Title: **MECHANISMS OF BLEEDING REDUCTION INDUCED BY APROTININ DURING CARDIOPULMONARY BYPASS : A CONTROLLED STUDY**

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Effectiveness of Aprotinin (Trasylol) on bleeding during cardiopulmonary bypass(CPB) has been well established. Mechanisms of action were investigated in a double blind study performed on 20 patients who underwent aorto coronary bypass and were randomly included in Placebo(P) or in Aprotinin(A) group.
Patients characteristics: age (A: 60.4±8.1, P: 62.8± 4.64 years), number of grafts (A: 2.6± .5, P: 2.6±.5) and preoperative Left Ventricular Ejection Fraction (A: 50 ± 8.3 %, P: 48 ± 5 %), no aspirin during 8 days prior to the operation.
Aprotinin Protocol: loading dose of 280 mg prior to incision, 280 mg into the membrane oxygenator prime, and a continuous infusion of 50 mg/h from anesthesia induction until ICU arrival. Heparinemia during CPB was kept over 4Units/ml. Blood loss from mediastinal drainage was recorded for each patient. Blood was sampled before anesthesia(1), 30 min after start of CPB(2), 5 min after aortic clamp release(3) and after heparin neutralization(4). Samples were studied to determine: 1° specific fibrin degradation products as D Dimers complex (DDE),
2° Platelet function by Ristocetin Agglutination,
3° tissue Plasminogen Activators (tPA),
4° βThromboglobulin (BTG) and platelets number.

RESULTS: ANOVA mean 1-4,

		1	2	3	4	ANOVA
DDE (ng/ml)	A	102	57	81	461	<.001
	P	280	338*	710**	1944**	
RA	A	100	103	100	92	<.001
(%control)	P	100	78*	61**	52**	
PLATELETS	A	250	125	133	111	ns
(1000/mm3)	P	276	122	143	135	
tPA (ng/ml)	A	8.3	6.7	10.6	18.4	ns
	P	6.8	10.6	11.8	18.4	
BTG (ng/ml)	A	117	117	180	290	ns
	P	98	106	182	283	
PK	A	100	73	69	73	ns
(%control)	P	100	69.5	62	68.8	

p<0.05 *, p<0.005 **

NEGATIVE CORRELATIONS
DDE2 vs RA(4) p<0.001, vs RA(3) p<0.008

DRAINAGE VOLUME		MEAN	SEM	WILCOXON
(ml)	A	277	±46	p≤ 0.04
	P	629	±189	

Those findings suggest that Aprotinin acts by plasmin inhibition with a resulting protective effect on platelet GPIb receptors break down on the platelet membrane. Moreover A inhibits tPA effects on the hemostatic clots of the wound closure
REFERENCES: Bidstrup BP et al, J Thorac. Cardiovasc. Surg., 1989, Vol97, 364.

A1206

TITLE: IS THE THROMBOELASTOGRAPH A CLINICALLY USEFUL PREDICTOR OF BLOOD LOSS AFTER BYPASS?

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The thromboelastograph (TEG) may assist recognition and management of coagulopathies after cardiopulmonary bypass (CPB).[1] Fig.1 displays TEG measurements: R and K reflect coagulation time; α is speed of clot formation; MA is maximum clot strength; A_{60} is clot strength 60 min later; whole blood clot lysis index (WBCLI=A_{60}/MA) measures clot breakdown. WBCLI<0.8 indicates fibrinolysis.[2] This study determined whether TEG measurements correlated with fibrin split products ≥10μg/ml (+FSP) and predicted blood loss after CPB.

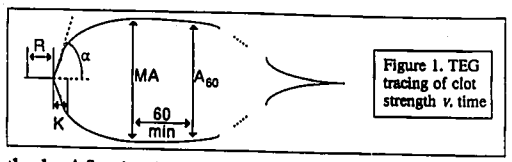


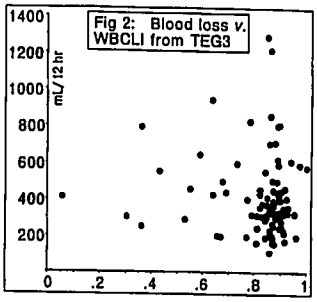
Figure 1. TEG tracing of clot strength *v.* time

Methods: After institutional approval and informed consent, patients undergoing cardiac surgery donated blood prior to skin incision (FSP1, TEG1), after protamine (TEG2), and again 2 hrs after sternal closure (FSP3, TEG3). Mass of blood drained *via* mediastinal tubes over 12 hrs determined blood loss. Correlation coefficients compared TEG data with blood loss. WBCLI cut-offs of 0.8 and 0.05 divided patients into groups. ("Tear-drop" TEG patterns occur at WBCLI<0.05.) Chi-sq statistic compared frequency data; unpaired t-test compared grouped continuous variables.

Results: No patient had +FSP prior to skin incision, but 16/88 had WBCLI<0.8 and 1/88 WBCLI=0. WBCLI after protamine (TEG2) predicted blood loss (table). After operation (TEG3), WBCLI correlated with neither +FSP nor blood loss (table). WBCLI (fig.2), R, K, and α did not correlate with blood loss; MA (r=.34) and A_{60} (r=.25) correlated poorly. +FSP after surgery did not affect R, K, α, A_{60}, or WBCLI, and minimally affected MA (65*v.* 61 P<.04).

TABLE:	WBCLI≥0.8	<0.8	≥0.05	<0.05
TEG2 Bld loss	384±188(SD)	525±321*	386±182	808±428#
TEG3 +FSP3	15/70	8/19	23/88	0/1
TEG3 Bld loss	400±220	463±221	413±222	412
	*N=16/86, P=0.023		#N=5/86, P=0.0001	

Discussion: TEG3 parameters predict neither presence of FSP nor post-op bleeding. Post-op TEG appears to provide no useful information. TEG2 did predict blood loss, confirming that fibrinolysis occurs and corrects with time. However, >1 hr is needed to measure WBCLI. By this time, fibrinolysis has subsided. TEG2 information is too tardy for therapeutic decisions.



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1. SPIESS BD, ET AL.: J CLIN MONIT 3:25-30, 1987.
2. KANG YG, ET AL.: ANESTHESIOLOGY 66:766-773, 1987.