PEDİYATRİK KALP CERRAHİSİNDE APROTİNİN

Dr Aynur Camkıran Fırat

GÖĞÜS KALP DAMAR ANESTEZİ VE YOĞUN BAKIM DERNEĞİ 26. ULUSAL KONGRESİ 17-18 Eylül 2020 E-KONGRE

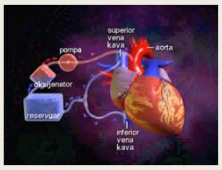
BAŞKENT ÜNİVERSİTESİ

Sunum Planı

- Pediyatrik kalp cerrahisi ile kanamanın ilişkisi
- Aprotinin nedir?
- Aprotinin ne işe yarar?
- Literatür eşliğinde tarihçesi
- Aprotinin yeniden piyasaya sunumu

Pediyatrik Kalp Cerrahisi

- KPB
  - *Koagülasyon, inflamasyon ve fibrinolizis aktivasyonu*
  - *Özellikle KPB'ın uzadığı durumlarda*
- Yenidoğan ve infantlarda daha belirgin
  - İmmatür doku ve organ fonksiyonları



Fibrinolizis aktivasyonu
Trombosit disfonksiyonu

Cardiopulmonary Bypass in Infants

Asli Dönmez, MD,* and Okan Yurdakök, MD†

Journal of Cardiothoracic and Vascular Anesthesia, Vol 28, No 3 (June), 2014: pp 778–788

Table 1. Comparison of Adult and Pediatric CPB

Parameter	Adult	Pediatric
Minimum CPB temperature	Rarely <25°-32°C	Frequently 15°-25°C
Use of total circulatory arrest	Rare	Common
Pump prime		
Dilution of blood volume	25%-33%	150%-300%
Whole blood or RBC added	Rare	Frequent
Perfusion pressure	50-80 mmHg	20-60 mmHg
Acid-base management strategy	Alpha-stat	pH-stat at temperature <28°-30°C
Glucose management		
Hyperglycemia	Frequent, requires insulin	Less common
Hypoglycemia	Rare	Common, reduced hepatic glycogen stores

Çocuklarda Perioperatif Kanamayı Artıran Diğer Faktörler

- ✓ Hemostatik sistemin immatüritesi
- ✓ KPB ile artan hemodilüsyon
- ✓ Siyanotik kalp hastalığının varlığı
- ✓ Cerrahi prosedürün karmaşıklığı

Pediyatrik Kalp Cerrahisi Sırasında Kanama

Sık görülen bir komplikasyon

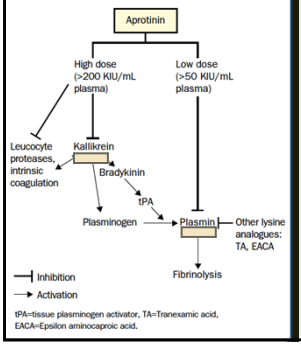
Antifibrinolitikler tercih edilmekte

Fibrinolizisin aktivasyonunun inhibisyonu

Trombosit disfonksiyonunun inhibisyonu

Kolaylaştırıcı faktörler (+)

Effects of aprotinin on fibrinolysis



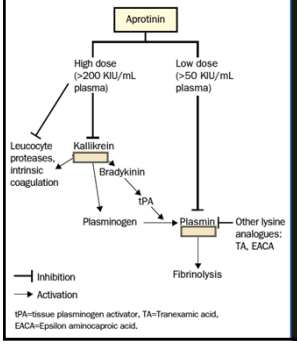
Aprotinin: pharmacological reduction of perioperative bleeding

THE LANCET • Vol 355 • April 15, 2000

- Nonspesifik serin proteaz inhibitörü
- Sığır akciğer dokusundan elde edilmekte
- Doz bağımlı inhibisyon
  - *Plasminin güçlü inhibitörü*
  - *Kallikrein üzerine daha az inhibisyon*
  - *Tripsin ve elastaz*

Fibrinolitik aktivitenin başlamasınından kaçınmak için profilaksi

Effects of aprotinin on fibrinolysis



tPA=tissue plasminogen activator, TA=Tranexamic acid, EACA=Epsilon aminocaproic acid.

Aprotinin: pharmacological reduction of perioperative bleeding

THE LANCET • Vol 355 • April 15, 2000

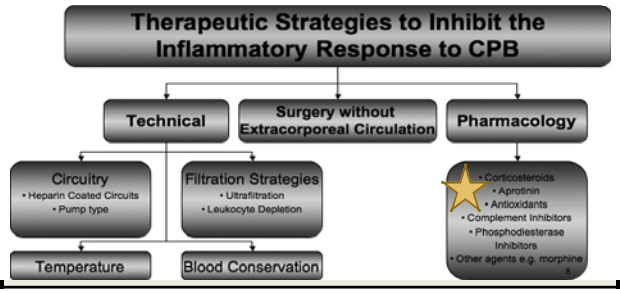
- Trombosit fonksiyonunun korunması (+)
- Perioperatif kanamayı azaltan güçlü bir antifibrinolitik
- Aprotinin kullanımında fibrinolitik aktivite belirteci D-dimer daha düşük
- İdeal olanı rekombinant insan aprotinin

9/18/20 7

The Inflammatory Response to Cardiac Surgery With Cardiopulmonary Bypass: Should Steroid Prophylaxis Be Routine?

John G.T. Augoustides, MD, FAHA, FASE

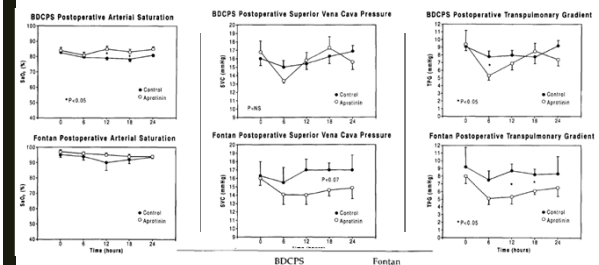
Journal of Cardiothoracic and Vascular Anesthesia, Vol 26, No 5 (October), 2012: pp 952-958



8

Aprotinin Improves Outcome of Single-Ventricle Palliation

(Ann Thorac Surg 1996;62:1329–36)



Characteristics	BDCPS Aprotinin	BDCPS Control	Fontan Aprotinin	Fontan Control
No. of patients	8	22	10	6
Age (mo)	10 ± 1	12 ± 1	70 ± 8	70 ± 23

9/18/20 9

Aprotinin Attenuates the Elevation of Pulmonary Vascular Resistance After Cardiopulmonary Bypass

J Korean Med Sci 2006; 21: 25-9

10 tane erkek, kırma köpek
Grup 1: Kontrol grubu
Grup 2: Aprotinin grubu

Before bypass: 50,000 KIU/kg continuous infusion for 20 min
After bypass: 10,000 KIU/kg/hr for 3 hr
Mixed in priming solution: 50,000 KIU/kg

Table 1. Comparison of post-bypass PVR/pre-bypass PVR between the control and the aprotinin groups

	Control	Aprotinin	*p*-value
PVR_1/PVR	1.28	1.58	NS
PVR_2/PVR	1.82	1.73	NS
PVR_3/PVR	1.9	1.66	NS
PVR_4/PVR	2.14	1.5	0.0047

PVR, pre-bypass PVR; $PVR_{0.5}$, post-bypass 0-3 hr PVR; NS, not significant.

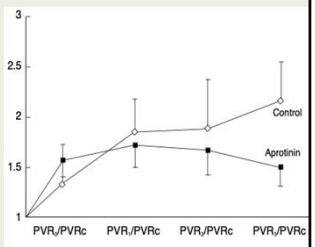


Fig. 1. The ratio of post-bypass over pre-bypass PVR in the control and the aprotinin groups.
PVR, prebypass PVR; $PVR_{0.5}$, postbypass 0-3 hr PVR.

Aprotinin Attenuates the Elevation of Pulmonary Vascular Resistance After Cardiopulmonary Bypass

J Korean Med Sci 2006; 21: 25-9

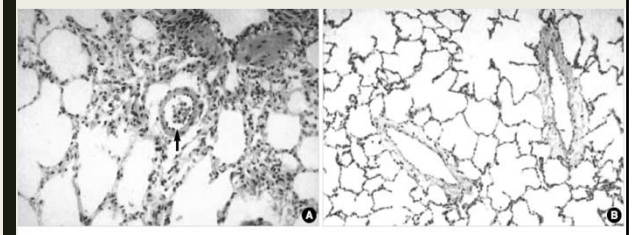
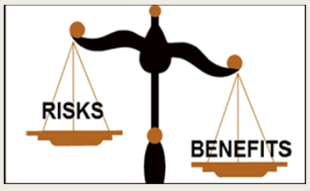


Fig. 3. Pathological findings of the lung. (A) Control group, Hematoxylin and eosin stain; original magnification × 100. (B) Aprotinin group, Hematoxylin and eosin stain; original magnification × 40.

9/18/20 11



ÇOCUKLARDA APROTİNİN GÜVENLİ Mİ?

- ✓ Alerjik reaksiyon
- ✓ Böbrek yetmezliği
- ✓ Anafilaktik reaksiyon
  - ✓ İlk 12 ay
- ✓ Mikrovasküler oklüzyon
- ✓ Strok

9/18/20 12

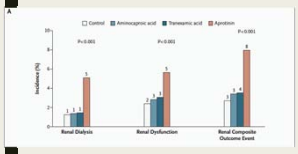
1960	• Akut pankreatit antiinflamatuvar
1987	**Effect of aprotinin on need for blood transfusion after repeat open-heart surgery** Lancet. 1987 Dec 5;2(8571):1289-91.
1993	• Yüksek riskli KABG lerde FDA onamı • Hepatik ve majör ortopedik cerrahide de popülarite (+) • Sistemik antiinflamatuvar etki nedeniyle konjenital kalp cerrahisi
1998	• Tüm KABG ler için FDA onamı
2006	• Mangano ve Karkouti çalışmaları, kullanımın sınırlanması
2007	• Üretici firma tarafından üretimin durdurulması
2012	• Distribütör firma değişimi

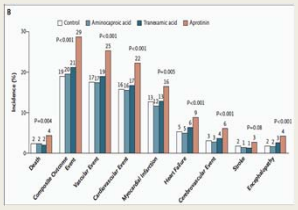
The risk of aprotinin: a conflict of evidence
www.thelancet.com Vol 367 April 29, 2006

The Risk Associated with Aprotinin in Cardiac Surgery
N Engl J Med 2006;354:353-65.

	Sedrakyan,[5] 2004	Levi,[6] 1999	Henry,[7] 2001
Mortality	0·96 (0·65–1·40)	0·55 (0·34–0·90)	0·87 (0·63–1·19)
Myocardial infarction	0·85 (0·63–1·14)	1·13 (0·76–1·67)	0·97 (0·69–1·36)
Renal failure	1·01 (0·55–1·83)	..	1·19 (0·79–1·79)
Stroke	0·53 (0·31–0·90)	..	0·43 (0·16–1·19)
Any thrombosis	..	..	0·64 (0·31–1·31)
Atrial fibrillation	0·90 (0·78–1·03)	..	..

Table: Relative risk estimates for aprotinin (95% CI) from three systematic reviews





The Risk Associated with Aprotinin in Cardiac Surgery

N Engl J Med 2006;354:353-65.

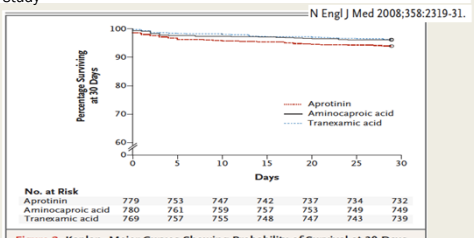
Bayer's Trasylol back in the dock as Canadian study is stopped

Bayer Türk Kimya San. Ltd. Şti.'den yapılan açıklamada, Bugün 08.11.2007 tarihi itibarıyla Kanada BART (BART çalışması yüksek riskli kardiyak operasyon hastaları üzerinde yapılan bağımsız, randomize ve kontrollü bir çalışmadır.) çalışmasından elde edilen nihai sonuçlar alınana ve değerlendirilene dek, T.C. Sağlık Bakanlığı ve dünya genelinde Ana Firma tarafından alınan karar uyarınca Trasylol® (aprotinin enjeksiyon) isimli preparatın ülkemizdeki pazarlama ve satışını, geçici olarak askıya almış ve ürünü geri çekmeye başlamıştır.

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

BART study

N Engl J Med 2008;358:2319-31.



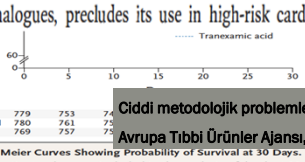
No. at Risk							
Aprotinin	779	753	747	742	737	734	732
Aminocaproic acid	780	761	759	757	753	749	749
Tranexamic acid	769	757	755	748	747	743	739

Figure 2. Kaplan–Meier Curves Showing Probability of Survival at 30 Days.
Among the 2328 patients who were included in the analysis of death at 30 days, patients in the aprotinin group had a reduced rate of survival as compared with those in the tranexamic acid group (P=0.05) and the aminocaproic acid group (P=0.06).

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

N Engl J Med 2008;358:2319-31.

Despite the possibility of a modest reduction in the risk of massive bleeding, the strong and consistent negative mortality trend associated with aprotinin, as compared with the lysine analogues, precludes its use in high-risk cardiac surgery.



No. at Risk							
Aprotinin	779	753	74				
Aminocaproic acid	780	761	75				
Tranexamic acid	769	757	75				

Figure 2. Kaplan–Meier Curves Showing Probability of Survival at 30 Days.
Among the 2328 patients who were included in the analysis of death at 30 days, patients in the aprotinin group had a reduced rate of survival as compared with those in the tranexamic acid group (P=0.05) and the aminocaproic acid group (P=0.06).

Ciddi metodolojik problemler

Avrupa Tıbbi Ürünler Ajansı, Şubat 2012

Aprotinin 10,000 KIU/ml Injection BP

4.1 Therapeutic indications

Aprotinin is indicated for prophylactic use to reduce blood loss and blood transfusion in adult patients who are at high risk of major blood loss undergoing isolated cardiopulmonary bypass graft surgery (i.e. coronary artery bypass graft surgery that is not combined with other cardiovascular surgery).

Paediatric population

The safety and efficacy in children below 18 years of age have not been established.

9/18/20

Comparative Analysis of Antifibrinolytic Medications in Pediatric Heart Surgery

J Thorac Cardiovasc Surg. 2012 March ; 143(3): 550–557

The Society of Thoracic Surgeons Congenital Heart Surgery Database (2004–2008)

-There were 22,258 patients (25 centers) included: median age 7.6m

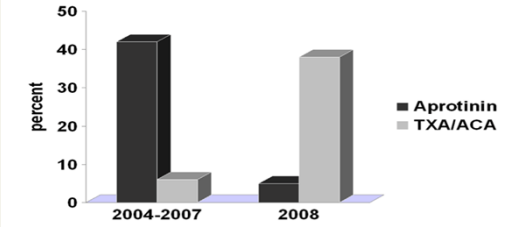


Figure 1.
Antifibrinolytic use in children undergoing heart surgery

9/

Comparative Analysis of Antifibrinolytic Medications in Pediatric Heart Surgery

J Thorac Cardiovasc Surg. 2012 March ; 143(3): 550–557

	Aprotinin	No drug	p-value	Aprotinin vs. No Drug	p-value
Overall	(n=7077)	(n=8644)			
In-hospital mortality	242 (3.4%)	317 (3.7%)	0.40	0.83 (0.68–1.04)	0.15
Bleeding requiring surgical invervention	122 (1.7%)	173 (2.0%)	0.20	0.76 (0.57–1.02)	0.07
Composite*	340 (4.8%)	455 (5.3%)	0.19	0.81 (0.68–0.97)	0.02
Dialysis	106 (1.5%)	102 (1.2%)	0.08	1.03 (0.74–1.45)	0.85
Neurologic deficit	113 (1.6%)	95 (1.1%)	0.007	1.18 (0.84–1.64)	0.34
Total LOS, days	8.7 (4.0–13.0)	7.9 (4.0–11.0)	<0.0001	1.02 (1.00–1.05)	0.11
ICU LOS, days	5.1 (2.0–8.0)	4.4 (2.0–7.0)	<0.0001	1.03 (0.99–1.06)	0.12
Duration of ventilation, days	3.4 (1.0–5.0)	3.0 (1.0–5.0)	<0.0001	1.04 (1.01–1.09)[a]	0.02
Neonate Subgroup	(n=1517)	(n=1700)			
In-hospital mortality	165 (10.9%)	207 (12.2%)	0.25	0.88 (0.66–1.17)	0.38
Bleeding requiring surgical invervention	49 (3.2%)	72 (4.2%)	0.14	0.91 (0.56–1.49)	0.71

Comparative Analysis of Antifibrinolytic Medications in Pediatric Heart Surgery

J Thorac Cardiovasc Surg. 2012 March ; 143(3): 550–557

	Aprotinin	No drug	p-value	Aprotinin vs. No Drug	p-value
Redo Sternotomy Subgroup	(n=2819)	(n=2239)			
In-hospital mortality	64 (2.3%)	67 (3.0%)	0.11	0.57 (0.37–0.87)	0.009
Bleeding requiring surgical invervention	45 (1.6%)	61 (2.7%)	0.006	0.50 (0.30–0.85)	0.01
Composite*	102 (3.6%)	118 (5.3%)	0.004	0.56 (0.40–0.80)	0.001
Dialysis	29 (1.0%)	21 (0.9%)	0.74	0.96 (0.45–2.02)	0.91
Neurologic deficit	51 (1.8%)	27 (1.2%)	0.08	1.22 (0.68–2.20)	0.51
Total LOS, days	7.5 (4.0–10.0)	8.1 (5.0–11.0)	0.001	0.94 (0.90–0.98)[b]	0.006
ICU LOS, days	3.8 (2.0–6.0)	4.1 (2.0–6.0)	0.0002	0.90 (0.84–0.95)[c]	0.0004
Duration of ventilation, days	2.3 (1.0–3.0)	2.7 (1.0–4.0)	0.005	0.93 (0.87–1.00) [d]	0.04

9/18/20 22

Safety of Aprotinin in Congenital Heart Surgery: Results from a Large Multi-center Database

Ann Thorac Surg. 2010 July ; 90(1): 14–21

Patient and Center Characteristics

Overall	No Aprotinin	Aprotinin	p
30372	17041 (56.1)	13331 (43.9)	

- ✓ 35 farklı merkez
- ✓ 2003-2007 yılları arasında
- ✓ Medyan yaş 7 ay

Table 3

a. Adjusted Outcomes

	OR (95% CI)	p
Mortality	1.00 (0.99, 1.01)	0.447
Dialysis	1.00 (0.99, 1.01)	0.975
	LSM Difference Aprotinin - No Aprotinin	
Total length of Stay (days)	−0.44 (−1.01, 0.13)	0.127
ICU length of Stay (days)	0.18 (−0.15, 0.51)	0.291

Aprotinin, transfusions, and kidney injury in neonates and infants undergoing cardiac surgery

Table 1 Most common procedures performed in the study population

Procedures (numbers)	Control (n=568)	Aprotinin group (n=390)
Ventricular septal defect repair	117	73
Tetralogy of Fallot repair	90	66
Arterial switch operation	66	63
Complete atrioventricular canal repair	48	19
Arterial switch operation and ventricular septal closure ± aortic arch repair	44	28
Total anomalous pulmonary vein connection repair	24	20
Aortic arch repair	23	14
Bidirectional cavo-pulmonary anastomosis	18	11
Aortic valvuloplasty	15	13
Truncus arteriosus repair	8	9
Modified Blalock–Taussig shunt	10	6
'Reparation à l'étage ventriculaire'	9	4
Anomalous origin of the left coronary artery from the pulmonary artery	8	7
First stage palliation of the hypoplastic left heart syndrome	8	6
Pulmonary stenosis repair	8	2
Konno procedure	4	1
Others	68	48

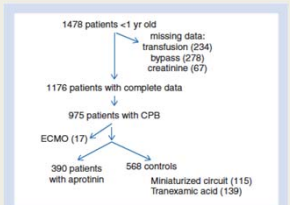


Fig 1 Patient enrolment process over a 42 month period. Aprotinin was suspended from prophylactic use starting in the 20th month. Patients with missing data concerning transfusion and/or CPB characteristics and/or postoperative creatinine measurements were excluded.

British Journal of Anaesthesia 108 (5): 830–7 (2012)

9/18/20 24

Aprotinin, transfusions, and kidney injury in neonates and infants undergoing cardiac surgery

British Journal of Anaesthesia 108 (5): 830–7 (2012)

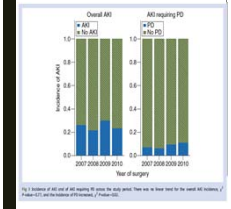


Table 4 Association between AKI, the prophylactic use of aprotinin, and blood product transfusions on the day of surgery, adjusted for the use of a miniaturized circuit (with reduced priming volume and reduced ultrafiltration), for the use of tranexamic acid, and for the year of surgery. Associations were assessed using inverse probability of treatment-weighted logistic regression models. Both incidence of AKI and incidence of severe injury PD were analysed

Variable	AKI		Severe AKI requiring dialysis	
	Adjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Use of aprotinin	0.62 (0.35–1.08)	0.09	1.40 (0.47–4.20)	0.54
Number of PRBC transfusions on day 0	1.64 (1.12–2.41)	0.01	2.07 (1.13–3.73)	0.02
Number of FFP transfusions on day 0	2.28 (1.68–3.09)	<0.001	3.11 (1.95–4.97)	<0.001
Number of platelet transfusions on day 0	1.33 (0.93–1.92)	0.12	2.20 (1.21–4.01)	0.01
Use of a miniaturized circuit	1.74 (0.82–3.68)	0.15	1.19 (0.41–3.50)	0.74
Priming volume (per 100 ml)	0.98 (0.66–1.43)	0.90	0.60 (0.32–1.14)	0.12
Ultrafiltration rate (per ml kg^{-1} h^{-1})	0.74 (0.59–1.03)	0.07	0.82 (0.57–1.16)	0.26
Use of tranexamic acid	0.92 (0.57–1.50)	0.74	0.86 (0.36–2.04)	0.73
Year of surgery	0.87 (0.65–1.16)	0.34	1.43 (0.87–2.36)	0.15

EACTA Annual Congress 2015

Gothenburg · Sweden · June 24 - 26, 2015

12:00 Aprotinin should be used in cardiac surgery - yes
J. Levy, Duke University School of Medicine

12:30 Aprotinin should not be used in cardiac surgery - no
A. Koster, University Hospital Bochum

Aprotinin: is it time to reconsider?
Eur J Anaesthesiol 2015; **32**:591 – 595

Antifibrinolytic Therapy for Cardiac Surgery
An Update
Anesthesiology 2015; 123:214–21

Use of antifibrinolytics in pediatric cardiac surgery: Where are we now?
Pediatric Anesthesia. 2019;29:435–440.

The Safety and Efficacy of Antifibrinolytic Therapy in Neonatal Cardiac Surgery

PLOS ONE | **Published:** May 8, 2015

Chih-Yuan Lin[1,3], Jeffery H. Shuhaiber[1], Hugo Loyola[1], Hua Liu[1], Pedro del Nido[1], James A. DiNardo[2], Frank A. Pigula[1]*

Table 1. Preoperative and intraoperative characteristics.

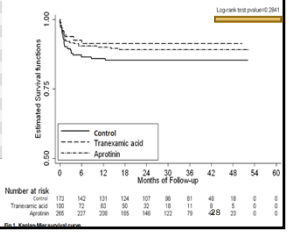
Characteristic	Group ANo antifibrinolytic(n = 184)	Group B Tranexamic acid only(n = 104)	Group C Aprotinin and both aprotinin and tranexamic acid(n = 276)	p-Value
Patients, n	177	100	275	
Male gender, n(%)	105 (59.3)	56 (56.0)	155 (58.4)	0.87
Age at surgery median (IQR) days	6 (4–12)	6 (4–12)	5 (4–8)	0.0036
Weight, mean (SD) Kg	3.06 (0.61)	3.26 (0.56)	3.10 (0.66)	0.0520
Prematurity, n	3	0	10	0.138
RACHS-1 score, median (IQR)	3 (3–6)	3 (3–4)	4 (3–6)	0.2850
Deep hypothermic circulatory arrest, median (IQR) min	32 (13–48)	31.5 (12.5–49)	17 (9–27)	0.0001
CPB time, median (IQR) min	128 (100–158)	142 (116–166)	138 (120–163)	0.0027
Aortic cross-clamp time, median (IQR) min	65 (48–84)	78 (54–99)	71 (57–86)	0.0971

The Safety and Efficacy of Antifibrinolytic Therapy in Neonatal Cardiac Surgery

PLOS ONE | **Published:** May 8, 2015

Table 3. Adjusted effect of antifibrinolytic therapy on odds ratio for death.

Risk factor	OR	P value	[95%CI for OR]
None	1.00*		
Transexamic Ac	0.27	0.092	0.06–1.23
Aprotinin	0.31	0.357	0.02–3.62
Gender(female ref)	1.27	0.720	0.33–4.79
Age at surgery	1.05	0.240	0.96–1.16
Days in Hospital	0.77	0.001	0.67–0.89
Days in CICU	1.35	<0.001	1.16–1.57
Cross-clamp Ao	0.96	0.039	0.93–0.99
CPB temp	1.21	0.012	1.04–1.41
CPB time	1.02	0.020	1.00–1.05
RACHS-1 level 1–2	1.00*		
RACHS-1 level 3	1.28	0.816	0.15–10.4
RACHS-1 level 4	0.73	0.831	0.04–12.6
RACHS-1 level 6	7.31	0.084	0.76–69.9
Creatinine pre-post	3.74	0.385	0.19–73.9
Transfusion < 24h	0.98	0.200	0.97–1.00



Aprotinin versus tranexamic acid in children undergoing cardiac surgery: an observational study

European Journal of Cardio-Thoracic Surgery 56 (2019) 688–695

Key question
Should aprotinin be reintroduced in children undergoing cardiac surgery?

Key finding(s)
Aprotinin is associated with higher exposure to blood products and severe postoperative morbidity or mortality.

Take-home message
There is insufficient evidence to reintroduce aprotinin in paediatric cardiac surgery apart from a well-designed study.

Çalışmanın amacı

- Transfüzyon miktarı, morbidite ve mortaliteyi karşılaştırmak

Aprotinin için

- Yüksek riskli subgrupta antifibrinolitik ve antiinflamatuvar etkinliğine bakmak

Aprotinin versus tranexamic acid in children undergoing cardiac surgery: an observational study

European Journal of Cardio-Thoracic Surgery 56 (2019) 688–695

Table 1: Preoperative characteristics and intraoperative data

Variables	TXA group (N = 1020)	Aprotinin group (N = 1142)	P-value
Male gender	594 (58.2)	637 (55.8)	0.250
Age (months)	9.6 (3.0–38.7)	16.0 (6.0–52.0)	<0.001
Preoperative weight (kg)	6.8 (4.3–13.5)	8.0 (5.0–15.0)	<0.001
Cyanotic heart disease (yes)	430 (42.2)	531 (46.5)	0.043
RACHS-1 score			0.008
Risk category 1–2	488 (47.8)	560 (49.0)	
Risk category 3–4	496 (48.7)	550 (48.2)	
Risk category 5–6	25 (2.5)	6 (0.5)	
CPB time (min)	109 (78–139)	112 (78–142)	0.268
Aortic cross-clamp time (min)	48.0 (30.0–69.0)	53.0 (32.0–76.0)	<0.001
Circulatory arrest	64 (6.3)	121 (10.6)	<0.001
MUF	972 (96.1)	1008 (88.5)	<0.001
Subgroups			
Neonates (N = 236)	144 (14.1)	92 (8.1)	0.009
Complex surgery (N = 1084)	524 (51.4)	560 (49.0)	0.007
Redo surgery (N = 377)	247 (24.2)	130 (11.4)	<0.001

European Journal of Cardio-Thoracic Surgery 56 (2019) 688–695

Table 4: Primary outcomes in the whole population and high-risk subgroups

Variables	TXA group (N = 1020)	Aprotinin group (N = 1142)	97.5% CI[a]	P-value
Exposure to blood products				
Overall	363 (59.8)	885 (77.5)	0.14–0.22	<0.001
Neonates (N = 236)	138 (95.9)	91 (99.0)	-0.01 to 0.07	0.091
Complex surgery (N = 1084)	346 (66.2)	445 (79.4)	0.08–0.19	<0.001
Redo surgery (N = 377)	93 (37.8)	68 (52.1)	0.03–0.15	0.003
Severe postoperative morbidity or mortality				
Overall	287 (28.1)	375 (32.8)	0.01–0.09	0.007
Neonates (N = 236)	87 (60.8)	72 (77.8)	0.05–0.30	0.002
Complex surgery (N = 1084)	211 (40.3)	244 (43.4)	-0.03 to 0.09	0.148
Redo surgery (N = 377)	33 (13.5)	113 (8.7)	-0.11 to 0.02	0.102

9/18/20 31

European Journal of Cardio-Thoracic Surgery 56 (2019) 688–695

Table 5: Secondary outcomes in the whole population

Variables	TXA group (N = 1020)	Aprotinin group (N = 1142)	99.7% CI[a]	P-value
Bleeding and transfusions				
Intraoperative blood loss (ml kg^{-1})	30.0 ± 27.2	48.5 ± 35.8	15.0–22.0	<0.001
PO blood loss (24 h) (ml kg^{-1})	14.9 ± 12.6	19.7 ± 19.5	2.8–7.0	<0.001
PO blood loss (total) (ml kg^{-1})	31.9 ± 58.8	39.8 ± 57.2	0.9–15.1	<0.001
RBC exposure	583 (57.2)	847 (74.2)	0.1–0.2	<0.001
FFP exposure	179 (17.5)	208 (18.2)	-0.1 to 0.1	0.652
Platelet exposure	71 (7.0)	123 (10.8)	0.0–0.1	0.005
RBC transfusion (ml kg^{-1})	13.9 ± 24.6	31.2 ± 35.4	13.9–20.8	<0.001
FFP transfusion (ml kg^{-1})	39.3 ± 29.2	34.3 ± 40.6	-5.4 to 0.1	0.503
Platelet transfusion (ml kg^{-1})	28.3 ± 29.5	28.3 ± 26.7	-0.5 to 2.3	0.774
Morbidity and mortality				
Infection	404 (39.6)	518 (45.4)	-0.0 to -0.1	0.004
Neurologic event	56 (5.5)	148 (13.0)	0.1–0.1	<0.001
Respiratory failure[b]	245 (24.0)	290 (25.4)	-0.1 to 0.1	0.428
Length of MV (h)	78.3 ± 140.8	99.5 ± 422.6	-21.8 to 64.6	0.170
PICU LOS (days)	9.9 ± 19.6	8.9 ± 21.2	-3.7 to 1.7	0.206
Hospital LOS (days)	21.9 ± 36.4	23.2 ± 33.0	-3.1 to 5.7	0.338
Renal failure[c]	36 (3.5)	30 (2.6)	-0.0 to 0.0	0.278
Prolonged inotropic support[d]	32 (41.8)	37 (57.7)	0.1–0.2	<0.001
Mortality (in hospital)	32 (3.1)	37 (3.5)	-0.0 to 0.0	0.681

9/18/20 32

European Journal of Cardio-Thoracic Surgery 56 (2019) 688–695

Table 3: Results of the matching using the covariate balancing propensity score

Retrospektif çalışma
13 yıl gibi uzun bir dönem

Variables			ASD (%)
Age (months)		9 ± 41.67	0.00
Preoperative weight (kg)		8 ± 11.39	0.00
ASA score		8 ± 0.49	0.00
Cyanotic heart disease (yes)		97	0.00
Redo surgery (yes)		85	0.00
RACHS-1		7 ± 0.81	0.00
CPB time (min)		6 ± 49.13	0.00

Table 4: Primary outcome

Variables			7.5% CI[a]	P-value
Exposure to blood products				
Overall			0.14–0.22	<0.001
Neonates (N = 236)			0.01 to 0.07	0.091
Complex surgery (N = 1084)			0.08–0.19	<0.001
Redo surgery (N = 377)			0.03–0.15	0.003
Severe postoperative morbidity c				
Overall			0.01–0.09	0.007
Neonates (N = 236)	87 (60.8)	72 (77.8)	0.05–0.30	0.002
Complex surgery (N = 1084)	211 (40.3)	244 (43.4)	-0.03 to 0.09	0.148
Redo surgery (N = 377)	33 (13.5)	113 (8.7)	-0.11 to 0.02	0.102

Key finding(s)

Aprotinin is associated with higher exposure to blood products and severe postoperative morbidity or mortality.

Take-home message

There is insufficient evidence to reintroduce aprotinin in paediatric cardiac surgery apart from a well-designed study.

SONUÇ OLARAK,

- Elimizdeki verilere göre, açık kalp cerrahisinde sırasında kullanılan aprotinin,
- Fibrinolizisi inhibe eder
- Trombosit fonksiyonlarının korunmasını sağlar
- Kan ürünlerinin kullanımını azaltır

9/18/20 34

Aprotinin pediyatrik kalp cerrahisinde kullanımı güvenli mi?

GÖĞÜS KALP DAMAR ANESTEZİ VE YOĞUN BAKIM DERNEĞİ 26. ULUSAL KONGRESİ 17-18 Eylül 2020 E-KONGRE

BAŞKENT ÜNİVERSİTESİ