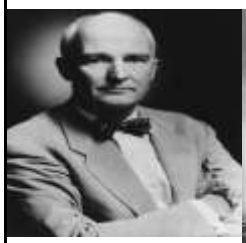
THE BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

THE KNOWN AND UNKNOWN

Figure 1. The Dodrill-GMR heart pump.

Stoney W. Circulation 2009;119:2844-2853

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY



John H. Gibbon, MD.

Gibbon-IBM heart-lung machine model II

Figure 6. C.

Stoney W. Circulation 2009;119:2844-2853

THI MILESTONES

1962 Texas Heart Institute founded by Denton A. Cooley, MD.
1968 First successful heart transplantation in the United States.
1969 First implantation in the world of an artificial heart in a human.
1975 First study funded by the National Heart, Lung, and Blood Institute of an implantable left ventricular assist device (LVAD) for post-cardiotomy support.
1976 First accredited School of Perfusion Technology in the United States.
1978 First bridge-to-transplant with an LVAD.
1981 Second implantation in the world of an artificial heart in a human.
1986 First implant of the HeartMate pneumatically powered LVAD, as a bridge to transplant.
1990 First cases of MAZE surgery performed at St. Luke's Episcopal Hospital for atrial fibrillation
1991 First patient in the world left the hospital with an electric, portable, battery-powered LVAD.
1999 Implantation of the AbioCor total artificial heart
2000 First site for clinical trials of the Jarvik 2000, a miniature, axial flow left ventricular assist device.
2001 100,000th open heart operation performed.
2006 1,000th heart transplant performed.
2011 First successful implantation of a continuous-flow total artificial heart in a human being
2012 THI founder Dr. Denton A. Cooley publishes his memoirs, *100,000 Hearts*, highlighting many historical firsts.

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

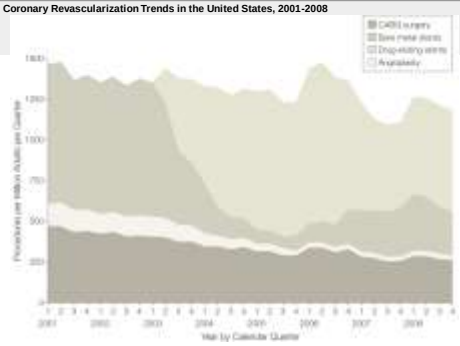
Cardiovascular Surgery in Jehovah's Witnesses
Report of 542 Operations Without Blood Transfusion
David A. Ott, MD; Denton A. Cooley, MD
JAMA. 1977;238(12):1256-1258.

Alteration of coagulation and selected clinical chemistry parameters in patients undergoing open heart surgery without transfusions.
Milam JD, Austin SF, Martin RF, Keats AS, Cooley DA.
Am J Clin Pathol. 1981 Aug;76(2):155-62.

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

From: **Coronary Revascularization Trends in the United States, 2001-2008**



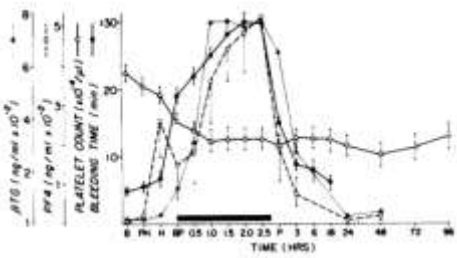
JAMA. 2011;305(17):1769-1776.

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

Procedures	
Total	51.4 million
Arteriography and angiocardiography using contrast material	
Cardiac catheterizations	1.0 million
Endoscopy of small intestine with or without biopsy	1.1 million
Endoscopy of large intestine with or without biopsy	499,000
Diagnostic ultrasound	1.1 million
Balloon angioplasty of coronary artery or coronary atherectomy	500,000
Hysterectomy:	498,000
Cesarean section	1.3 million
Reduction of fracture:	671,000
Insertion of coronary artery stent	454,000
Coronary artery bypass graft	395,000
Total knee replacement	719,000
Total hip replacement	332,000

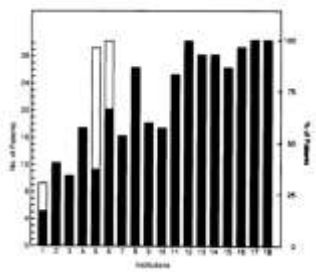
SOURCE: CDC/NCHS National Hospital Discharge Survey, 2010.

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY



Harker L. Blood 1980 56: 824-834

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY



Goodnough J Am Med Assoc 1991;265:86-90.

RBC Transfusion Guideline for Physicians

This algorithm is intended for use as a recommended guideline; individual patient situations may require varying treatment

For use in patients who meet the following :
1. First time CV surgery
2. Age < 65 years
3. No history of CHF
4. Hemodynamically stable (no pressors, no IABP)

Hgb Monitoring

If initial Hgb ≥ 8g/dl and CT output < 300 ml/hr in 1st hour post-op & ≤ 100 ml/hr in subsequent hours, continue to monitor

If CT output **exceeds** 300ml/hr 1st hour post-op, or > 100ml/hr in subsequent hours, recheck Hgb, order coagulogram and PFS, then follow microvascular bleeding algorithm (on back of this page)

If CT output > 500 ml **total** in **first 8 hours** post-op, repeat H&H.

If Hgb < 8g/dl go to RBC therapy guidelines

RBC Therapy

If Hgb< 8g/dl and CT output > 150 ml/hr consider transfusing (**2** units) RBC

If Hgb < 8 and CT output < 150 ml/hr, consider transfusing (**1** unit) RBC

Also consider fluid volume effect on Hgb levels

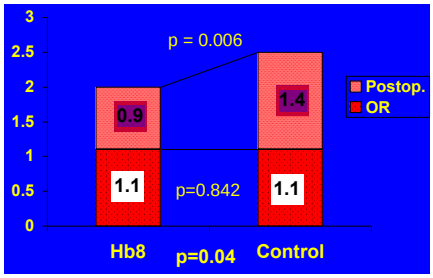
Recheck H&H 30 minutes after transfusion complete

If CT output remains < 150cc/hr, consider continuing **single** RBC transfusions followed by H&H checks 30 minutes after transfusion until target Hgb of ≥ 8g/dl is reached

SIGNS AND SYMPTOMS OF ANEMIA: weakness, pale skin, tachycardia or irregular heartbeat, shortness of breath, chest pain, dizziness, cognitive problems, numbness or coldness in extremities, headache

Transfusion protocol Hb8

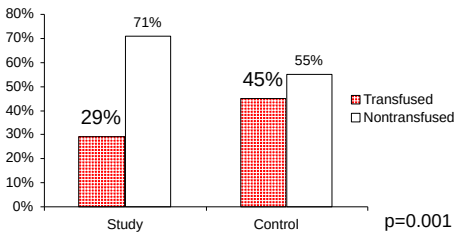
RBC transfusion rate (units per patient)



Bracey A. Transfusion 1999; 39:1070.

Transfusion protocol Hb 8

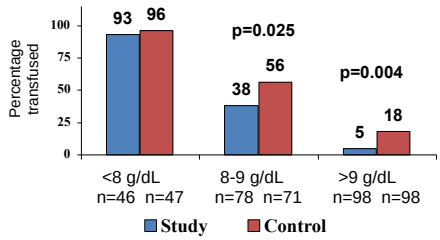
Transfusion incidence in postoperative period



Bracey A. Transfusion 1999; 39:1070

Transfusion protocol Hb8

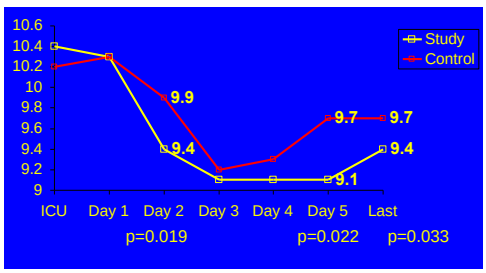
Transfusion incidence in subgroups of patients by lowest Hb during postoperative period



Bracey A. Transfusion 1999; 39:1070

Transfusion protocol Hb8

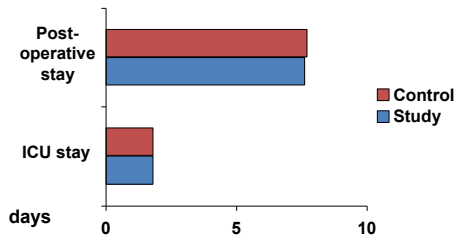
Daily mean nadir hemoglobin levels in subgroups of patients with nadir postoperative Hb between 8 and 9 g/dL.



Bracey A. Transfusion 1999; 39:1070

Transfusion protocol Hb8

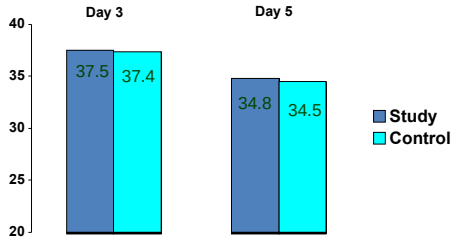
Outcome measures



Bracey A. Transfusion 1999; 39:1070

Transfusion Protocol Hb 8

Self-assessment of fatigue



Bracey A. Transfusion 1999; 39:1070

Transfusion Protocol Hb 8

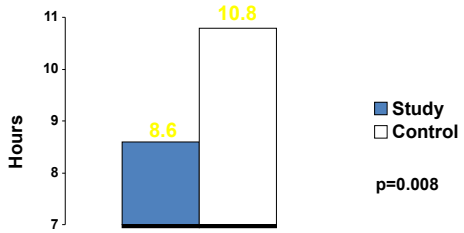
Outcome Measures

	Study group (212) (%)	Control group (216) (%)
Atrial arrhythmia	30 (14)	40 (19)
Ventricular arrhythmia	13 (6)	9 (4)
Myocardial infarction	1 (0.5)	0 (0)
Neurologic deficit	11 (5)	9 (4)
Pulmonary complications	57 (27)	64 (30)
Renal failure	8 (4)	5 (2)
Infection	5 (2)	3 (1)

No statistically significant differences were found.

Bracey A. Transfusion 1999; 39:1070

Transfusion protocol Hb8
Duration of mechanical ventilation
in patients with postoperative Hb between 8 - 9



Bracey A. Transfusion 1999; 39:1070

From: **Transfusion Requirements After Cardiac Surgery: The TRACS Randomized Controlled Trial**

JAMA. 2010;304(14):1559-1567. doi:10.1001/jama.2010.1446

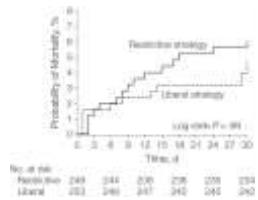


Figure Legend:

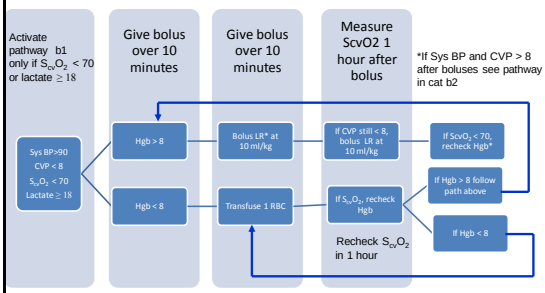
Time zero was just after randomization (12 hours before surgery). Hazard ratio, 1.28 (95% confidence interval, 0.60-2.73) (P = .99) for restrictive strategy vs liberal strategy.

CVRR Resuscitation Algorithm

- All pump patients will have lactate and $S_{cv}O_2$ measured on ICU admission
- Hemodynamically unstable patients (category a) will be treated according CVRR Resuscitation algorithm
- Hemodynamically stable patients (category b) with elevated lactate $\geq$ 18 and $S_{cv}O_2$ < 70% will trigger intervention for treatment of occult hypoperfusion according to CVRR Resuscitation algorithm
- Response to therapy will be monitored by:

a. $S_{cv}O_2$ drawn 1 hour post intervention (continue intervention if $S_{cv}O_2$ remains < 70% after bolus or RBC transfusion x 2.
b. Lactate drawn 18±2 hours after initial specimen

Category b1



*LR = lactated Ringer's solution

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

Outcomes: pre *vs* post-implementation of pathway

	Pre-implementation[1] N = 21	Post-implementation N = 53	p value
ICU LOS (hours)	116.9	64.0	0.27
Hospital LOS (days)	16.0	11.0	0.049
ICU Readmission Rate	28.6%	7.7%	0.026
Length of MV (hours)	64.2	43.7	0.67
Complication* Rate	47.6%	26.4%	0.10
Complications*/Patient	1.24	0.49	0.076

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

Outcomes: follow-up lactate at goal *vs* not at goal

	Follow-up Lactate at goal N = 33	Follow-up Lactate NOT at goal N = 14	p value
ICU LOS (hours)	50.3	105.3	0.065
Hospital LOS (days)	10.0	13.5	0.17
ICU Readmission Rate	9.1%	7.1%	1.000
Length of MV (hours)	18.4	117.0	0.173
Complication* Rate	15.2%	50.0%	0.025
Complications*/Patient	0.2	1.1	0.066

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

Blood use in patients undergoing repeat coronary artery bypass graft procedures: multivariate analysis

A.W. Bracey, R. Radovancevic,B. Radovancevic,H.A. McAllister Jr,W.K. Vaughn,D.A. Cooley

Variable	
Pre-operative anemia	P < 0.0003
ASA exposure	P < 0.0094
Prolonged CPB time	P < 0.0001

Bracey 1995 Transfusion; 35: 850–854

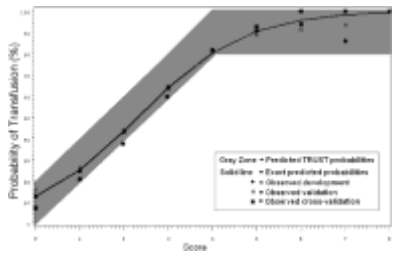
BLOOD INTERFACE IN TRANSFUSION IN CV SURGERY

TRANSFUSION PREDICTOR – TRUST SCORE

Variable	score
Hb level < 13.5 g/dL	1
Weight < 77 kg	1
Female sex	1
Age > 65 years	1
Nonelective surgery	1
Serum creatinine level > 1.36 mg/L	1
Previous cardiac surgery	1
Nonisolated surgery	1

Alghamdi TRANSFUSION 2006;46:1120-1129.

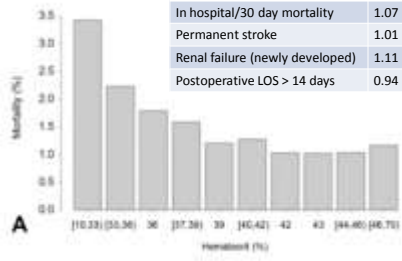
Development and validation of Transfusion Risk Understanding Scoring Tool (TRUST) to stratify cardiac surgery patients according to their blood transfusion needs



Alghamdi TRANSFUSION 2006;46:1120-1129.

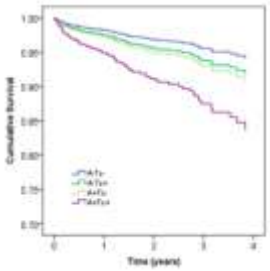
BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

Variable	OR (95% CI)	P value
In hospital/30 day mortality	1.07 (0.94-1.23)	0.3013
Permanent stroke	1.01 (0.90-1.13)	0.8623
Renal failure (newly developed)	1.11 (1.03-1.20)	0.0066
Postoperative LOS > 14 days	0.94 (0.86-1.04)	0.2316

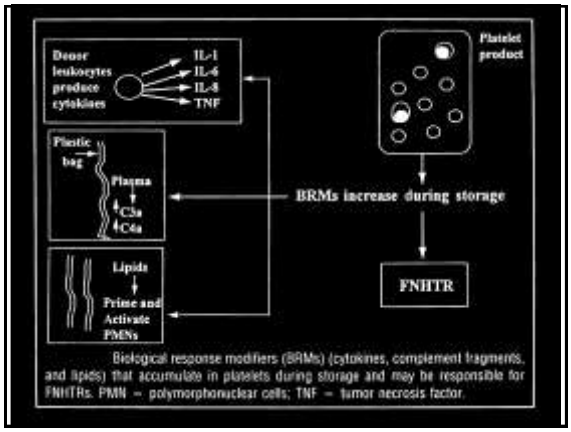


Williams ML. Ann Thorac Surg 2013;96:1628-34.

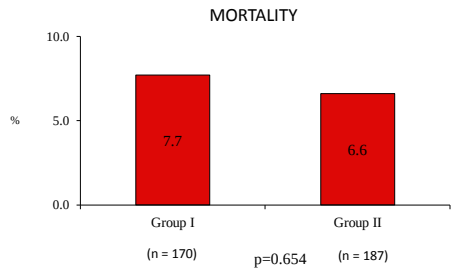
BLOOD INTERFACE IN CARDIOVASCULAR SURGERY



Engoren M. Ann Thorac Surg 2014;97:514–21

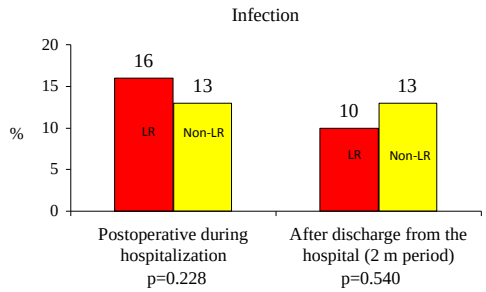


Leukoreduction - CV Surgery



Bracey A. Transfusion 2002;**42 Suppl**: 5S.

Leukoreduction - CV Surgery



Bracey A. Transfusion 2002;**42 Suppl**: 5S.

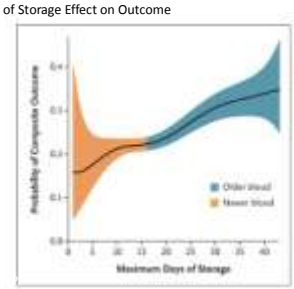
BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

Variable	Group I - LR	Group II – non-LR	P value
Post-operative LOS (d)	11 ± 8	10 ± 7	0.491
Mechanical ventilation (h)	23 ± 37	18 ± 26	0.177
ICU stay (h)	68 ± 57	61 ± 60	0.264

Bracey A. Transfusion 2002;**42 Suppl**: 5S.

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

Model of Storage Effect on Outcome



Koch NEJM 2008;358:1229

BLOOD STORAGE

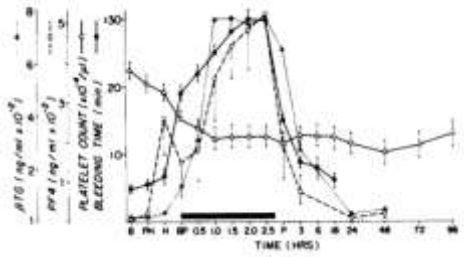
- RECESS (Steiner) – CVS complex case population (redo, multiple procedure)
  - primary outcome – MODS
  - secondary outcome discharge death, oxygenation, endorgan function troponin, creatinine
  - randomize to < 8-10 days vs >21 days
  - screen 7200 to get 800 in each arm
  - physiologic substudy will address O2 delivery, deformability/flow

RECESS – MODS SCORE

Clinical components of the multiple organ dysfunction score

Organ system	0	1	2	3	4
Respiratory (PaO2/FiO2)	>300	226-300	151-225	76-150	≤ 75
Renal (creatinine)	≤100	101-200	201-350	351-500	>500
Hepatic (bilirubin)	≤20	21-60	61-120	121-240	>240
CV (PAR) (HR x CVP/MAP)	≤10.0	10.1-15.0	15.1-20.0	20.1-30.0	>30.0
Heme (plat ct)	> 120	81-120	51-80	21-50	≤20
Neuro (Glascow Coma Score)	15	13-14	10-12	7-9	≤6

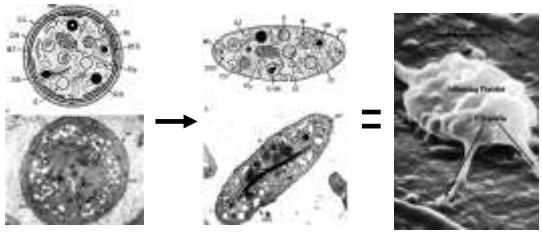
BLOOD INTERFACE IN CARDIOVASCULAR SURGERY



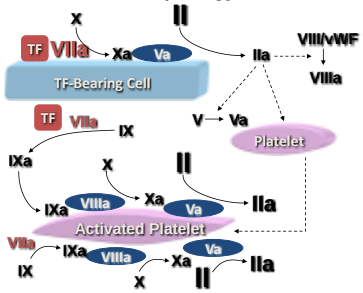
Harker L. Blood 1980 56: 824-834

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

Platelet Ultrastructure - Activation

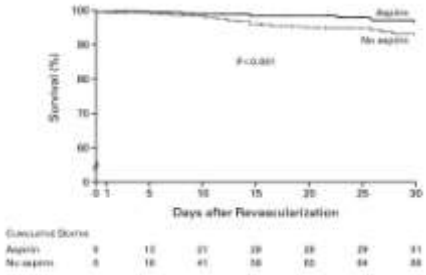


Normal Hemostasis: Pivotal role of TF/VIIa



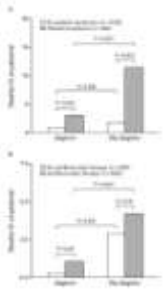
Hoffman et al. Blood Coagul Fibrinolysis 1998;9(suppl 1):S61.

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY



Mangano DT. N Engl J Med 2002;347:1309-1317.

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY



Mangano DT. N Engl J Med 2002;347:1309-1317.

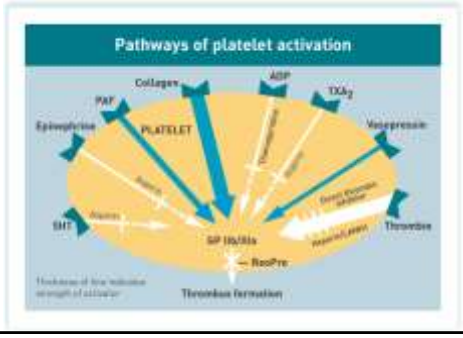
BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

Study	No Pats.	Chest Tube Drainage	Transfusion	Re-exploration
Goldman (1991)	351	Increased	Increased	Increased
Sethi (1990)	772	Increased	Increased	Increased
Goldman (1988)	555	Increased	Not Inc.	Increased
Kallis (1994)	100	Increased	Increased	Increased
Ferraris (1988)	34	Increased	Increased	Increased
Kawande (1987)	36	Increased	Increased	Increased

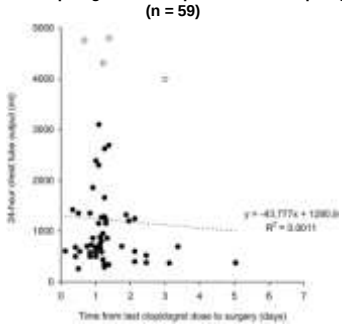
Randomized trials –
1. Increased chest tube output 200-400 ml.
2. Increased RBC transfusion 0.5 – 1 RBC unit.

Ferraris VA. Int J Angiol 2011;20:1-18.

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY



Relationship between 24-h postoperative chest tube output and time to surgery after last clopidogrel dose in patients with clopidogrel exposure (n = 59)



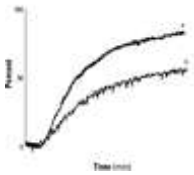
Hongo, R. H. et al. J Am Coll Cardiol 2002;40:231-237

BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

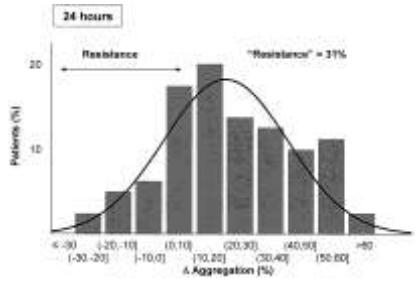
- Platelet function assays
  1. Platelet aggregation
  2. PFA-100
  3. VerifyNow
  4. Thromboelastograph (TEG)
  5. Platelet works
  6. Flow cytometry P-selectin (research)
  7. Cone and plate(let) analyzer (research)
  8. Thrombovision T-Guide (trial phase)
  9. VASP Phosphorylation (flow-research)

PLATELET FUNCTION ASSAYS

- Gold standard
- Technically difficult
- Agonists: ADP, epinephrine, collagen, arachidonic acid, ristocetin
- Advantages: graphs dynamics of aggregation

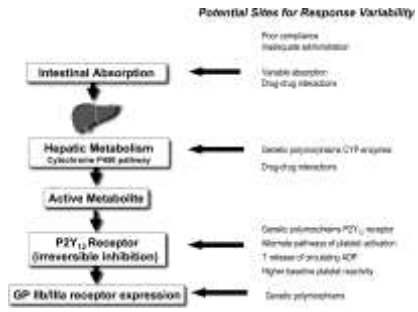


Interindividual variability in platelet response to clopidogrel after stenting



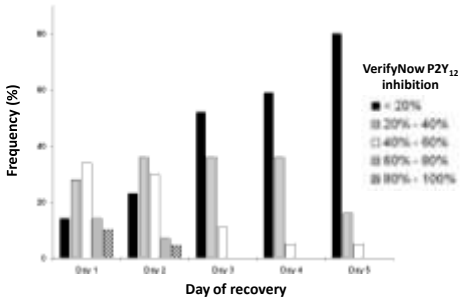
O'Donoghue, M. et al. Circulation 2006;114:e600-e606

Proposed mechanisms for interindividual variability in platelet inhibition in response to clopidogrel

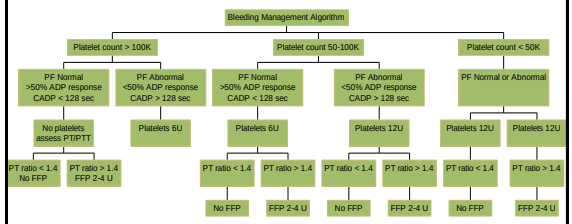


O'Donoghue, M. et al. Circulation 2006;114:e600-e606

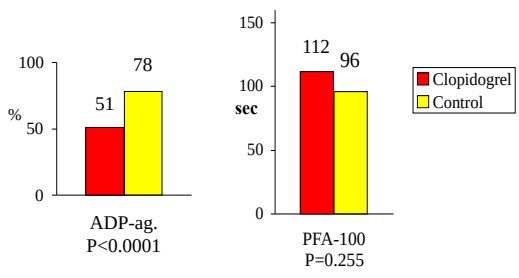
Frequency distribution of platelet inhibition after cessation of daily clopidogrel therapy



Transfusion Triggers – Transfusion Algorithms



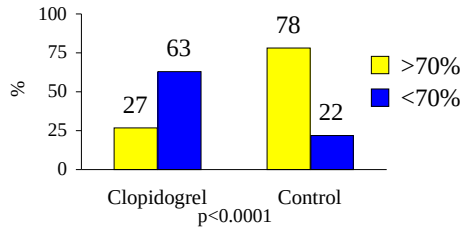
Platelet Function Before CPB in the Prospective Groups



Chen L. J Thorac Cardiovasc Surg 2004;128:425.

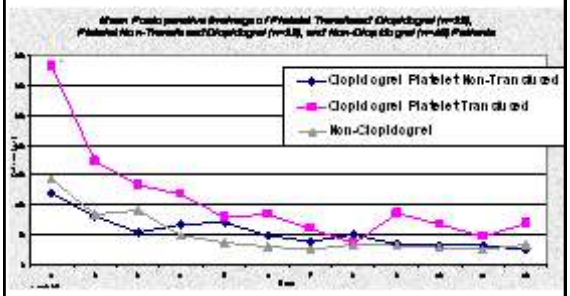
CABG after Receipt of Clopidogrel

Incidence of Reduced Platelet Function
(ADP aggregation - normal function >70%)



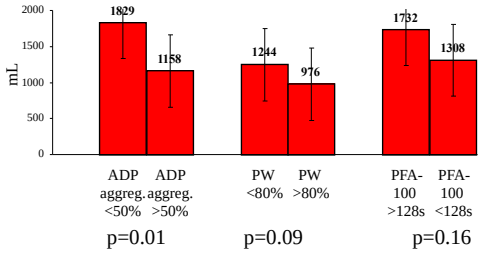
Chen L. J Thorac Cardiovasc Surg 2004;128:425.

PLATELET FUNCTION ASSAYS



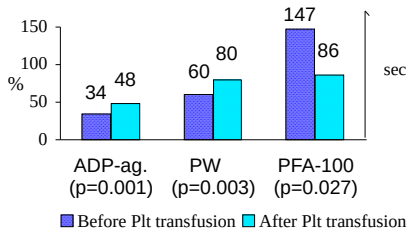
Chen L. J Thorac Cardiovasc Surg 2004;128:425.

Total Chest Tube Blood Loss



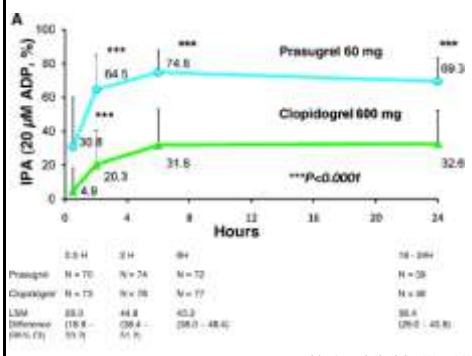
Chen L. J Thorac Cardiovasc Surg 2004;128:425.

Effect of Platelet Transfusion on Platelet Function



Chen L. J Thorac Cardiovasc Surg 2004;128:425.

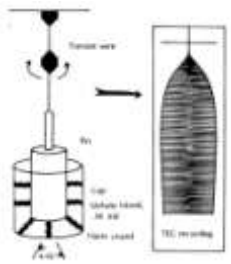
Figure 3. LD-phase platelet function measures.



Wiviott S D et al. *Circulation.* 2007;116:2923-2932

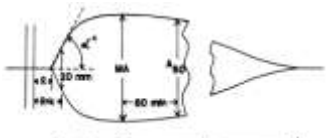
BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

TEG

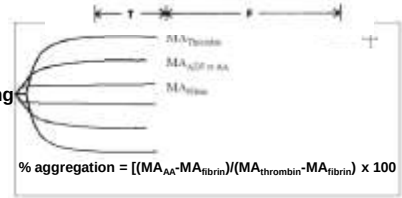


BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

Standard TEG



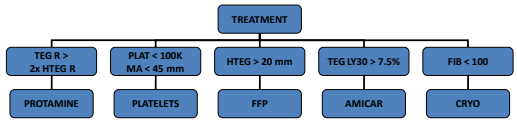
Platelet mapping TEG



% aggregation = $[(MA_{AA}-MA_{fibrin})/(MA_{thrombin}-MA_{fibrin}) \times 100$

PLATELET FUNCTION ASSAYS

MICROVASCULAR BLEEDING MANAGEMENT using TEG algorithm



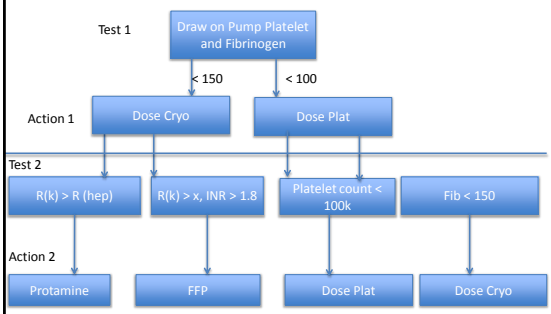
Shores-Lesserson. Anesth Analg 1999;88:312-9

Perioperative blood management

Microvascular bleeding management using algorithm based on TEG results

	TEG	CONTROL
FFP vol. (ml)	36 ± 142	217 ± 463*
PLAT vol. (ml)	34 ± 94	83 ± 160
RBC incidence	22/53(42%)	31/52(60%)
FFP incidence	4/53(8%)	16/52(31%)**
PLAT incidence	7/53(13%)	15/52(29%)*

Shores-Lesserson. Anesth Analg 1999;88:312-9 *p<.05 **p<.01



BLOOD INTERFACE IN CARDIOVASCULAR SURGERY

- Unresolved questions
  1. What is the lowest tolerable hemoglobin? Is there a better measure of oxygen supply?
  2. How best can one assess the coagulation system – pre, during and post surgery? Is there a role for platelet function assessment?
  3. Are further design enhancements drug therapies possible to decrease inflammation, avoid coagulation activation?

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Barnard and Michelson *N Engl J Med* 1995;333:1051.