The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

DRUG THERAPY

Prevention and Treatment of Major Blood Loss

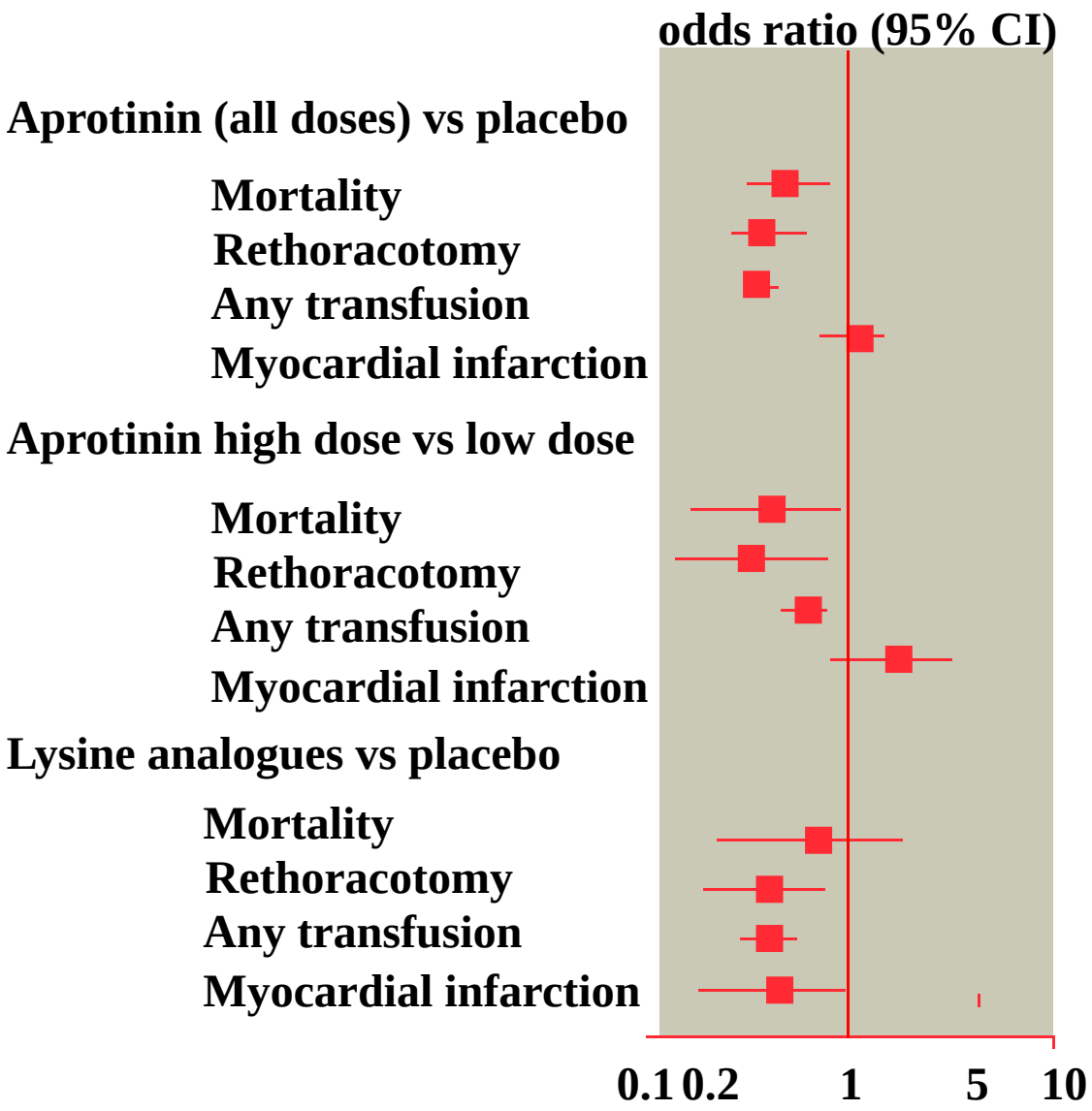
Pier Mannuccio Mannucci, M.D., and Marcel Levi, M.D., Ph.D.

N Engl J Med 2007;356:2301-11.

antifibrinolytics
EHS 2008
michael spannagl lmu münchen

Effectiveness of Antifibrinolytics

Meta-analysis of Antifibrino-lytics (72 trials, 8409 patients)

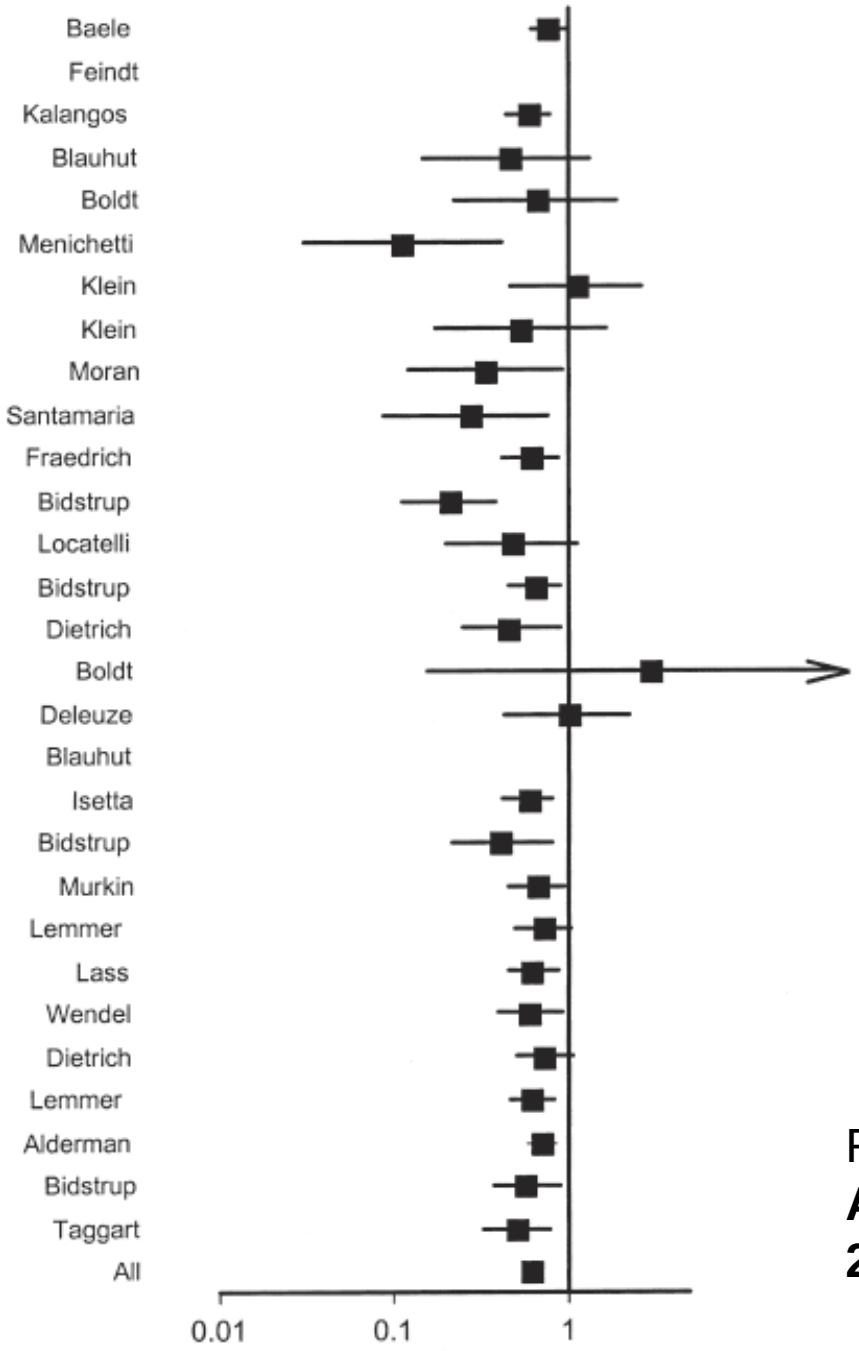


Levi et al
Lancet 354, 1940 (1999)

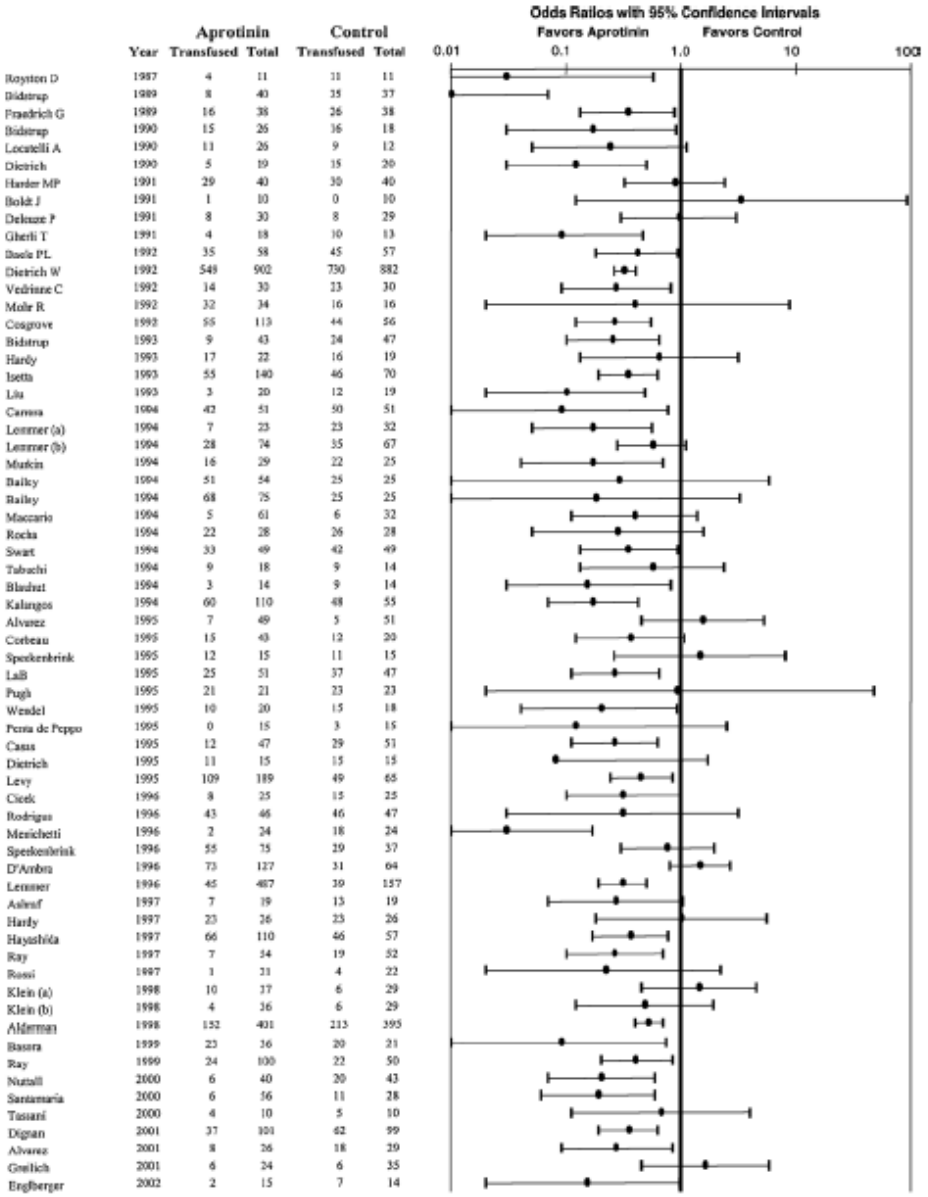
„ Aprotinin remains the hemostatic agent of choice.....Evidence of the efficacy of lysine analogues is not as solid as that for aprotinin, so these agents should be used only as a second choice in high-risk cardiac surgery...“

N Engl J Med 2007;356:2301-11.

Relative risk ratio for primary CABG and high-dose aprotinin. Randomized trials



Ferraris VA et al.
Ann Thorac Surg 2007; 83:S27-86



	Year	Aprotinin Transfused	Aprotinin Total	Control Transfused	Control Total
Royston D	1987	4	11	11	11
Bidstrup	1989	8	40	35	37
Fraedrich G	1989	16	38	26	38
Bidstrup	1990	15	26	16	18
Locatelli A	1990	11	26	9	12
Dietrich	1990	5	19	15	20
Harder MP	1991	29	40	30	40
Boldt J	1991	1	10	0	10
Deleuze P	1991	8	30	8	29
Gherli T	1991	4	18	10	13
Boele PL	1992	35	58	45	57
Dietrich W	1992	549	902	730	882
Vedrinne C	1992	14	30	23	30
Mohr R	1992	32	34	16	16
Cosgrove	1992	55	113	44	56
Bidstrup	1993	9	43	24	47
Hardy	1993	17	22	16	19
Isetta	1993	55	140	46	70
Liu	1993	3	20	12	19
Carrera	1994	42	51	50	51
Lemmer (a)	1994	7	23	23	32
Lemmer (b)	1994	28	74	35	67
Mutcin	1994	16	29	22	25
Bailey	1994	51	54	25	25
Bailey	1994	68	75	25	25
Maccario	1994	5	61	6	32
Rocha	1994	22	28	26	28
Swart	1994	33	49	42	49
Tabuchi	1994	9	18	9	14
Blauhut	1994	3	14	9	14
Kalangos	1994	60	110	48	55
Alvarez	1995	7	49	5	51
Corbeau	1995	15	43	12	20
Speekenbrink	1995	12	15	11	15
LaBi	1995	25	51	37	47
Pugh	1995	21	21	23	23
Wendel	1995	10	20	15	18
Perna de Peppo	1995	0	15	3	15
Casas	1995	12	47	29	51
Dietrich	1995	11	15	15	15
Levy	1995	109	189	49	65
Cicek	1996	8	25	15	25
Rodrigus	1996	43	46	46	47
Mesrichetti	1996	2	24	18	24
Speekenbrink	1996	55	75	29	37
D'Ambra	1996	73	127	31	64
Lemmer	1996	45	487	39	157
Aslesf	1997	7	19	13	19
Hardy	1997	23	26	23	26
Hayashida	1997	66	110	46	57
Ray	1997	7	34	19	52
Rossi	1997	1	21	4	22
Klein (a)	1998	10	27	6	29
Klein (b)	1998	4	36	6	29
Alderman	1998	152	401	213	395
Basora	1999	23	36	20	21
Ray	1999	24	100	22	50
Nuttall	2000	6	40	20	43
Santamaria	2000	6	36	11	28
Tassani	2000	4	10	5	10
Dignan	2001	37	101	62	99
Alvarez	2001	8	26	18	29
Greilich	2001	6	24	6	35
Engberger	2002	2	15	7	14

Figure 1 Proportion of patients transfused.

Aprotinin Trials

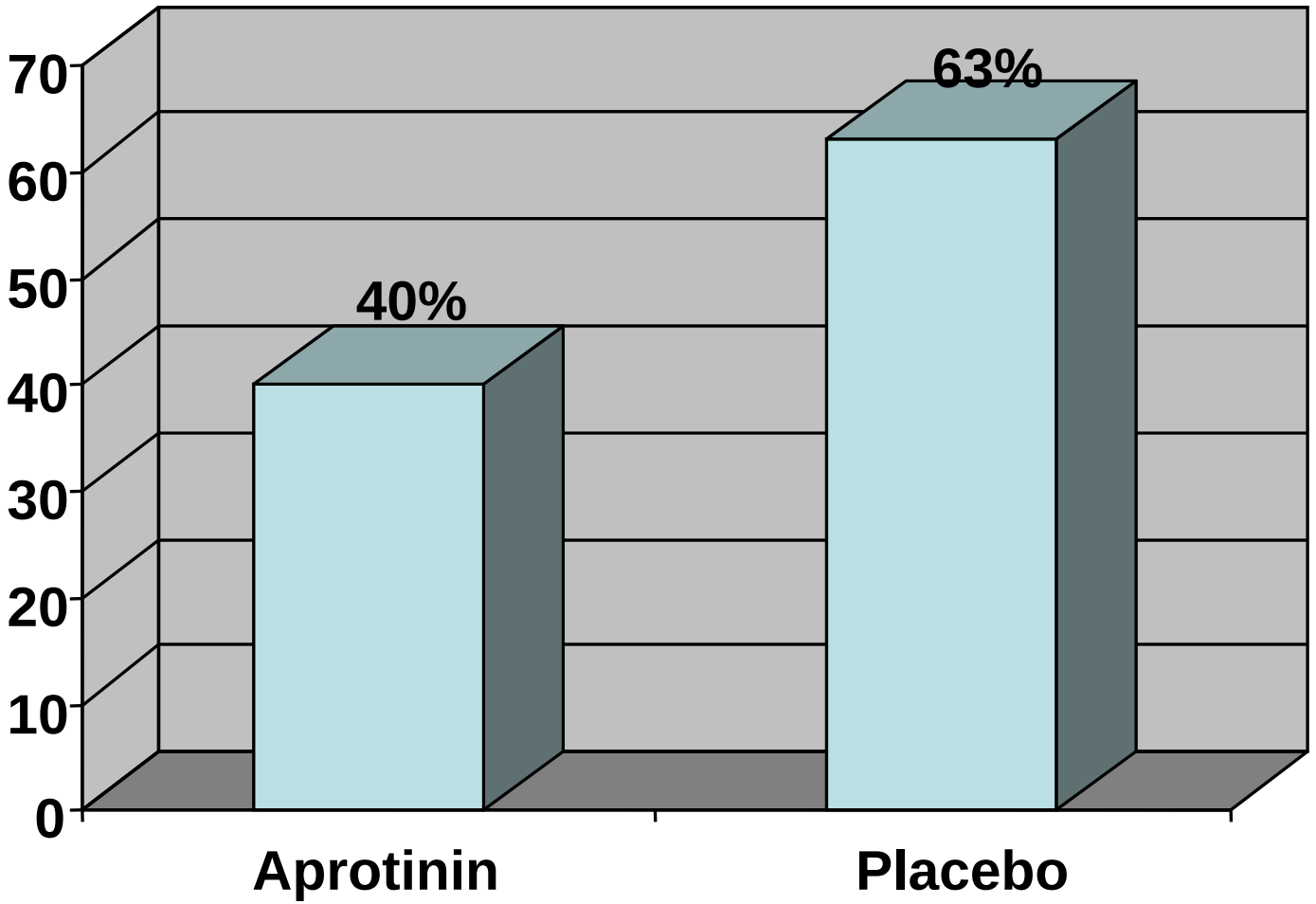
Rate of Re-exploration Tx vs. Aprotinin

Table 5. Rates of return to the operating room for postoperative hemorrhage in patients treated with aprotinin and with tranexamic acid (results are pooled from 17 high-dose aprotinin studies and 11 tranexamic acid studies).

	Treatment		*No treatment*			
	Reexplore		*Reexplore*			
	Yes	*No*	*Yes*	*No*	*RR*	*CI*
Aprotinin	18	1099	56	1043	0.316	0.188-0.53
TxA	14	354	17	362	0.848	0.429-1.674

Ferraris VA et al. : Perioperative blood transfusion and blood conservation in cardiac surgery:
the Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists clinical practice guideline.
Ann Thorac Surg 2007; 83:S27-86

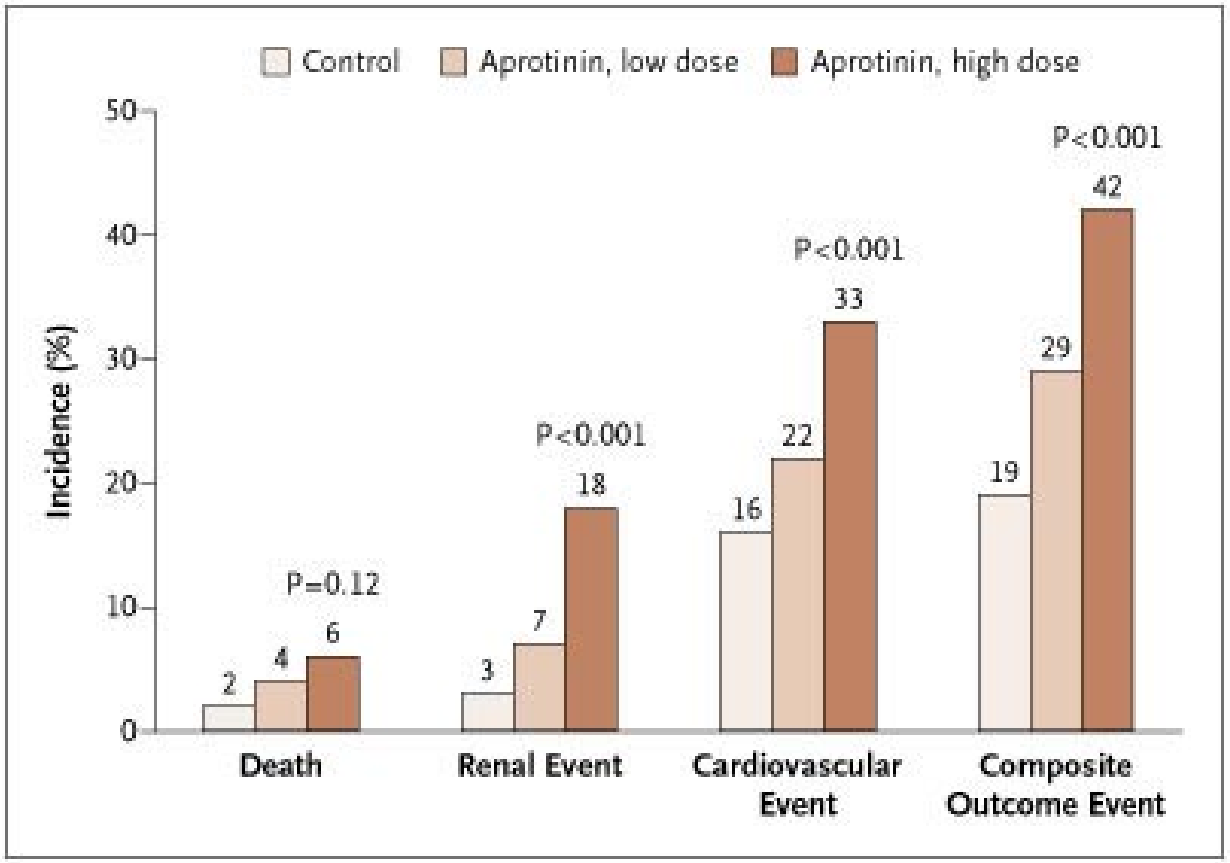
Patients with allogeneic Blood



„...risk reduction corresponded to more than 250 patients prevented from receiving any blood transfusion per 1000 CABG procedures“

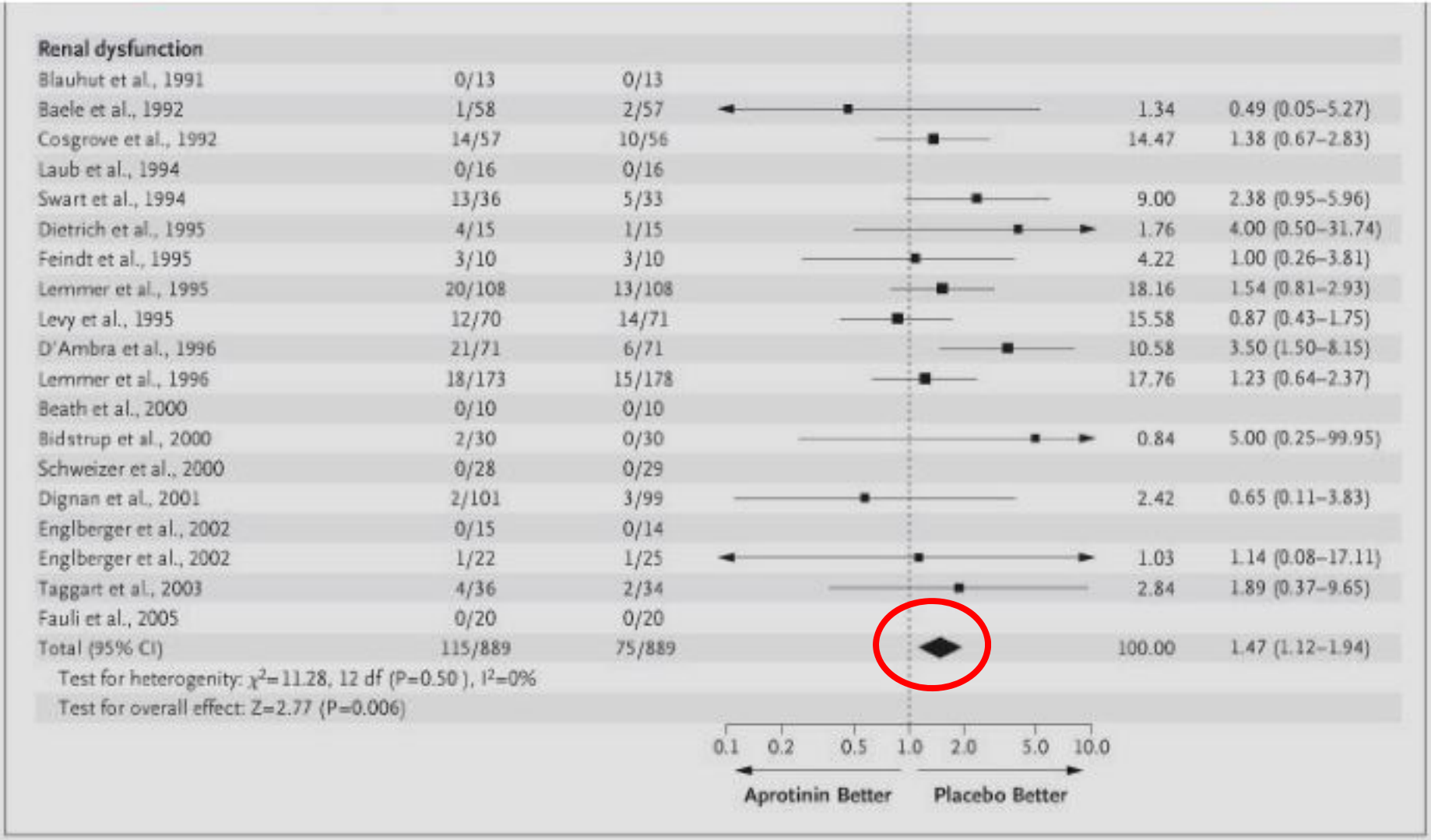
„Dose-Dependency“

Renal event = dialysis or dysfunction



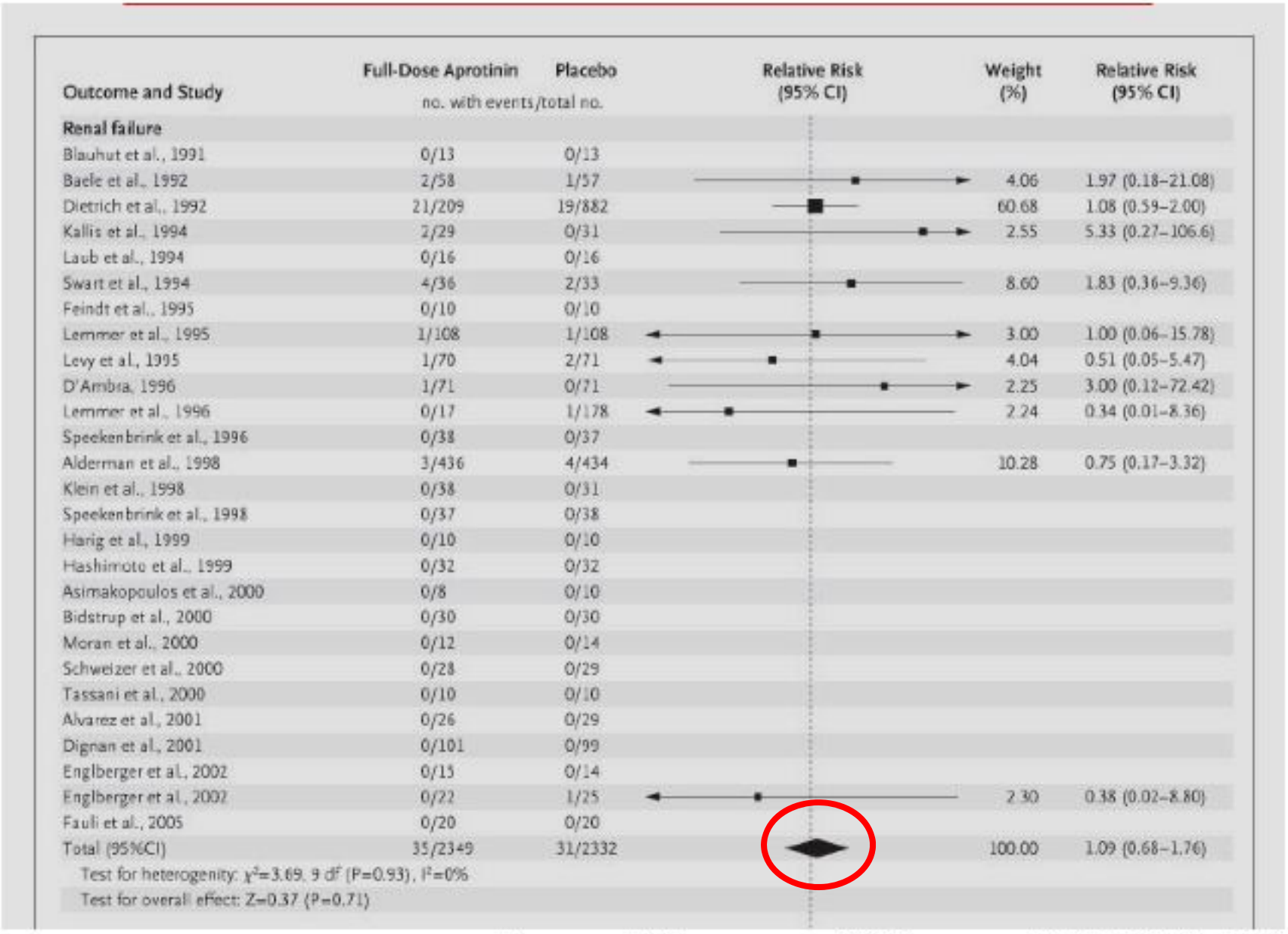
Mangano DT. N Engl J Med 2006;354(4):353-65

Renal Dysfunction and Aprotinin (Creatinine increase at least 0.5 mg/dl)



Brown, Birkemeyer, O´Connor, NEJM 354:18 (2006)

Renal Failure and Aprotinin (Creatinine >= 2 mg/dl or Dialysis))



Outcome and Study	Full-Dose Aprotinin (no. with events/total no.)	Placebo (no. with events/total no.)	Weight (%)	Relative Risk (95% CI)
Renal failure				
Blauhut et al., 1991	0/13	0/13		
Baele et al., 1992	2/58	1/57	4.06	1.97 (0.18–21.08)
Dietrich et al., 1992	21/209	19/882	60.68	1.08 (0.59–2.00)
Kallis et al., 1994	2/29	0/31	2.55	5.33 (0.27–106.6)
Laub et al., 1994	0/16	0/16		
Swart et al., 1994	4/36	2/33	8.60	1.83 (0.36–9.36)
Feindt et al., 1995	0/10	0/10		
Lemmer et al., 1995	1/108	1/108	3.00	1.00 (0.06–15.78)
Levy et al., 1995	1/70	2/71	4.04	0.51 (0.05–5.47)
D'Ambra, 1996	1/71	0/71	2.25	3.00 (0.12–72.42)
Lemmer et al., 1996	0/17	1/178	2.24	0.34 (0.01–8.36)
Speekenbrink et al., 1996	0/38	0/37		
Alderman et al., 1998	3/436	4/434	10.28	0.75 (0.17–3.32)
Klein et al., 1998	0/38	0/31		
Speekenbrink et al., 1998	0/37	0/38		
Harig et al., 1999	0/10	0/10		
Hashimoto et al., 1999	0/32	0/32		
Asimakopoulos et al., 2000	0/8	0/10		
Bidstrup et al., 2000	0/30	0/30		
Moran et al., 2000	0/12	0/14		
Schweizer et al., 2000	0/28	0/29		
Tassani et al., 2000	0/10	0/10		
Alvarez et al., 2001	0/26	0/29		
Dignan et al., 2001	0/101	0/99		
Englberger et al., 2002	0/15	0/14		
Englberger et al., 2002	0/22	1/25	2.30	0.38 (0.02–8.80)
Fauli et al., 2005	0/20	0/20		
Total (95%CI)	35/2349	31/2332	100.00	1.09 (0.68–1.76)
Test for heterogeneity: χ^2=3.69, 9 df (P=0.93), I^2=0%				
Test for overall effect: Z=0.37 (P=0.71)				

Brown, Birkemeyer, O´Connor, NEJM 354:18 (2006)

Karkouti

- Case control study using propensity scores
- Aprotinin n=449; Tranexamic acid n=449
- No statistically significant difference (p=0.08) in renal failure
  - 25/449 (5.6%) aprotinin group
  - 14/449 (3.1%) tranexamic acid group
- Higher incidence of renal dysfunction in aprotinin patients (p=0.01)
  - 107/449 (24%) aprotinin group
  - 75/449 (17%) tranexamic acid group
  - renal dysfunction was more pronounced in aprotinin treated patients with abnormal preoperative renal function

Karkouti et al. Transfusion 2006 on-line

Antifibrinolytics

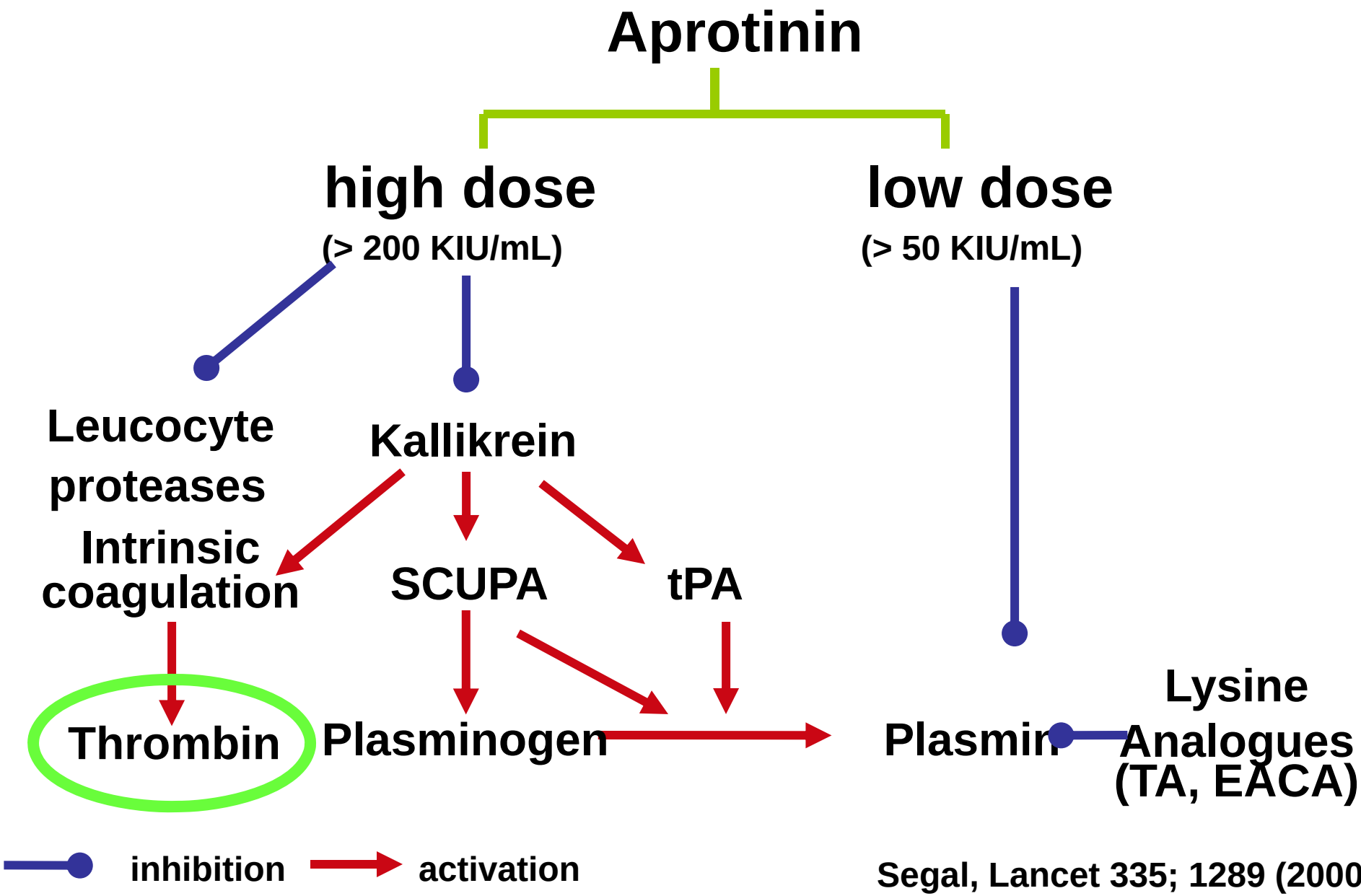
- *Tranexamsäure* – Cyklokapron®

- *Aprotinin* – Trasylol®

not to forget - Immunization!

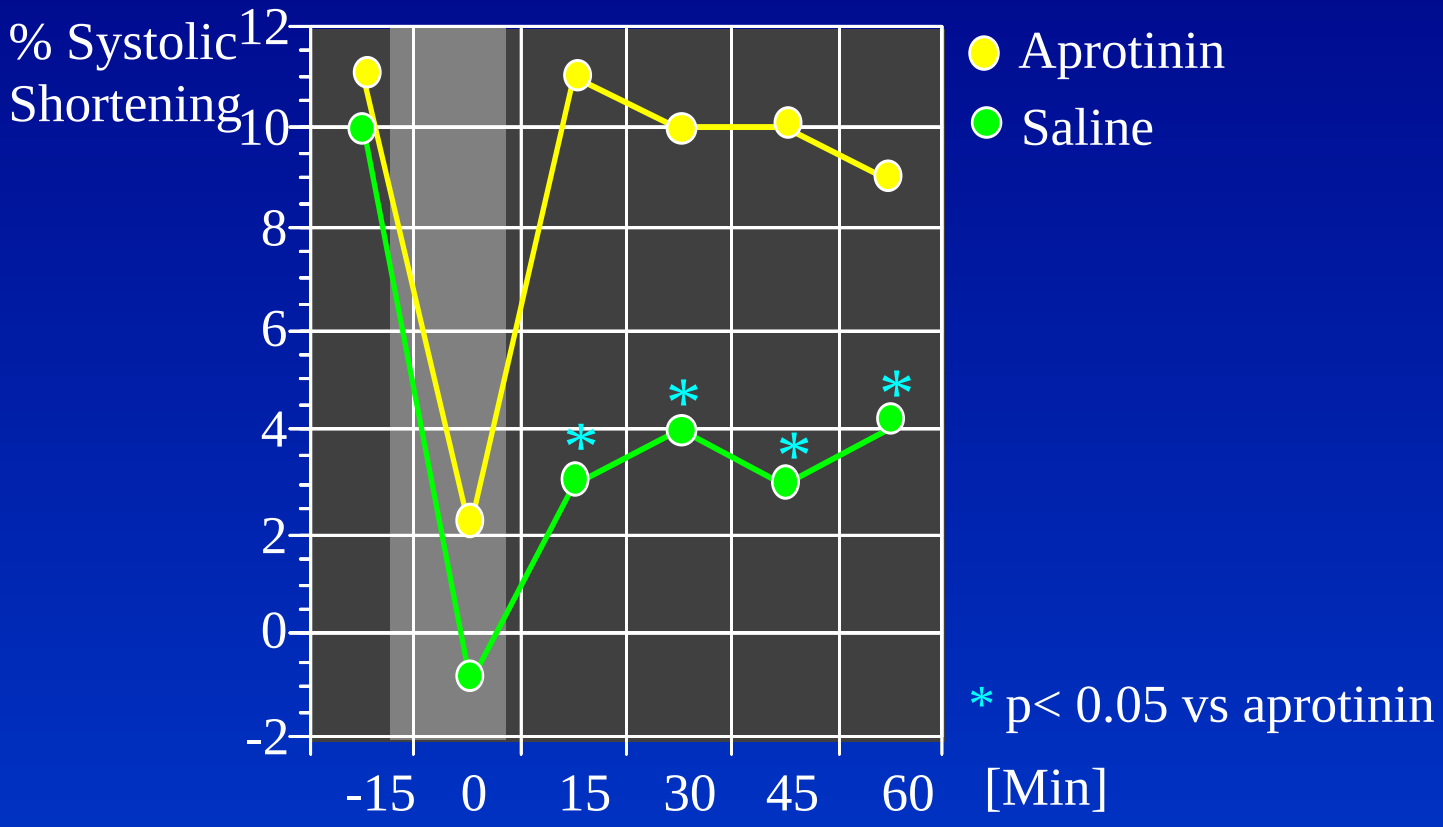
05.11.2007

Aprotinin Dosage and Hemostasis



Segal, Lancet 335; 1289 (2000

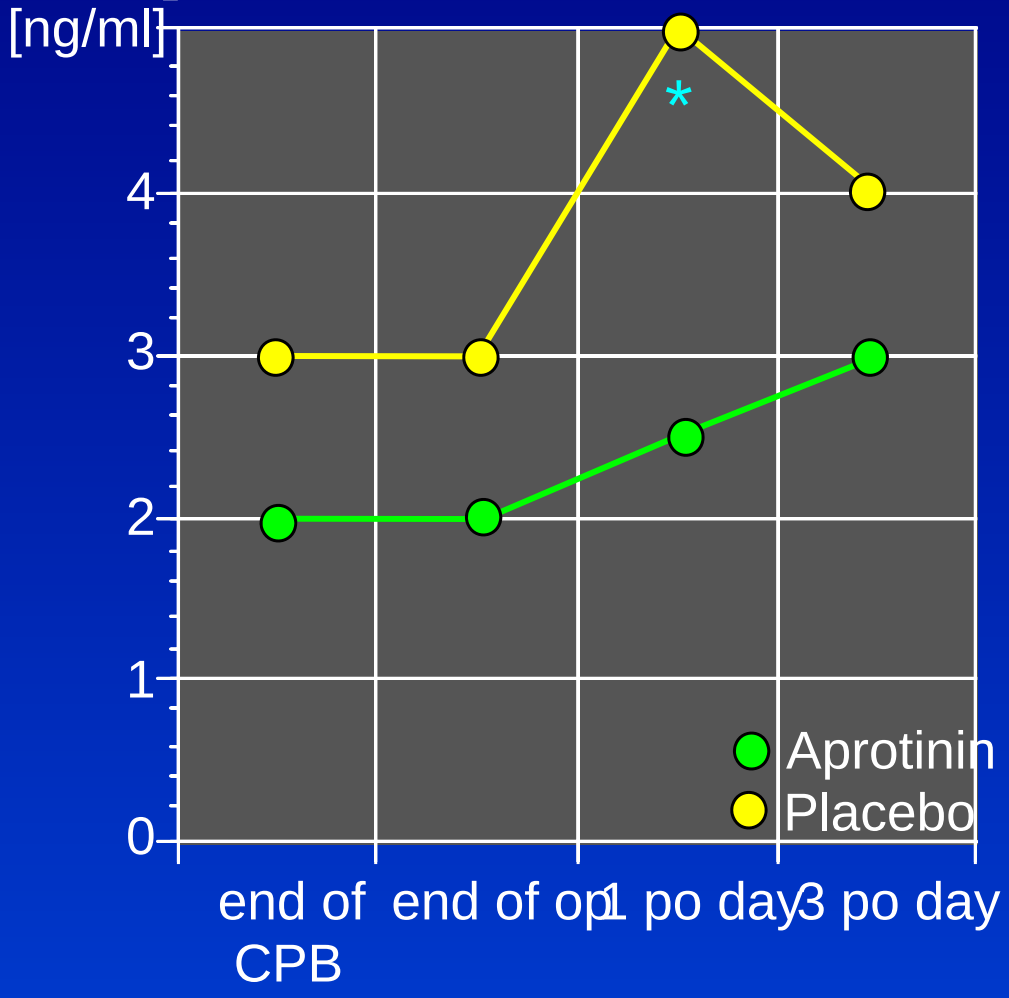
Aprotinin in stunned myocardium



Aprotinin 30000 KIU/kg before the onset of regional myocardial ischemia or placebo in dogs with 15 min interruption of the circumflex coronary artery blood flow

McCarthy, Anesth Analg 89:1096, 199

Troponin T Release and Aprotinin

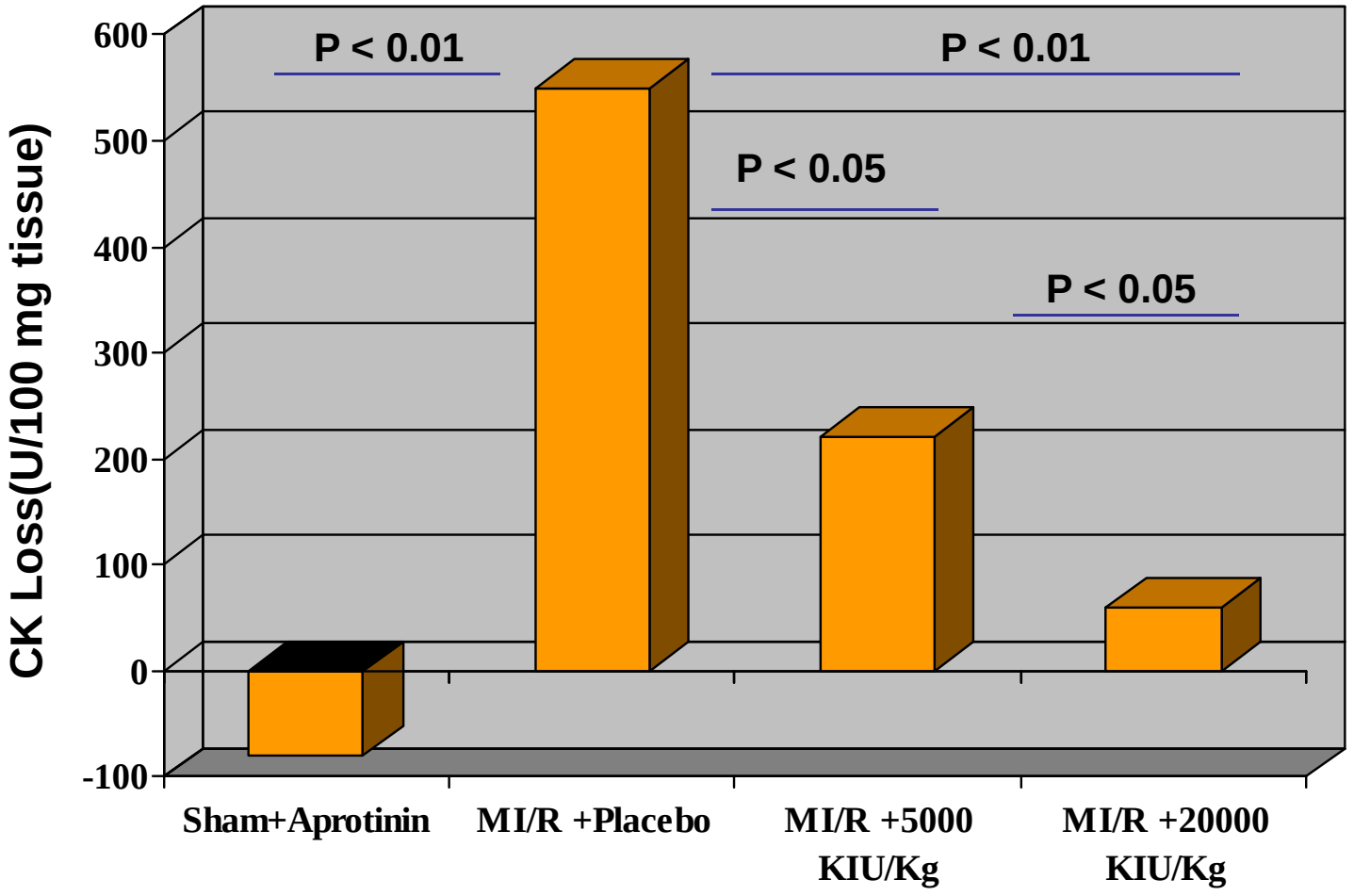


40 patients undergoing CABG, double-blind high-dose aprotinin (60.000 KIU/kg + 7.000 KIU/kg*h) or placebo, two Q-wave infarctions in the control group with the highest values (excluded)

* p< 0.05 vs aprotinin

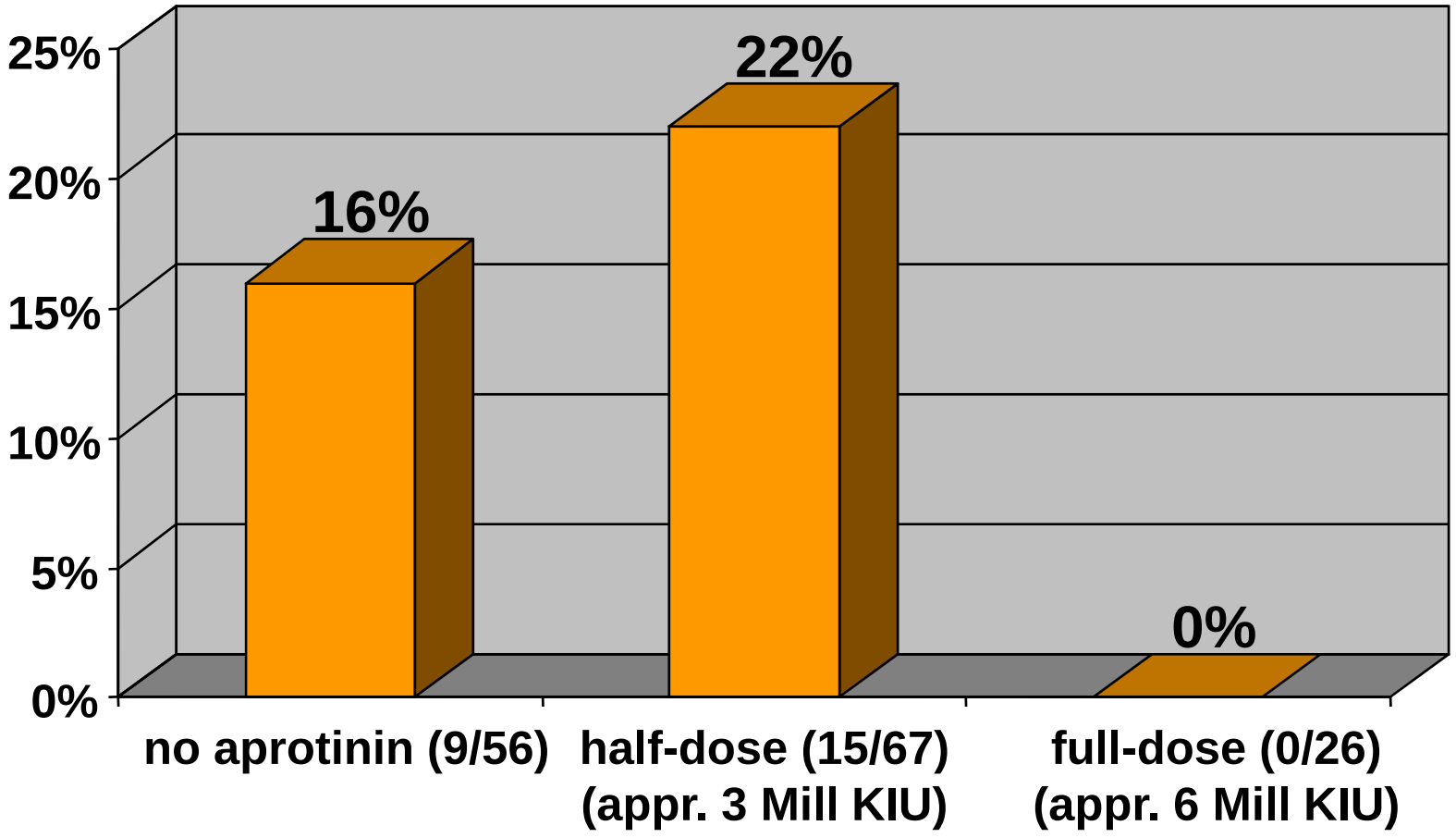
Wendel, J Thorac Cardiovasc Surg, 109:1164

Aprotinin - Regional Ischemia and Reperfusion in a Beating Heart Rat Model



Pruefer, JTCS, 124, 942

Stroke after Cardiac Surgery

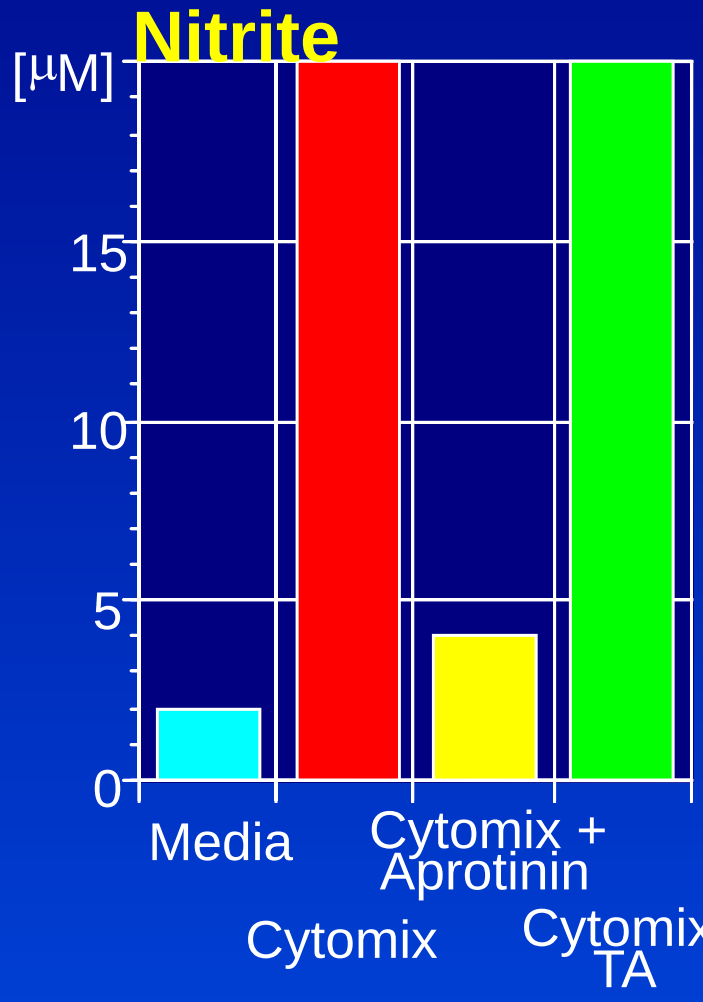


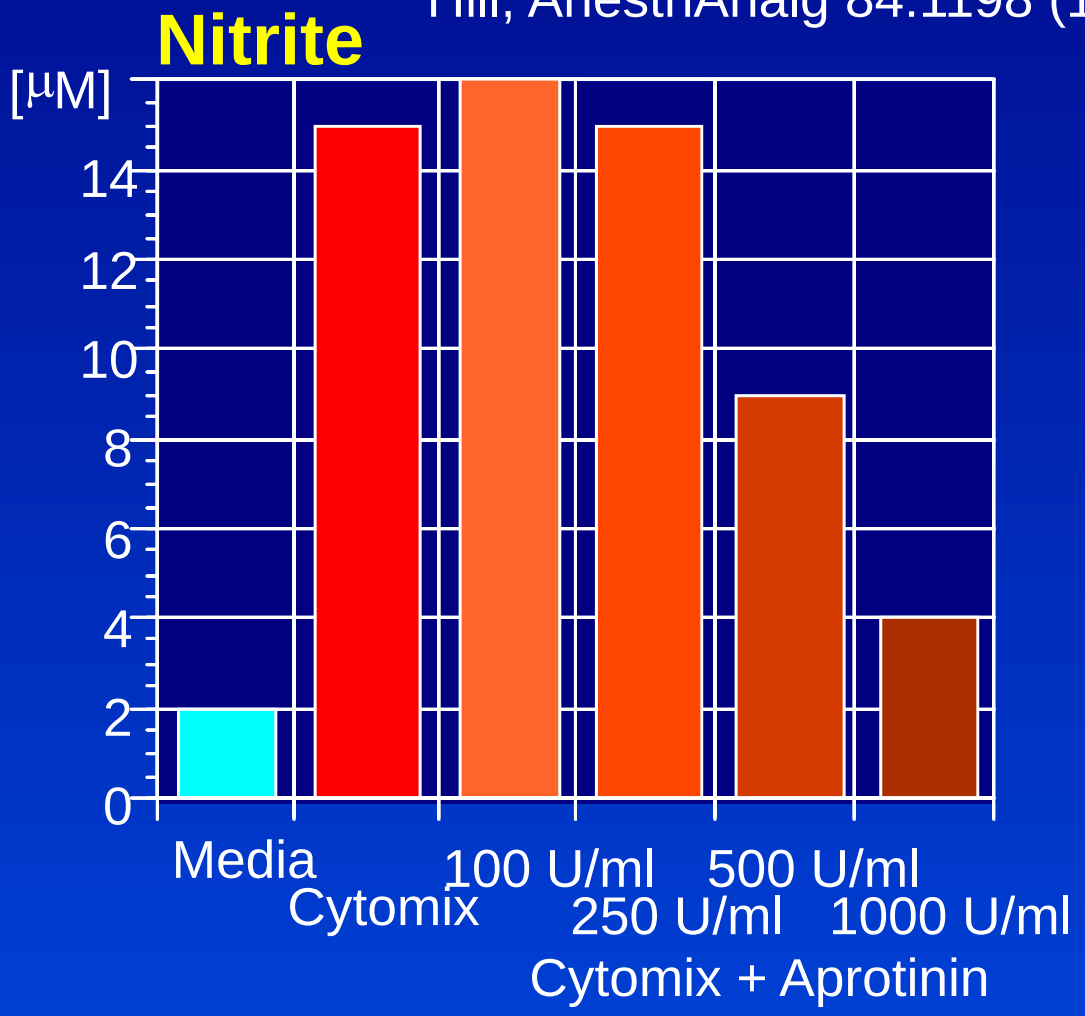
Frumento, Ann Thorac Surg 75:479 (2003)

Aprotinin but not TA inhibits cytokine -ind iNOS expression

(measured on murine bronchial epithelial cells)

Hill, AnesthAnalg 84:1198 (19





Drugs and Bleeding Tendency

- **Synthetic Antifibrinolytics**

  Tranexamic-acid

  ε - Aminocaproic-acid

- **Aprotinin**
- **Nafamostat Mesilate (KK Inh**

Anesthesiology 2001; 94:8–14

Tranexamic Acid Administration after Cardiac Surgery

A Prospective, Randomized, Double-blind, Placebo-controlled Study

Valter Casati, M.D., Ferdinando Bellotti, M.D.,† Chiara Gerli, M.D.,† Annalisa Franco, M.D.,† Michele Oppizzi, M.D.,* Mariangelo Cossolini, M.D.,* Giliola Calori, M.D.,‡ Stefano Benussi, M.D.,§ Ottavio Alfieri, M.D.,‖ Giorgio Torri, M.D.#*

Tranexamic Acid Reduces Bleeding and the Need for Blood Transfusion in Primary Myocardial Revascularization

Deeb Zabeeda, MD, Benjamin Medalion, MD, Michael Sverdlov, MD, Shaul Ezra, MD, Arie Schachner, MD, Tiberiu Ezri, MD, and Amram J. Cohen, MD*

Departments of Anesthesia and Cardiothoracic Surgery, The Edith Wolfson Medical Center, Holon, Israel

Prophylactic Tranexamic Acid and ϵ-Aminocaproic Acid for Primary Myocardial Revascularization

Jean-François Hardy, MD, Sylvain Bélisle, MD, Charles Dupont, MSc, François Harel, MSc, Danielle Robitaille, MD, Micheline Roy, RT, and Lyne Gagnon, RT

Departments of Anesthesia, Biostatistics, and Hematology, Montreal Heart Institute, University of Montreal, Montreal, Quebec, Canada

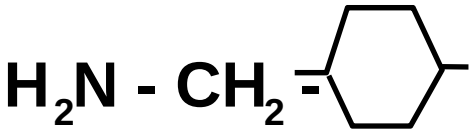
Anesthesiology
1999; 91:430–5

The Effect of Prophylactic ϵ-Aminocaproic Acid on Bleeding, Transfusions, Platelet Function, and Fibrinolysis during Coronary Artery Bypass Grafting

Christopher A. Troianos, M.D., Richard W. Sypula, M.D.,† Donna M. Lucas, M.D.,‡ Frank D'Amico, Ph.D.,§ Thomas R. Mathie, B.S.,‖ Manish Desai, B.S.,‖ Roberta T. Pasqual, Ph.D.,# Ronald V. Pellegrini, M.D.,***

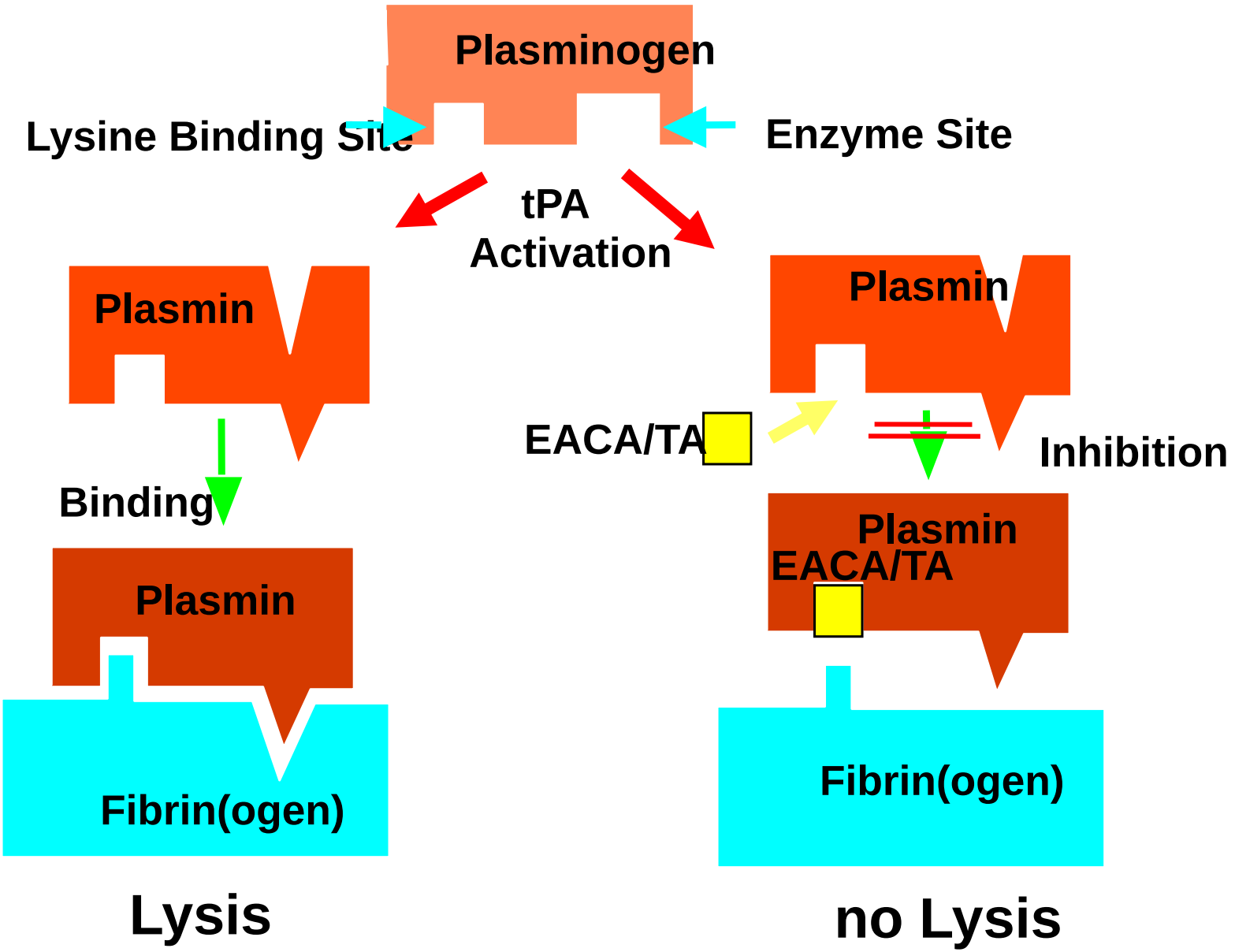
Lysin Analoge

$H_2N - CH_2 - (CH_2)_4 - COOH$ ε -Amonocaproic acid (EACA



Tranexamic Acid (TA)

Mode of Action of Lysine Analogues



Metaanalysis

Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion

Henry DA, Moxey AJ, Carless PA, O'Connell D, McClelland B, Henderson KM, Sly K, Laupacis A, Fergusson D

This is a reprint of a Cochrane review, prepared and maintained by the Cochrane Collaboration and published in *The Cochrane Library* 2003, Issue 4

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Update Software Ltd, Summertown Pavilion, Middle Way, Oxford OX2 7LG, UK

Tx vs Control

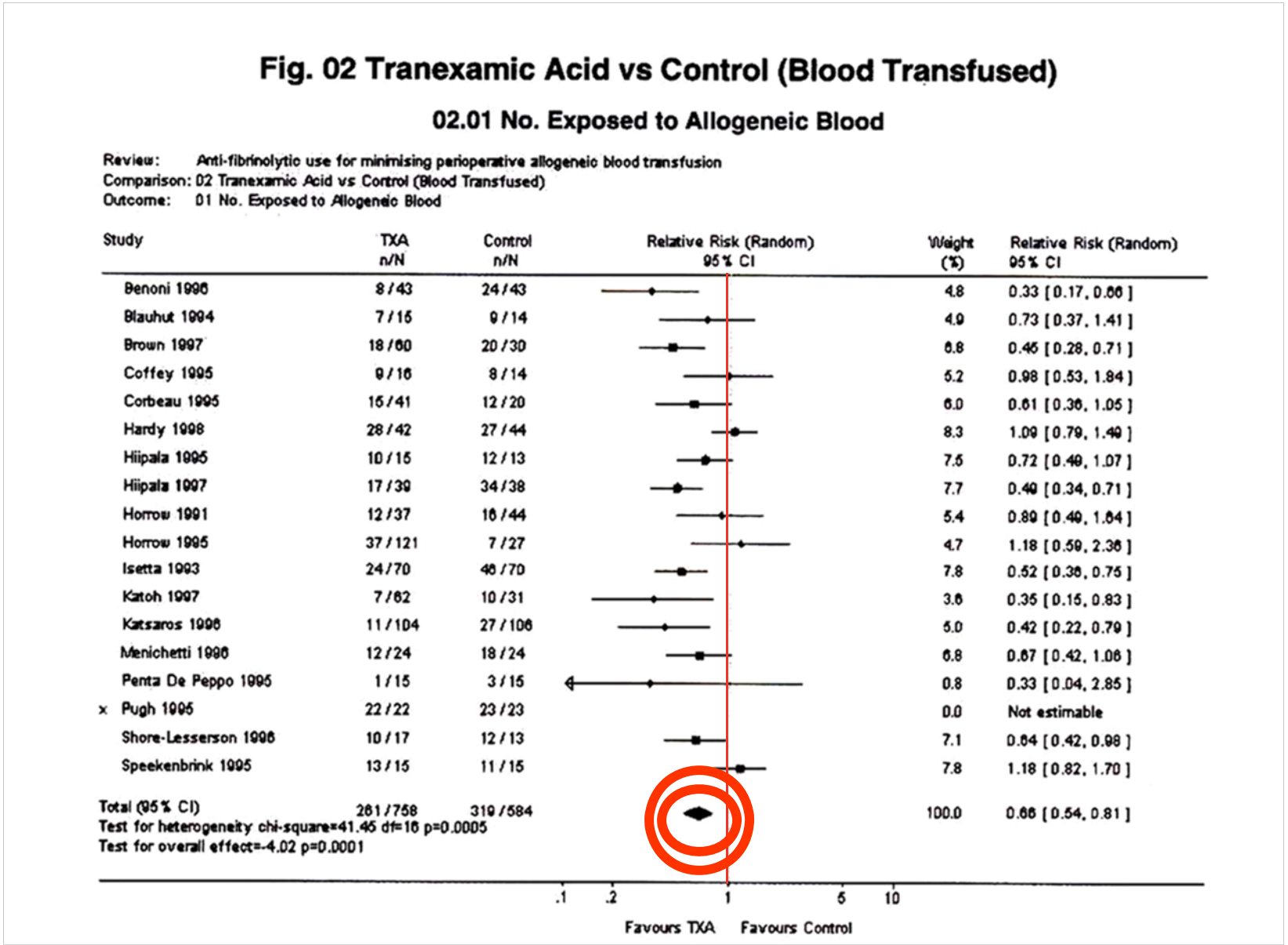


Fig. 02 Tranexamic Acid vs Control (Blood Transfused)

02.01 No. Exposed to Allogeneic Blood

Review: Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion
Comparison: 02 Tranexamic Acid vs Control (Blood Transfused)
Outcome: 01 No. Exposed to Allogeneic Blood

Study	TXA n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Benoni 1996	8 / 43	24 / 43		4.8	0.33 [0.17, 0.66]
Blauhut 1994	7 / 15	9 / 14		4.9	0.73 [0.37, 1.41]
Brown 1997	18 / 60	20 / 30		6.8	0.45 [0.28, 0.71]
Coffey 1995	9 / 16	8 / 14		5.2	0.98 [0.53, 1.84]
Corbeau 1995	15 / 41	12 / 20		6.0	0.61 [0.36, 1.05]
Hardy 1998	28 / 42	27 / 44		8.3	1.09 [0.79, 1.49]
Hiipala 1995	10 / 15	12 / 13		7.5	0.72 [0.49, 1.07]
Hiipala 1997	17 / 39	34 / 38		7.7	0.49 [0.34, 0.71]
Horrow 1991	12 / 37	16 / 44		5.4	0.89 [0.49, 1.64]
Horrow 1995	37 / 121	7 / 27		4.7	1.18 [0.59, 2.36]
Isetta 1993	24 / 70	46 / 70		7.8	0.52 [0.36, 0.75]
Katoh 1997	7 / 62	10 / 31		3.6	0.35 [0.15, 0.83]
Katsaros 1996	11 / 104	27 / 106		5.0	0.42 [0.22, 0.79]
Menichetti 1996	12 / 24	18 / 24		6.8	0.67 [0.42, 1.06]
Penta De Peppo 1995	1 / 15	3 / 15		0.8	0.33 [0.04, 2.85]
x Pugh 1995	22 / 22	23 / 23		0.0	Not estimable
Shore-Lesserson 1996	10 / 17	12 / 13		7.1	0.64 [0.42, 0.98]
Speekenbrink 1995	13 / 15	11 / 15		7.8	1.18 [0.82, 1.70]
Total (95% CI)	261 / 758	319 / 584		100.0	0.66 [0.54, 0.81]

Test for heterogeneity chi-square=41.45 df=16 p=0.0005
Test for overall effect=-4.02 p=0.0001

.1 .2 1 5 10

Favours TXA Favours Control

Studies TA vs Aprotinin

Authors	Procedure	Drug	N	Total dose (70 kg/4 h)	Blood Loss	Blood Transfusion	Proportion Transfused
Bennett-Guerrero et al [18]	Repeat ACB/ and/or valve	Aprotinin	99	6×10^6 KIU	AP < EACA[a]	AP < EACA[b]	
		EACA	105	19 g			
Blauhut et al [19]	Primary ACB	Aprotinin	14	5×10^6 KIU	AP < Pla[a]	AP < Pla[a]	AP < Pla[a]
		Tranexamic	15	1 g	TA < Pla[b]	TA < Pla[b]	TA < Pla[a]
		Placebo	14		AP < TA[b]	AP < TA[b]	AP < TA[a]
Boughenou et al [20]	Primary valve	Aprotinin	17	6×10^6 KIU	TA < AP[b]	TA < AP[b]	
		Tranexamic	18	2 g			
Corbeau et al [21]	Primary ACB or AVR	Aprotinin	43	6×10^6 KIU	AP < Pla[a]	AP < Pla[b]	
		Tranexamic	41	2.1 g	TA < Pla[a]	TA < Pla[b]	
		Placebo	20		AP < TA[a]	AP < TA[b]	
Cousin et al [22]	Primary or repeat ACB and/or valve	Aprotinin	20	6×10^6 KIU	AP H < Pla[a]	Pla < AP H[a]	
		Aprotinin L	30	1.75×10^6 KIU	AP L < Pla[a]	Pla < AP L[b]	
		Tranexamic	20	2.1 g	TA < Pla[b]	Pla < TA[b]	
		Placebo	20		AP < TA[b]	TA < AP[b]	
Eberle et al [23] (nonrandomized control)	Primary ACB	Aprotinin	20	6×10^6 KIU	AP < Pla[a]	AP > Pla[b]	AP > Pla[b]
		EACA	20	40 g	EACA < Pla[a]	EACA > Pla[b]	EACA > Pla[b]
		Placebo	10		AP < EACA[b]	AP < EACA[b]	AP < EACA[b]
Jamieson et al [24] (two trials)	Repeat valve	Aprotinin	24	6×10^6 KIU	AP < Pla[a]	AP < Pla[a]	
		Placebo-AP	36				
		Tranexamic	22	10 mg	TA < Pla[a]	TA < Pla[a]	
		Placebo-TA	19		AP = TA	AP < TA[b]	
Landymore et al [25]	Primary ACB	Aprotinin L	48	1×10^6 KIU	AP < Pla[a]	AP < Pla[a]	
		Tranexamic	56	1 g	TA < Pla[a]	TA < Pla[a]	
		EACA	44	9 g	EACA < Pla[a]	EACA < Pla[a]	
		Placebo	50		AP < EACA < TA[a]	AP = EACA < TA[a]	
Menichetti et al [26]	Primary ACB	Aprotinin	24	6×10^6 KIU	AP < Pla[a]		AP < Pla[a]
		Tranexamic	24	1.5 g	TA < Pla[a]		TA < Pla[a]
		Placebo	24		AP < TA[a]		AP < TA[a]
Mongan et al [27] (nonconcurrent control)	Primary ACB	Aprotinin	75	7×10^6 KIU	AP < Pla[a]	AP < Pla[a]	AP < Pla[a]
		Tranexamic	75	2 g	TA < Pla[a]	TA < Pla[a]	TA < Pla[a]
		Placebo	30		AP < TA[b]	AP = TA	AP = TA
Penta de Peppo et al [28]	Primary ACB and/or valve	Aprotinin	15	6×10^6 KIU	AP < Pla[a]	AP < Pla[b]	AP < Pla[b]
		Tranexamic	15	1.4 g	TA < Pla[b]	TA < Pla[b]	TA < Pla[b]
		Placebo	15		AP < TA[a]	AP < TA[b]	AP < TA[b]
Pugh et al [29] (single-blinded)	Primary ACB	Aprotinin	21	2×10^6 KIU	AP < Pla[a]	AP < Pla[a]	
		Tranexamic	22	5 g	TA < Pla[a]	TA < Pla[a]	
		Placebo	23		AP < TA[b]	AP < TA[b]	
Speckenbring et al [30]	Primary ACB	Aprotinin	15	6×10^6 KIU	AP < Pla[a]	AP < Pla[b]	
		Tranexamic	15	1 g	TA < Pla[a]	TA < Pla[b]	
		Placebo	15		AP < TA[b]	AP < TA[b]	
Trinh-Duc et al [31]	ACB, valve Aorta, ASD	Aprotinin	29	6×10^6 KIU	AP < EACA[b]	AP < EACA[b]	AP < EACA[b]
		EACA	27	20 g			

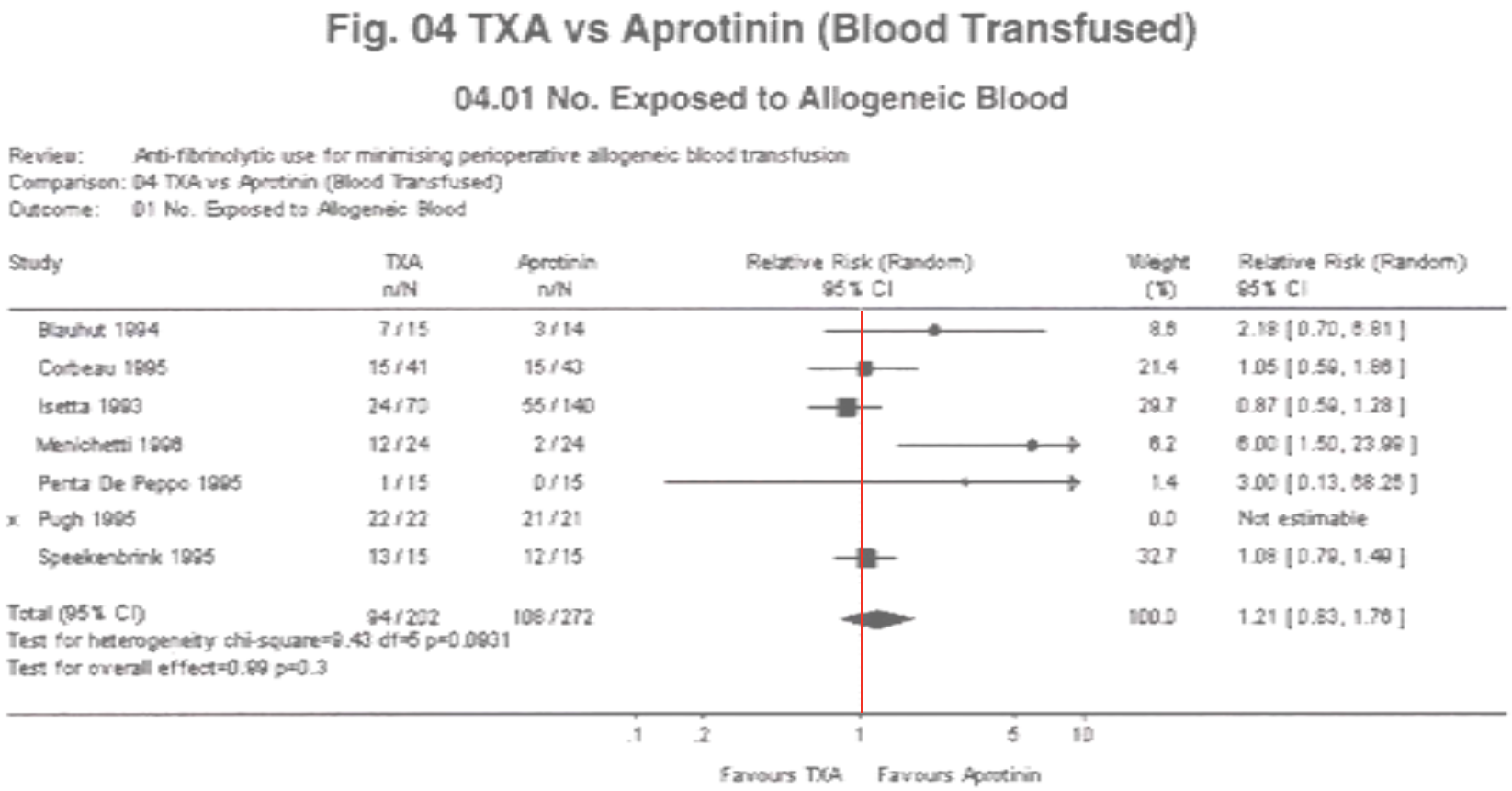
[a] $p \leq 0.05$. [b] Not significant.

ACB = aortocoronary bypass surgery; AVR = aortic valve replacement; Aorta = aortic dissection repair; AP = aprotinin group; Aprotinin H = high dose aprotinin; Aprotinin L = low dose aprotinin; ASD = atrial septal defect repair; EACA = ε-aminocaproic acid; KIU = kallikrein inhibitory units; Pla = placebo; TA = tranexamic acid group; Valve = valve replacement surgery.

Wong,
Ann Thorac Surg
2000;69:808

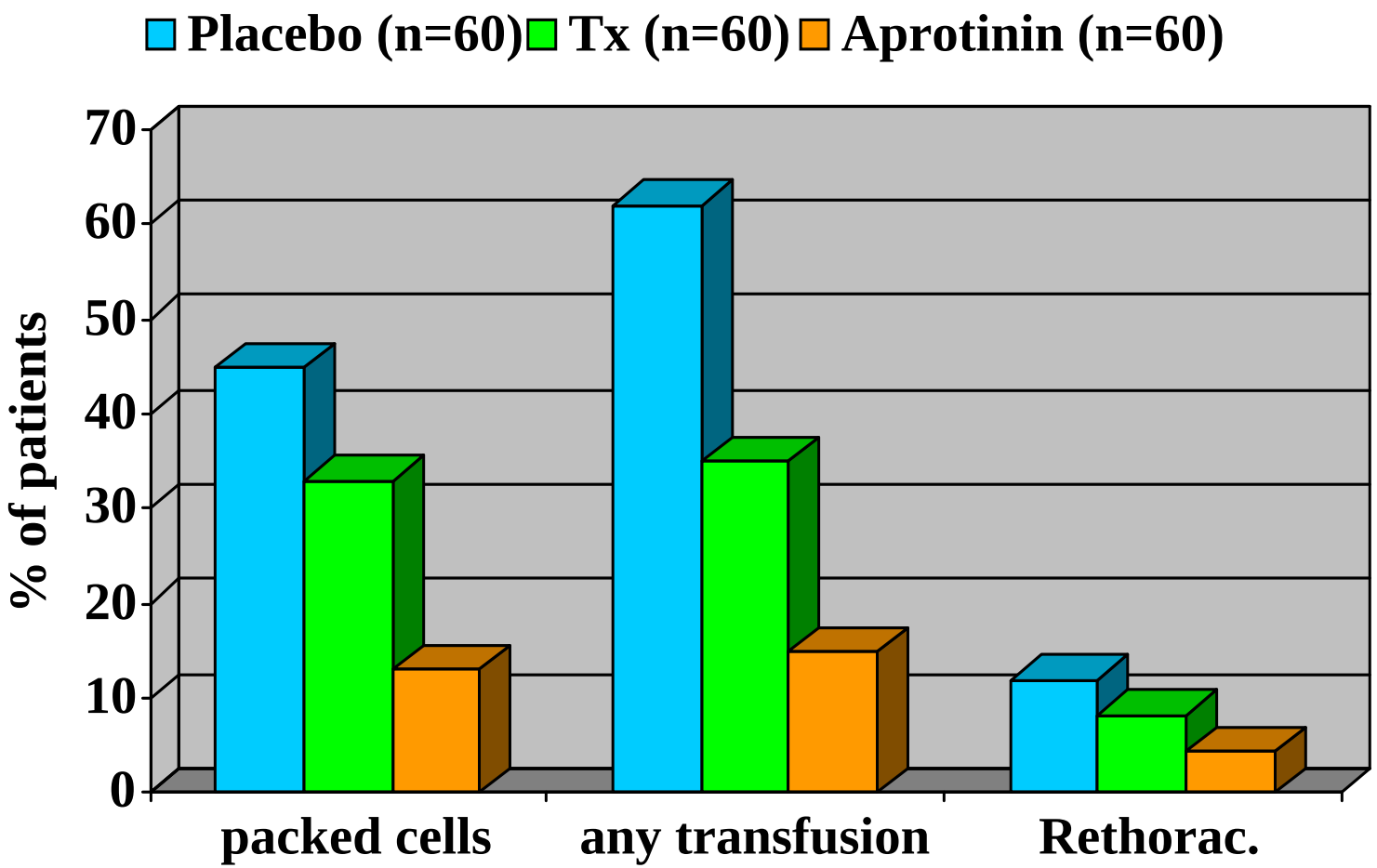
Tranexamic Acid vs. Aprotinin

21% relative risk increase for allogeneic transfusion with Tranexamic Acid



Aprotinin vs. Tranexamic Acid

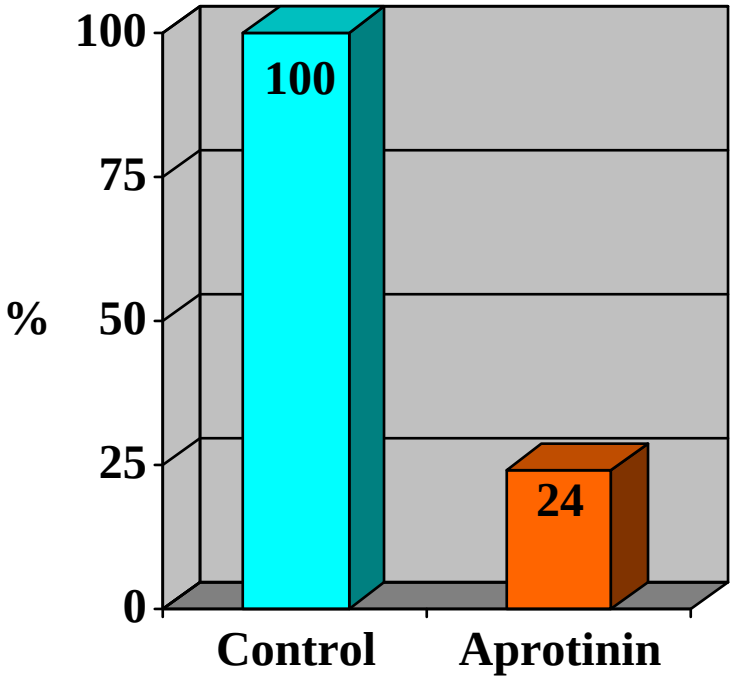
TA dosage: 61 mg/kg = 5g/patient)



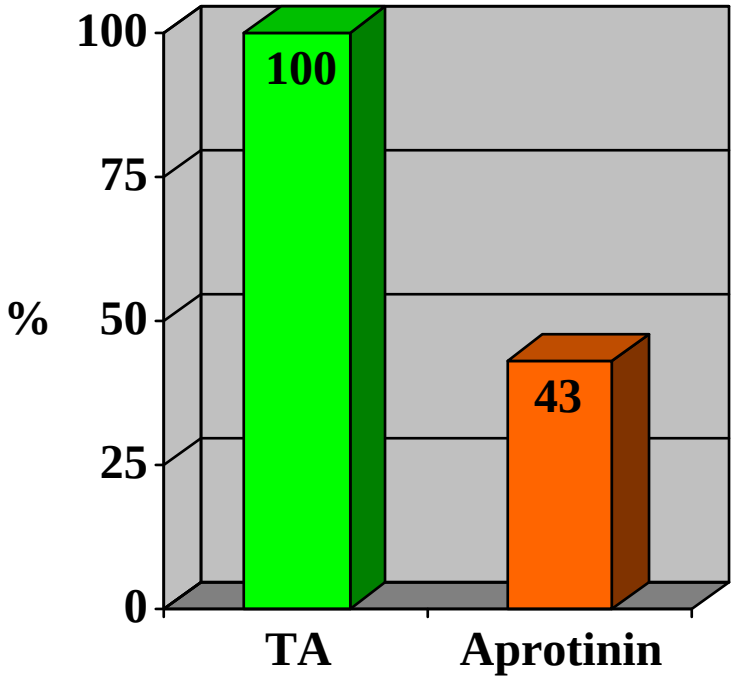
Diprose P, Br J Anaesth 2005;94:271-8

Relative Risk Receiving any Allogeneic Transfusion

Aprotinin vs Control



Aprotinin vs Tranexamic Acid

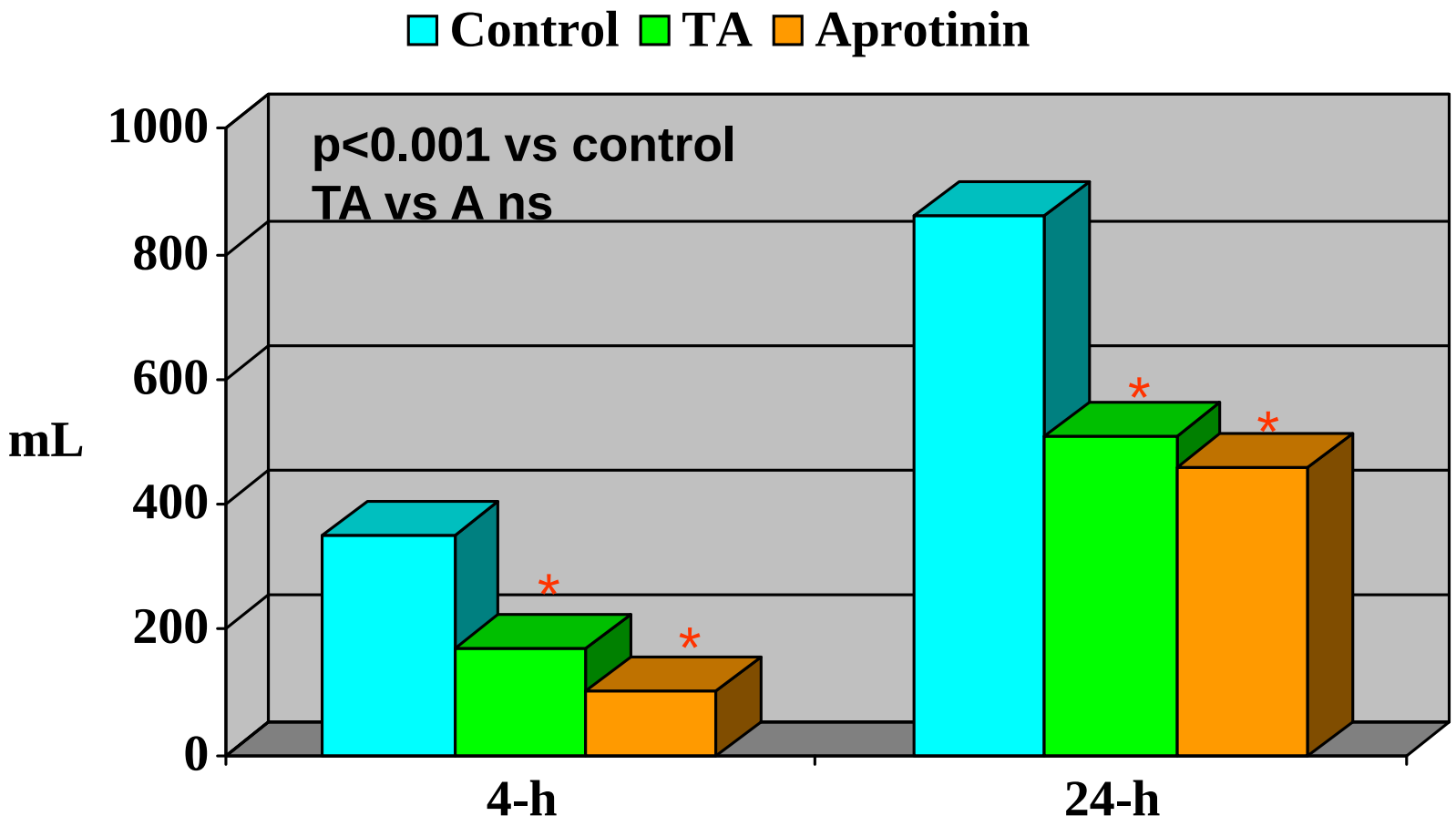


Aprotinin vs Control: 0.24 (95% CI 0.13 - 0.46; p<0.0001

Aprotinin vs TA: 0.43 (95% CI 0.21 - 0.86; p<0.0195

Diprose P, Br J Anaesth 2005;94:271-8

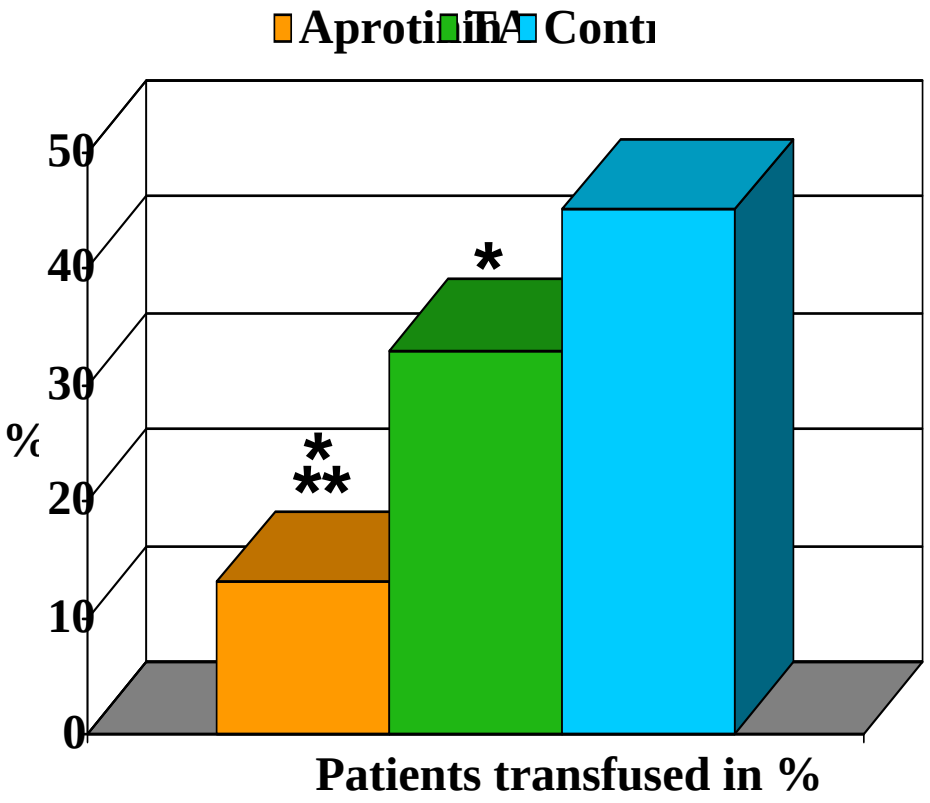
Blood Loss and TA

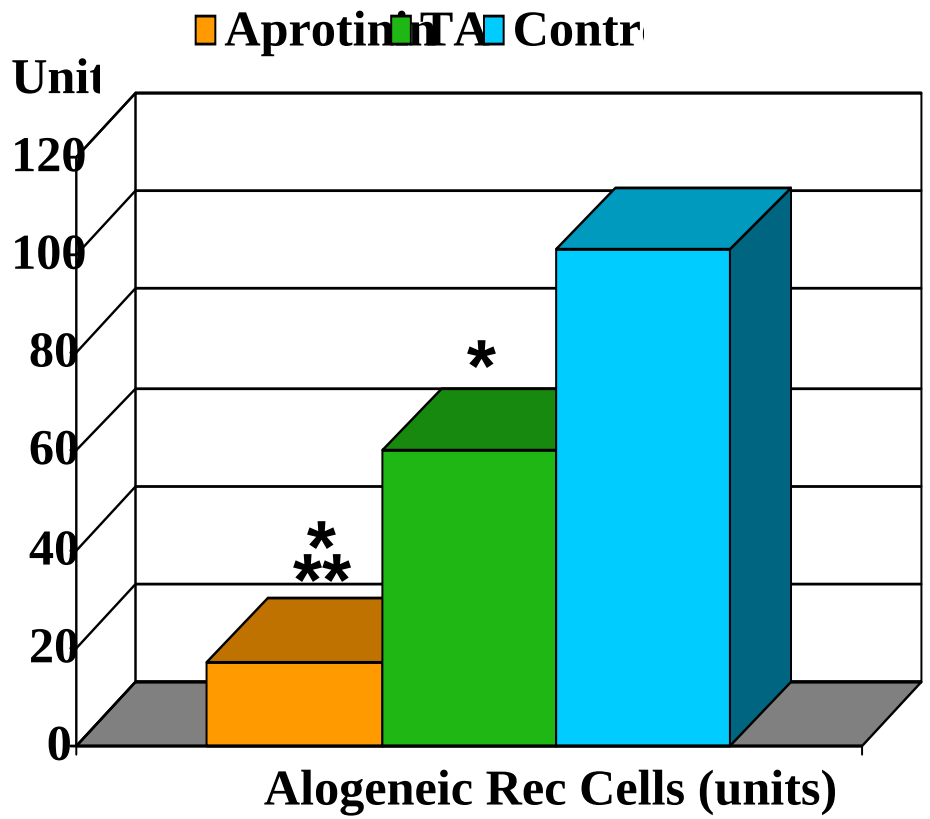


Diprose P, Br J Anaesth 2005;94:271-8

Aprotinin vs. Tranexamic Acid

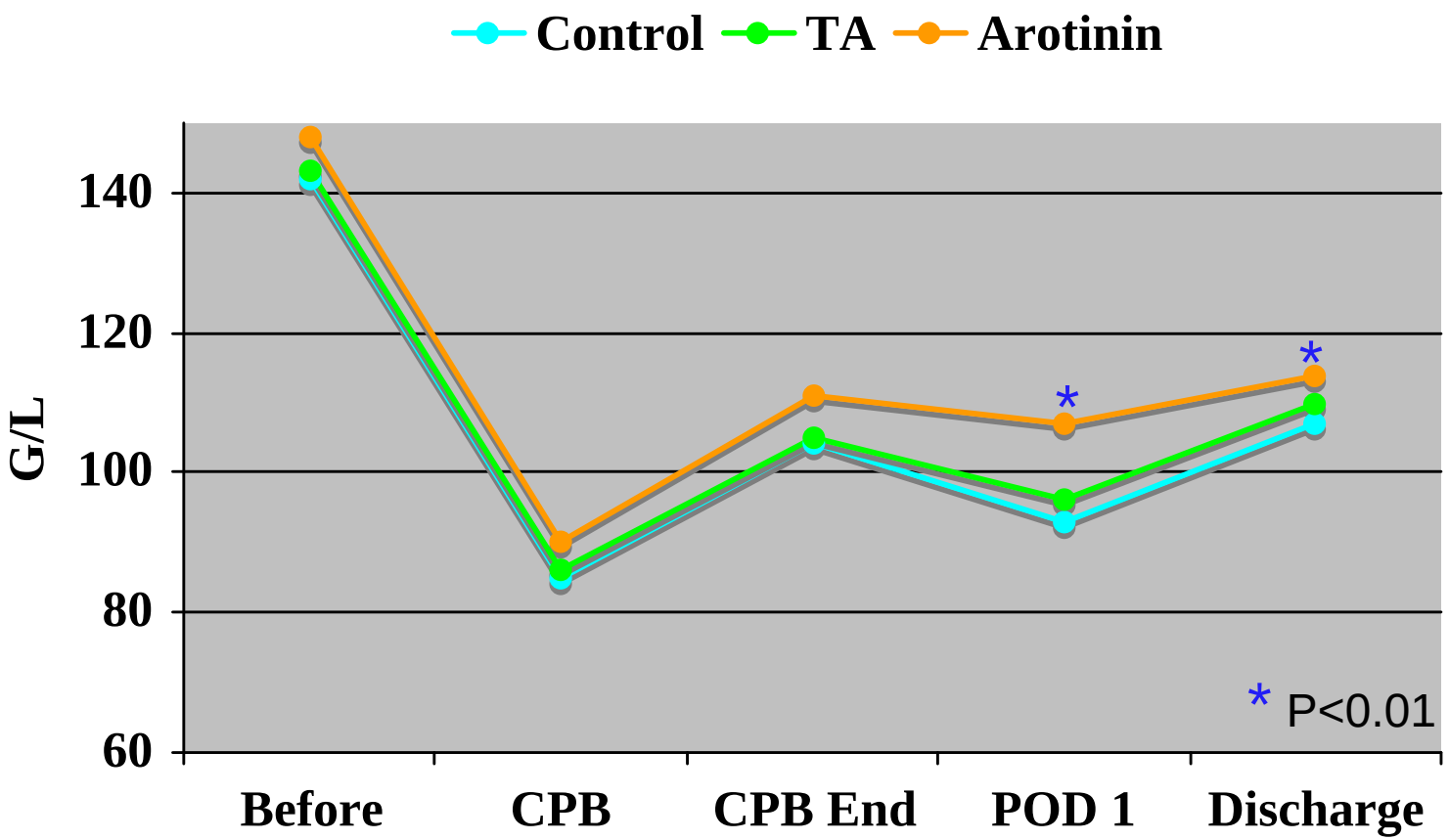
TA dosage: 61 mg/kg = 5g/patient)





Diprose P, Br J Anaesth 2005;94:271-8

Hemoglobin



Diprose P, Br J Anaesth 2005;94:271-8

FACHINFORMATION (Zusammenfassung der Merkmale des Arzneimittels/SPC)

CYKLOKAPRON®-INJEKTIONSLÖSUNG

Dosierung bei Patienten mit eingeschränkter Nierenfunktion

Serum-Kreatinin		Dosis i. v.	Verabreichung
µmol/l	mg/100 ml		
120 bis 249	1,35 bis 2,82	10 mg/kg KG (2 Ampullen)	alle 12 Stunden
250 bis 500	2,82 bis 5,65	10 mg/kg KG (2 Ampullen)	alle 24 Stunden
> 500	> 5,65	5 mg/kg KG (1 Ampulle)	alle 24 Stunden

Stand Dezember 2006

TA dosage: 2.5 - 100 mg/kg !!

Conclusion Tranexamicacid

- ***Pure antifibrinolytic***
- ***TA effectively reduces bleeding tendency***
- ***In patients with increased bleeding tendency, TA seems to be slightly less effective compared to Aprotinin***
- ***Apparently, no effect on inflammatory response, no effect on thrombin generation***
- ***Dosage undefined***

Discussion

- ***No allogeneic Blood - Major Advantage ??***

- ***Primary Prophylaxis to reduce Blood Loss***

$\not=$

Severe perioperative Bleeding Complications

Heart Surgery

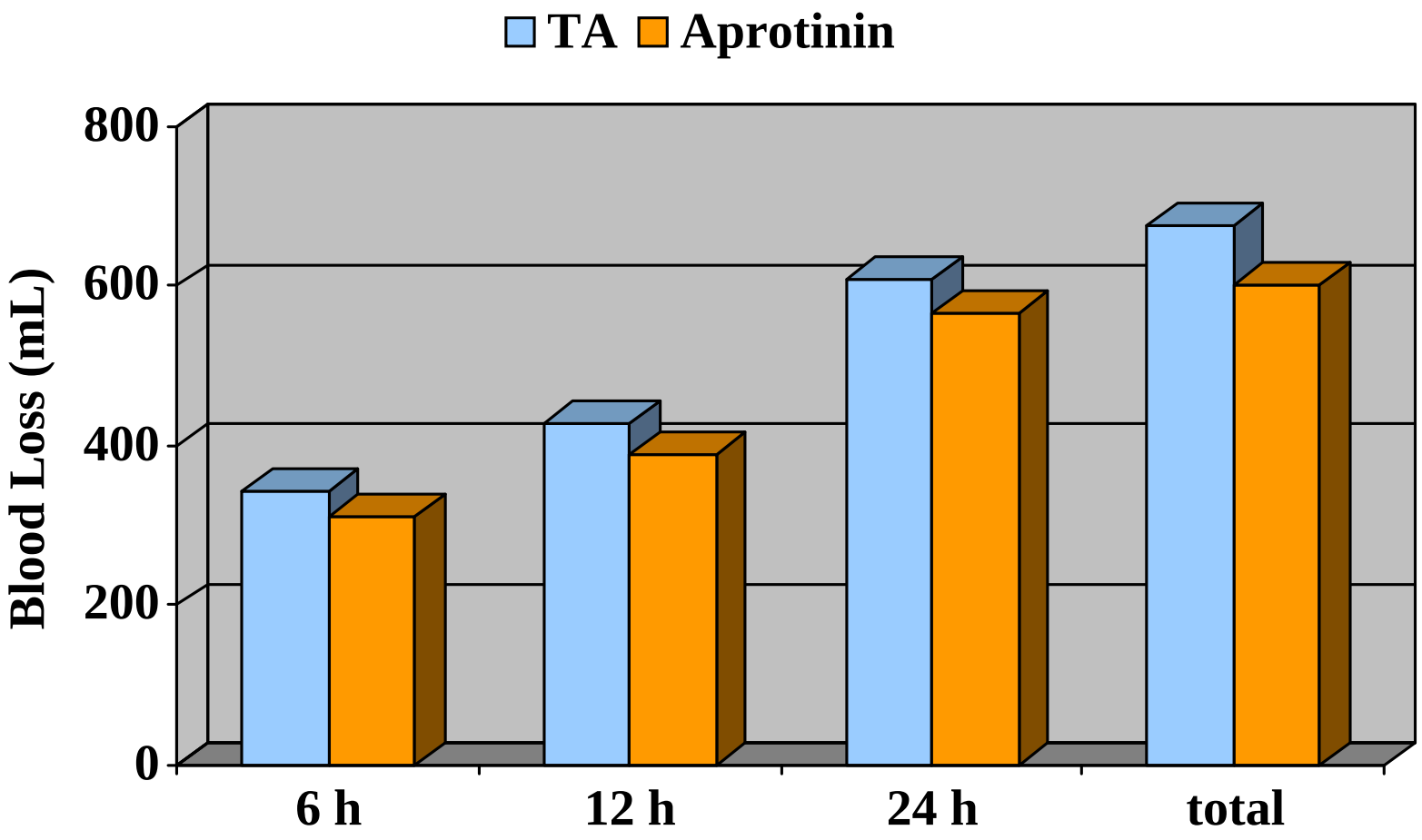
Organ Transplantation

Polytrauma **(Aprotinin better?)**

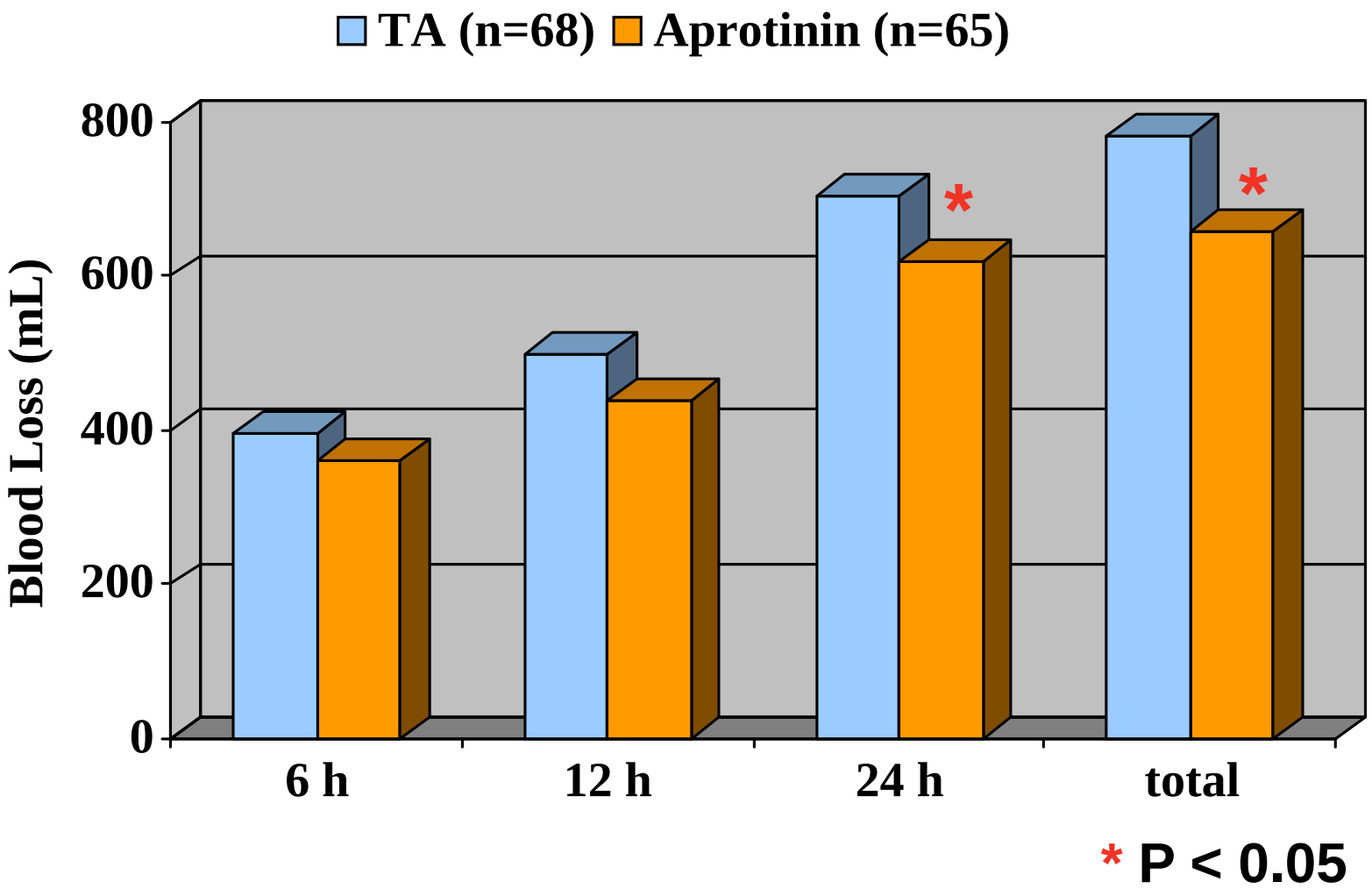
Procedural Characteristics

	TA	*Aprotinin*
CABG (n)	68	65
AVR (n)	39	40
Combined	3	5
CPB (min)	87±26	88±25
AoX (min)	60±17	62±17
Rethoracothomy (n)	3	2
Mortality (n)	1	3

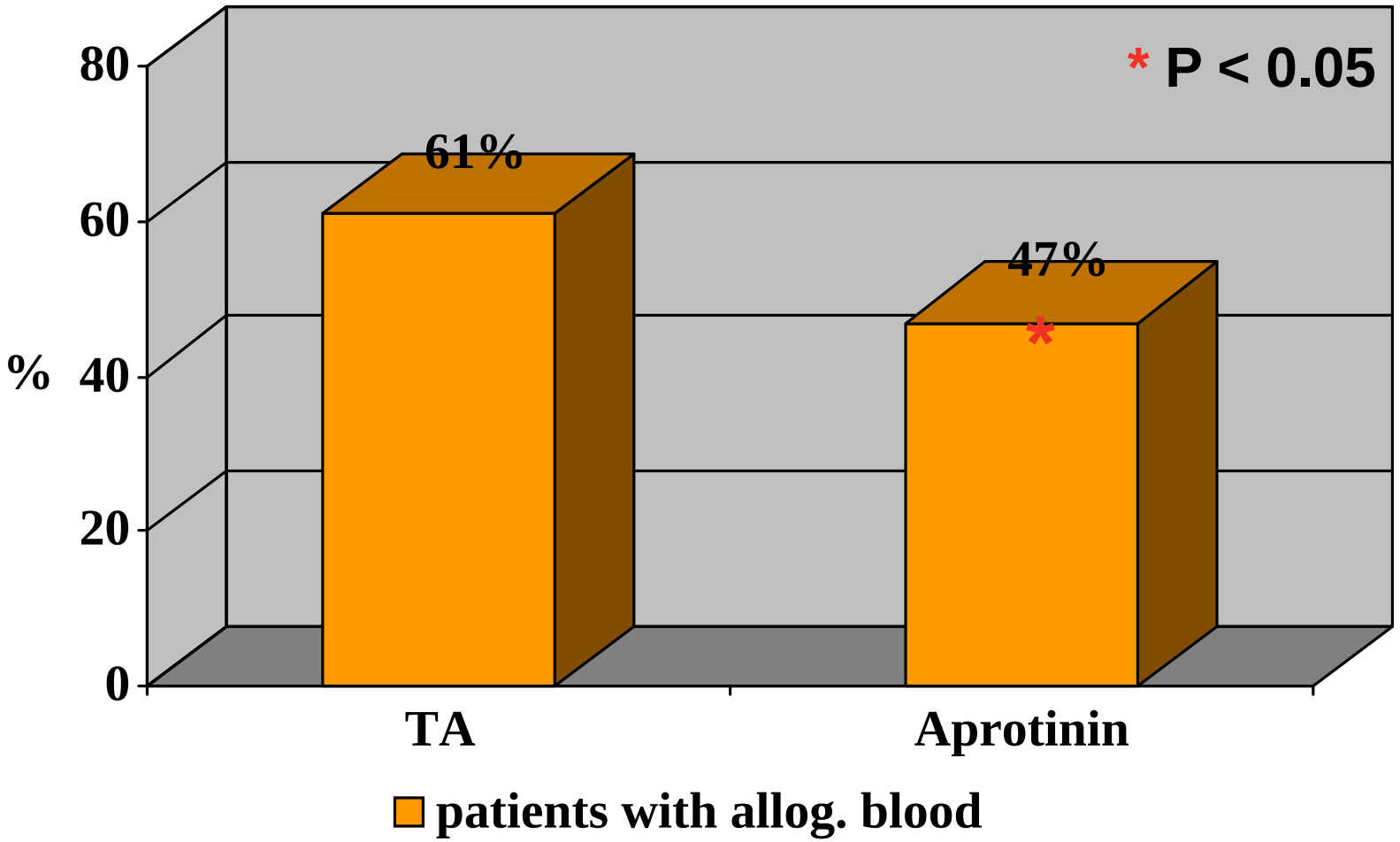
Blood Loss (ITT)



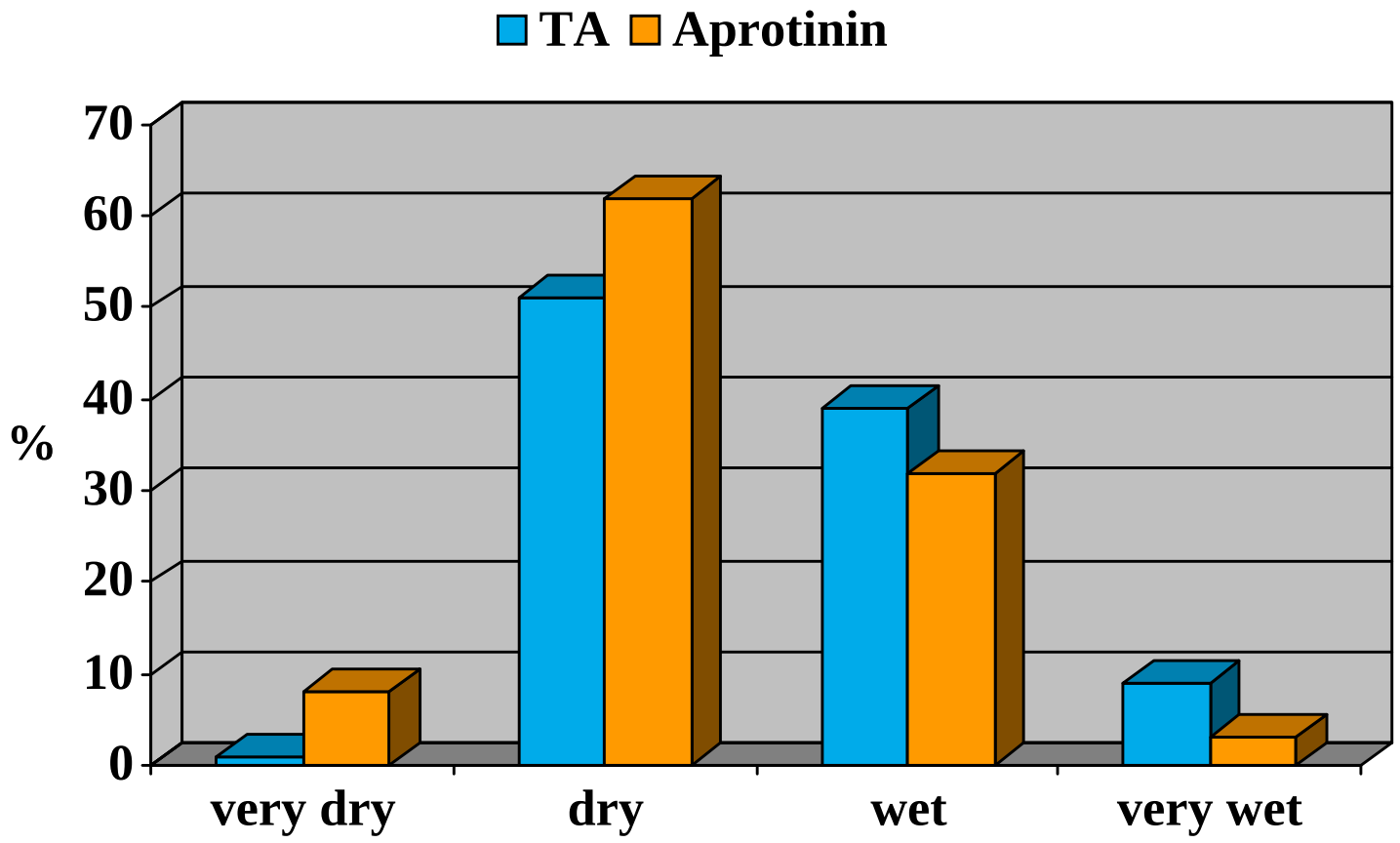
Blood Loss CABG (ITT)



Allogeneic Blood

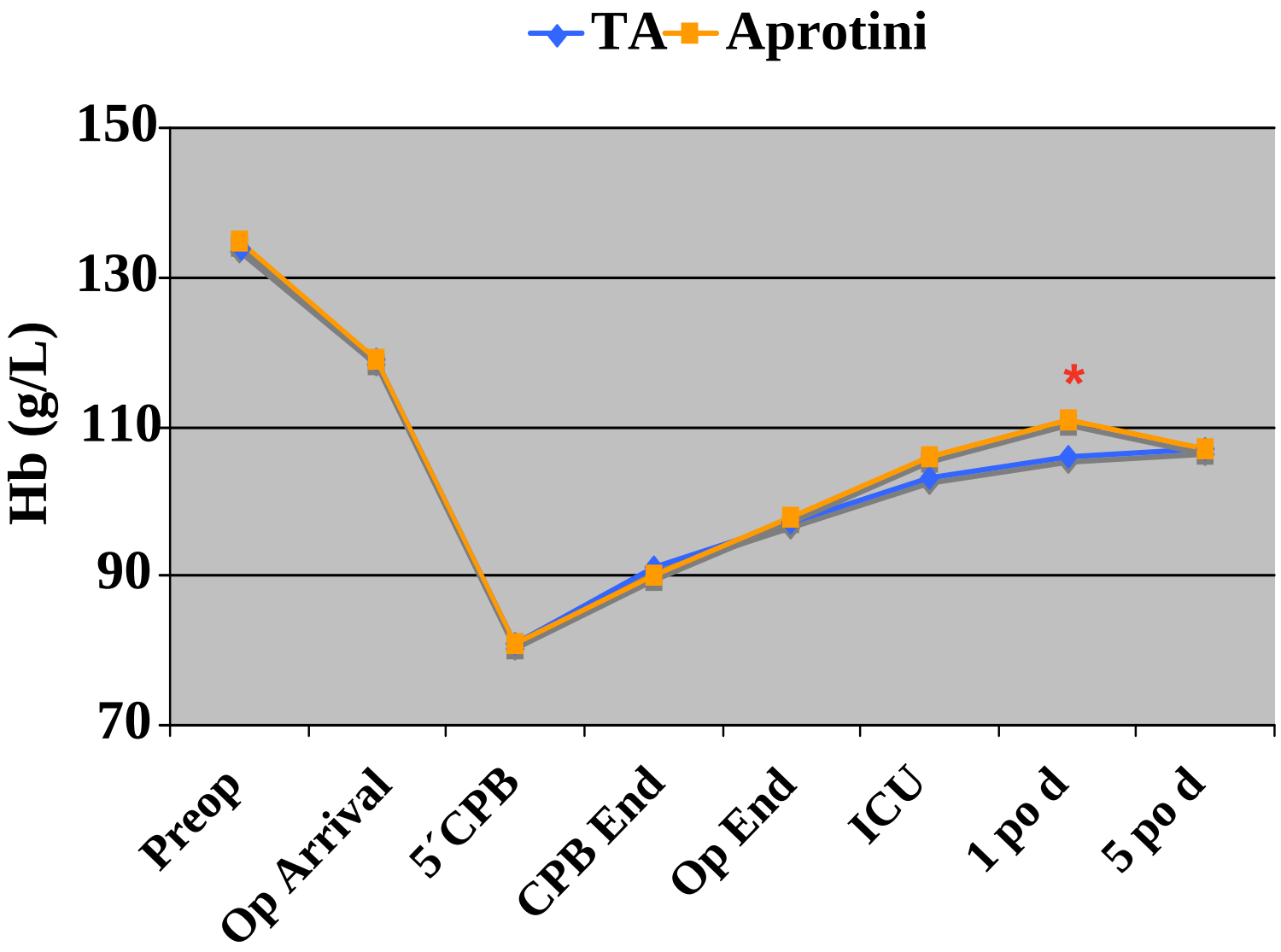


Assessment of Bleeding Tendency Surgeon and Anesthesiologist

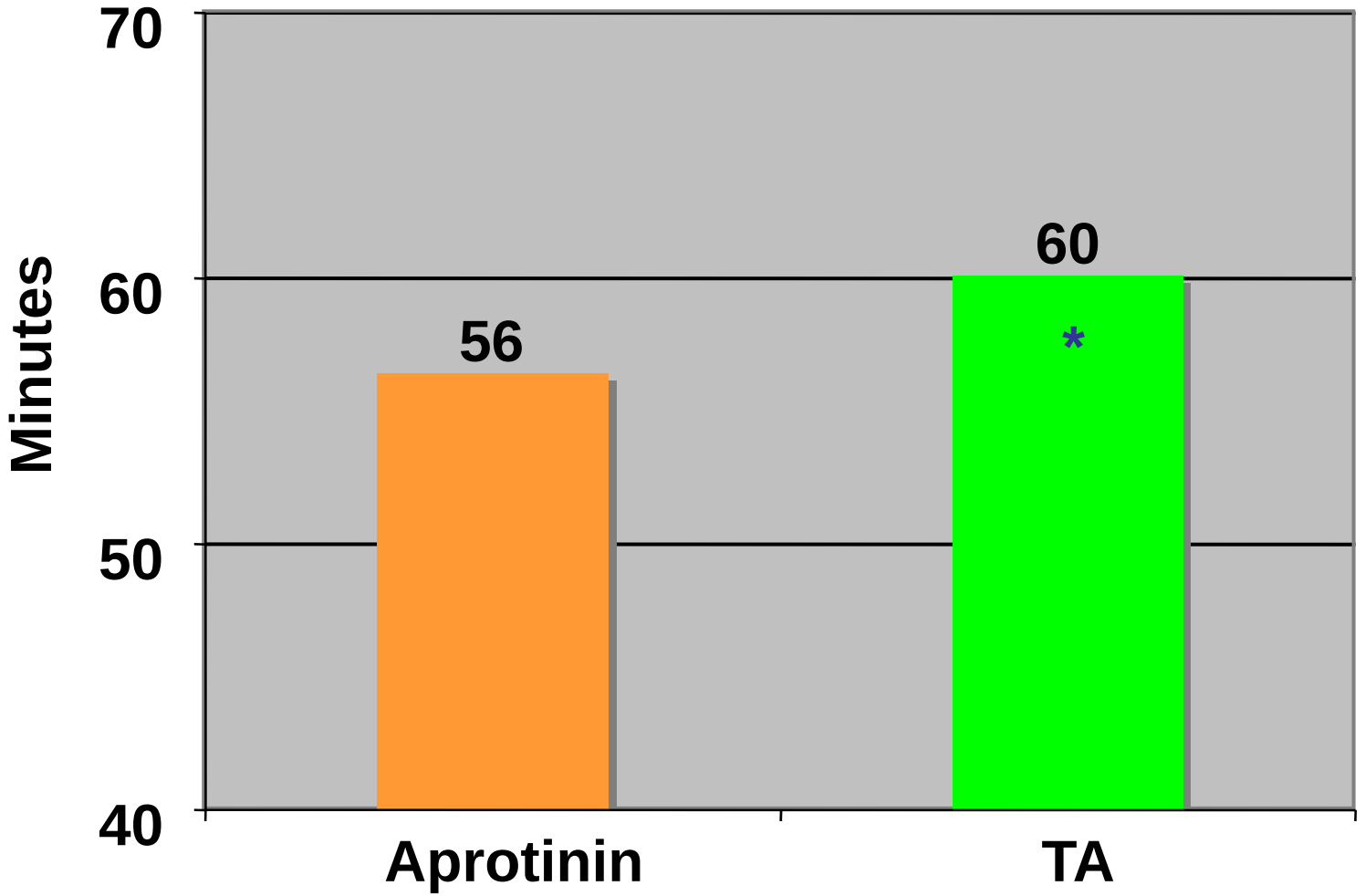


P = 0.018

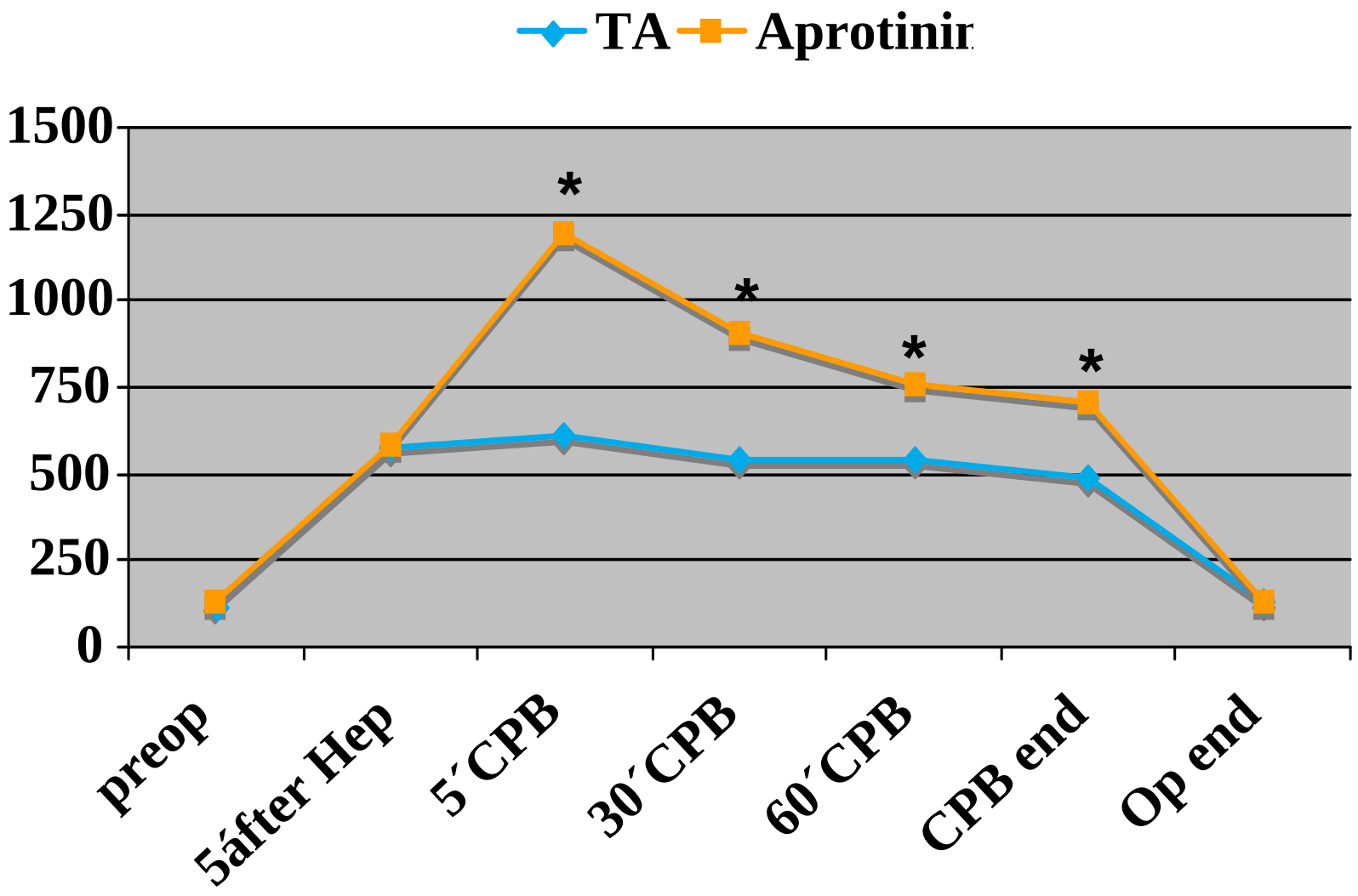
Hemoglobin (ITT)



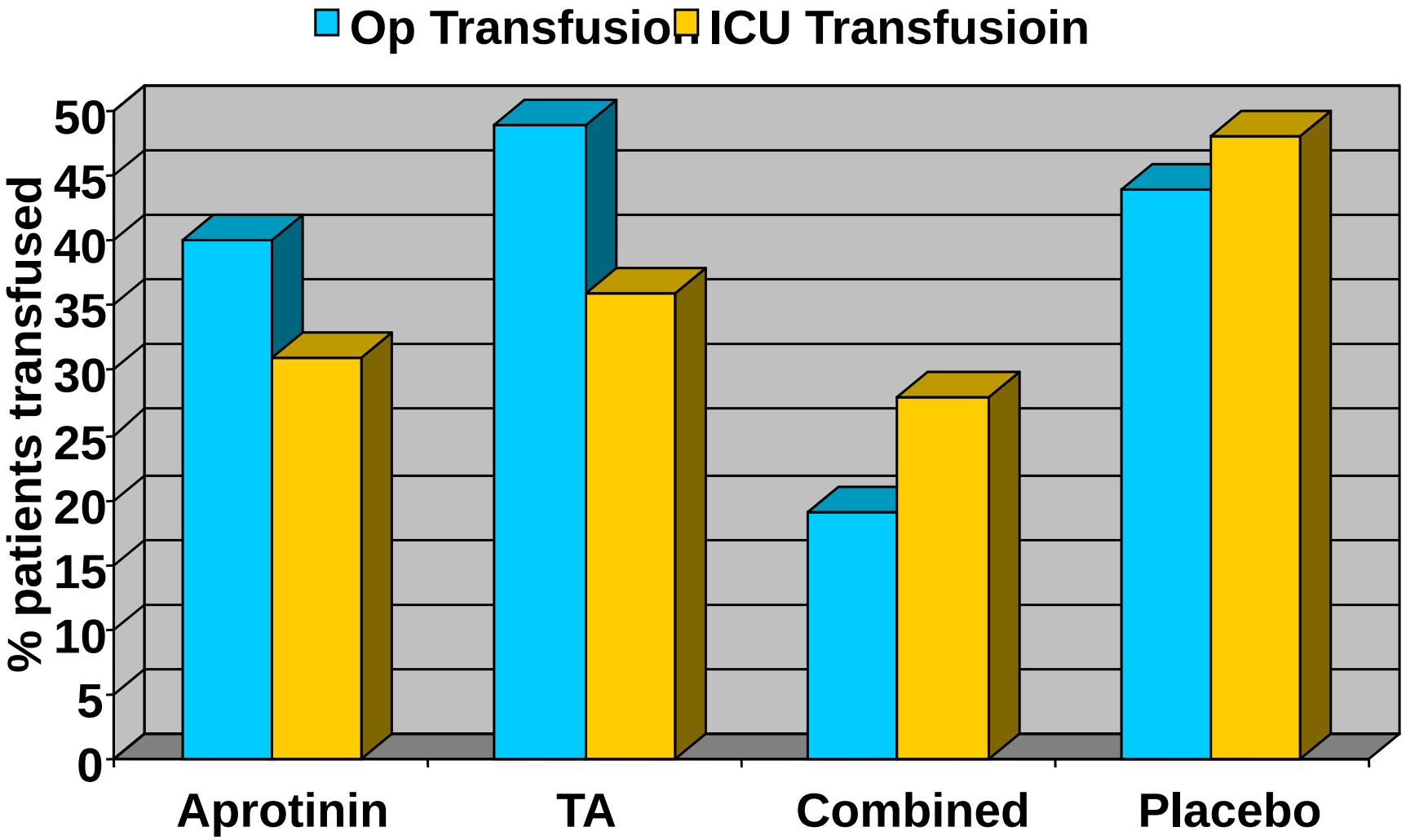
Chest Closure Time (CPB - Op End)



Celite ACT


TA
Aprotinir
1500
1250
1000
750
500
250
0
*
*
*
*
preop
5áfter Hep
5´CPB
30´CPB
60´CPB
CPB end
Op end

Tranexamicacid and Aprotinin



Nutall, Anesthesiology, 92:674 (200

Are antifibrinolytic drugs equivalent in reducing blood loss and transfusion in cardiac surgery? A meta-analysis of randomized head-to-head trials

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- Significant Reduction of blood loss Aprotinin vs. Tranexamicacid (106 ml)

  Clinical Relevance?

- Transfusion requirements, Rethorakotomie not different

Was scheinen (meinen) wir zu wissen ?

Aprotinin nicht effektiver als 50-100 mg/kg Tranexamsäure:

Primäre HCH

Pugh SC, J Cardiothorac Vasc Anesth, 1995;9:240 / Speekenbrink, Ann Thorac Surg, 1995;59:438 / Casati V, J Thorac Cardiovasc Surg, 2000;120:520 / Hekmat K, Curr Med Res Opin, 2004;20:121

ASS-Vorbehandlung

Bernet F, J Card Surg, 1999;14:92

Komplexe HCH (Re-OP´s, Doppeleingriffe)

Wong BI, Ann Thorac Surg, 2000;69:808 / Karkouti K, Transfusion, 2006;46:327

Risikoprofil: *wahrscheinlich* höher bei Aprotinin

Mangano DT, NEJM, 2006;354:353 / Karkouti K, Transfusion, 2006;46:327 / Mangano DT, JAMA 2007;297:471

Zur Anzeige wird der QuickTime™ Dekompressor „TIFF (Unkomprimiert)“ benötigt.

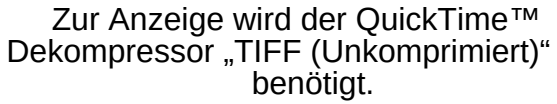

Figure 4. Adverse outcomes by antifibrinolytic agent compared with placebo. The RRs of adverse outcomes (mortality, stroke, and myocardial infarction) by antifibrinolytic agent vs placebo are plotted. The RR (diamond) and 95% CIs (horizontal bars) summarize the effect using a random-effects model. Effects left of 1.0 favor the antifibrinolytic agent over placebo; effects to the right favor placebo over antifibrinolytic agent. When the horizontal bars cross 1.0, the effect is not significantly different from the comparison group; this is the case for all agents for all adverse events (mortality, stroke, myocardial infarction) plotted here.

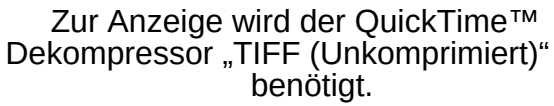

Figure 2. Total blood loss by antifibrinolytic agent compared with placebo. The WMD of total blood loss (mL) by antifibrinolytic agent, each compared with placebo. WMD (diamond) and 95% CIs (horizontal bars) summarize the effect using a random-effects model. All antifibrinolytic effects are to the left of the 0, representing a significant reduction in total blood loss over placebo.