, MD,[†] Daniel Dirkmann, MD,[*] Alexander A. Hanke, MD,[‡] Niels Rahe-Meyer, MD,[‡,§] and Kenichi A. Tanaka, MD, MSc[¶]

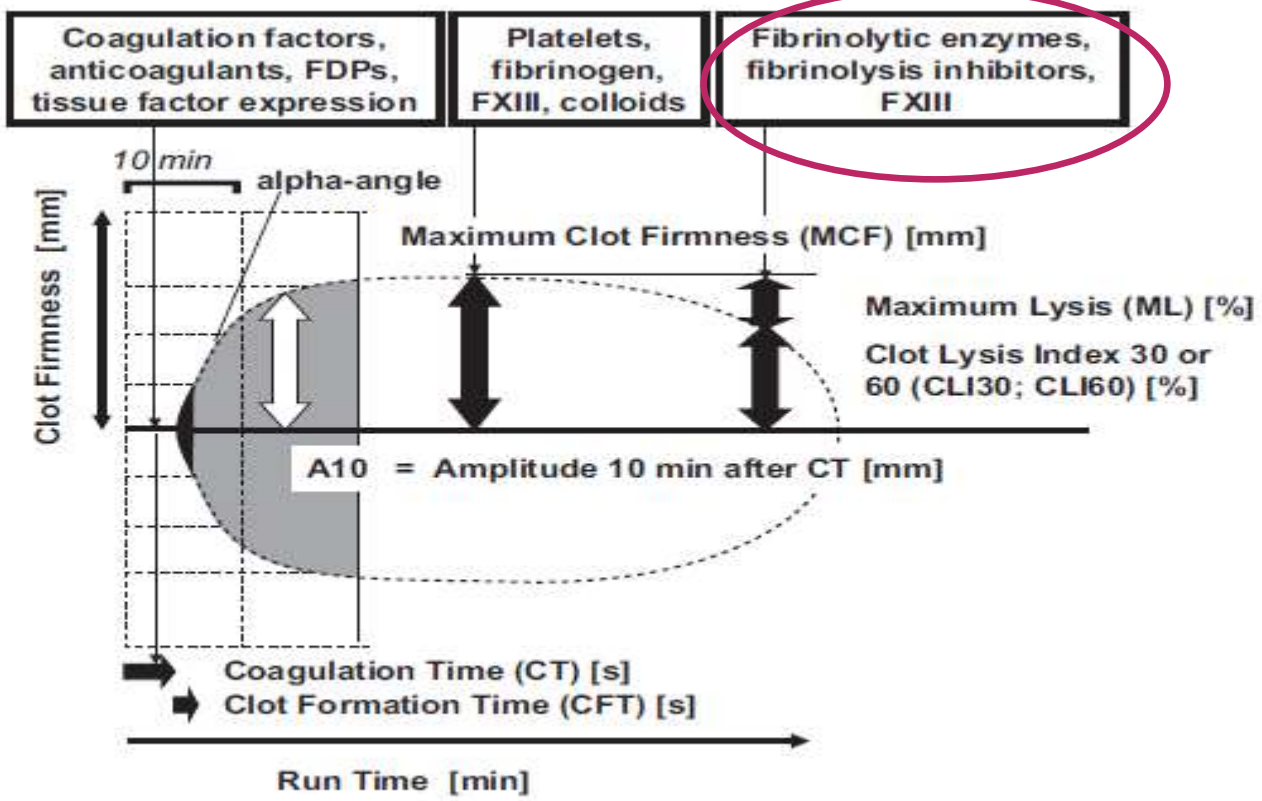


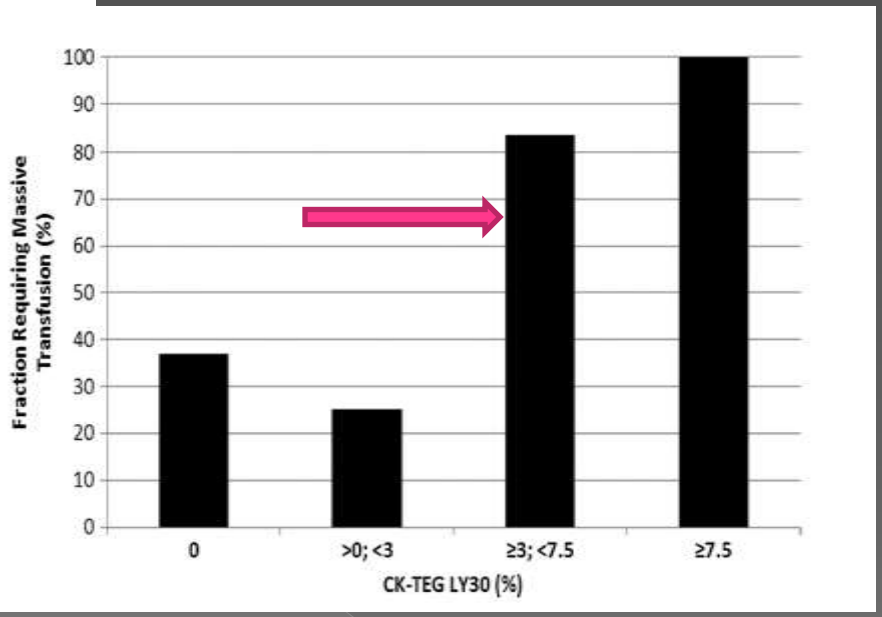
Fig 1. ROTEM parameters. FDPs, fibrin(ogen) degrading products; FXIII, coagulation factor XIII.

WTA 2013 PLENARY PAPER

Fibrinolysis greater than 3% is the critical value for initiation of antifibrinolytic therapy

Michael P. Chapman, MD, Ernest E. Moore, MD, Christopher R. Ramos, MD, Arsen Ghasabyan, MPH, CCRC, Jeffrey N. Harr, MD, MPH, Theresa L. Chin, MD, John R. String Angela Sauaia, MD, PhD, Christopher C. Silliman, MD, PhD, *and* Anirban Banerjee, PhD, *Aurora*

evidence that profound hypotension is linked to hyperfibrinolysis, neither the nature of the linkage nor the direction of the causality is clear.[3,12,19,27] Complicating these investigations are not only platelet effects but also the possibility of proteases other than plasmin being involved in pathologic fibrinolysis. It



Derin hipotansiyona hiperfibrinolizis eşlik etmektedir!

Muhtemelen **plazmin dışındaki proteazlar** da patolojik fibrinolizis oluşumunda rol almaktadır!

SON SÖZ

DR.OSCAR RATNOFF (1969)

" Epsilon aminokaproik asit yararlı bir silahtır. Bütün potansiyel olarak öldürücü silahlarda olduğu gibi, kullanımındaki anahtar **tedbir**dir!!!"