STS Webinar Series

The Society of Thoracic Surgeons

Patient Blood Management Guideline Webinar: A Discussion with the Authors

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Key Takeaway 1:

Use of synthetic antifibrinolytic agents such as epsilon-aminocaproic acid (EACA) or tranexamic acid reduce blood loss and blood transfusion during cardiac procedures and are indicated for blood conservation.

Class I, Level A

Tranexamic Acid ATACAS Investigators

- 31 sites, 7 countries, 2006-2015, n=4631
- 2x2 factorial design, DB, randomized, CABG
- ASA vs placebo; tranexamic acid vs placebo
- 1°outcome- composite death+thrombotic 30d
- TxA 100 mg/kg 1st 1526 patients to 1/2012
- TxA50 mg/kg after seizures noted
- Groups demographically similar

Myles PS et al: N Engl J Med 2017;376:136-148

Results Multicenter TxA Study

	TxA n=2311	Placebo n=2320	P value
1° Outcome (%)	386(16.7)	420(18.1)	0.22
MI 30d (%)	269(11.6)	300(12.9)	0.19
Reoperation (%)	32(1.4)	65(2.8)	0.001
Tot Products (U)	3(2-6)	4(2-8)	<0.001
Mech Vent hr	8(5-14)	9(6-16)	<0.001
Seizures (%)	15(0.7)	2(0.1)	0.002

Myles PS et al: N Engl J Med 2017;376:136-148

Outcomes and Adverse Events

	TA (2311)	Placebo (2320)	Risk Ratio	P
Composite (%)	16.7	18.1	0.92 (0.81-1.05)	0.22
MI	11.6	12.9	0.90 (0.77-1.05)	0.19
Reop any cause (%)	1.4	2.8	0.49 (0.32-0.75)	0.001
Units transfused	3 (2-6)	4 (2-8)		<0.001
Seizures (%)	0.7	0.1	7.62 (1.77-68.7)	0.002

Myles PS et al: N Engl J Med 2017;376:136-148

Key Takeaway 2:

In patients undergoing cardiac surgery, a restrictive perioperative allogeneic RBC transfusion strategy is recommended in preference to a liberal transfusion strategy for perioperative blood conservation, as it reduces both transfusion rate and units of allogeneic RBCs without increased risk for mortality or morbidity.

Class I, Level A

There is a ***competing risks dilemma*** to the perioperative management of anemia in cardiac surgery patients

Finding the balance

- Potential deleterious effects of **anemia induced tissue hypoxemia**

VS

- Potential inherent deleterious **risk of allogeneic RBC transfusions to treat that anemia**

What level of anemia is safe? What is a clinically relevant transfusion trigger?

New data since the 2011 Guidelines

- Several RCTs involving >8000 patients across 4 countries
- Has also enabled meta-analyses that are more robust than previous

- All RCT studies included
- restrictive trigger between 7 and 8 g/dL - [more anemia]
  - liberal trigger between 8 and 10 g/dL - [more transfusions]

- ~30% reduction in RBC transfusion with restrictive measures

- Meta-analyses – no difference in mortality, reoperations, MI, stroke

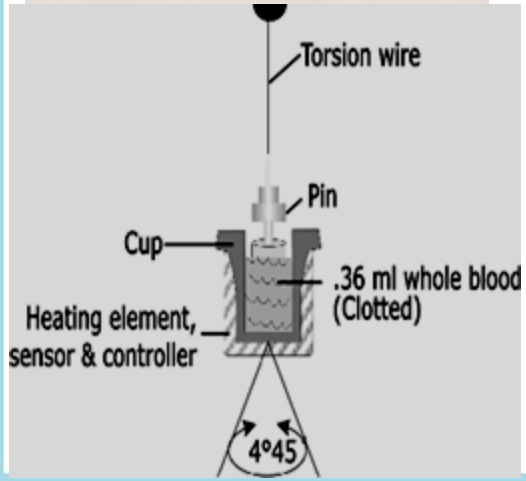
Overall, best evidence from multiple recent RCTs, systematic reviews, and meta-analyses clearly establish that the use of restrictive RBC transfusion strategies reduces both the probability and amount of RBC transfusion without increasing the risk of mortality or major morbidity in patient undergoing cardiac surgery

Key Takeaway 3:

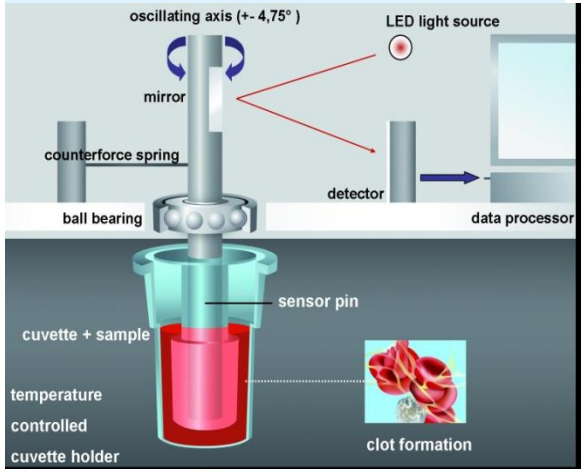
Goal directed transfusion algorithms which incorporate point of care testing, such as with viscoelastic devices, are recommended to reduce periprocedural bleeding and transfusion in cardiac surgical patients.

Class I, Level B-R

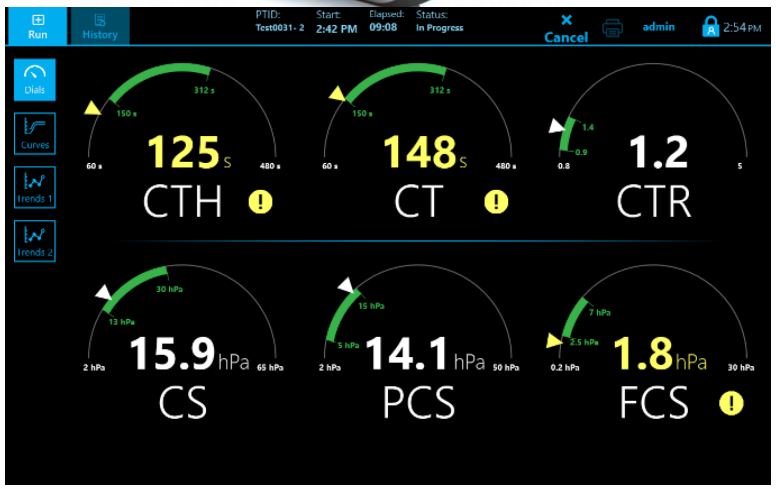
TEG



ROTEM

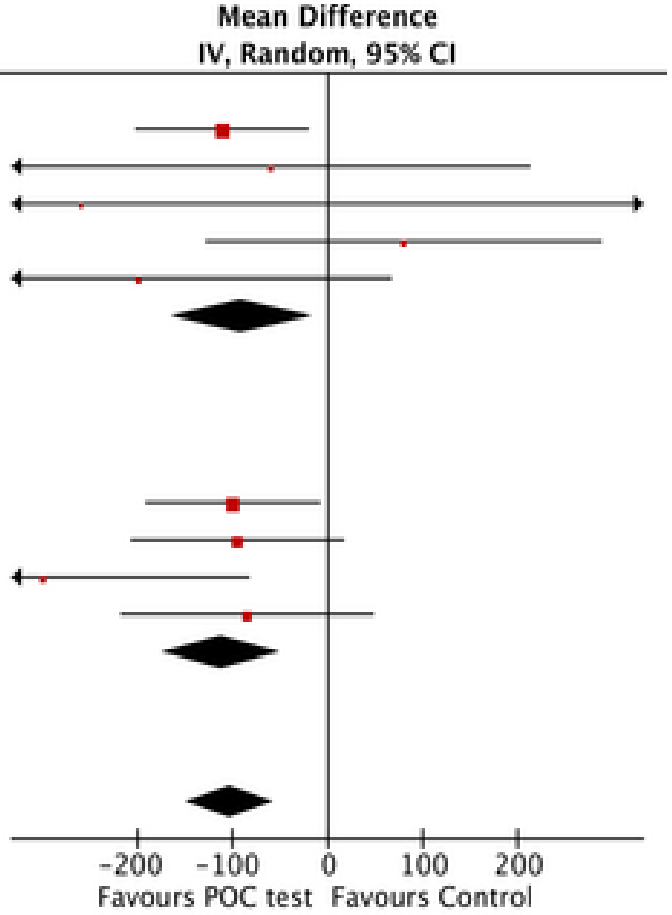


QUANTRA



POC Algorithm vs. Control- Bleeding

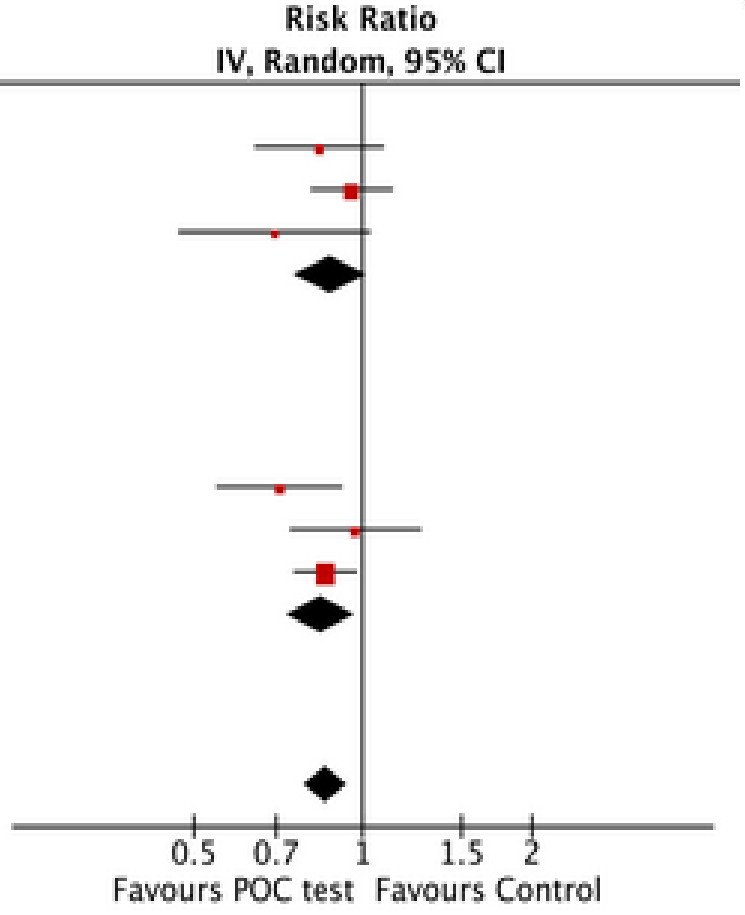
Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI
14.1.1 TEG/ROTEM only				
Ak 2009	-110.9	46.144	26.9%	-110.90 [-201.34, -20.46]
Girdauskas 2010	-60	139.388	2.9%	-60.00 [-333.20, 213.20]
Nuttall 2001	-260	355.654	0.5%	-260.00 [-957.07, 437.07]
Royston 2001	80	105.798	5.1%	80.00 [-127.36, 287.36]
Shore-Lesserson 1999	-199	135.433	3.1%	-199.00 [-464.44, 66.44]
Subtotal (95% CI)			**38.5%**	**-90.55 [-166.11, -14.99]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.71$, df = 4 (P = 0.45); $I^2 = 0\%$				
Test for overall effect: Z = 2.35 (P = 0.02)				
14.1.2 TEG/ROTEM+PFT				
Agarwal 2014	-100	46.512	26.5%	-100.00 [-191.16, -8.84]
Avidan 2004	-95	56.775	17.8%	-95.00 [-206.28, 16.28]
Weber 2012	-300	110.356	4.7%	-300.00 [-516.29, -83.71]
Westbrook 2009	-85	67.52	12.6%	-85.00 [-217.34, 47.34]
Subtotal (95% CI)			**61.5%**	**-111.79 [-174.49, -49.09]**
Heterogeneity: $Tau^2 = 295.14$; $Chi^2 = 3.22$, df = 3 (P = 0.36); $I^2 = 7\%$				
Test for overall effect: Z = 3.49 (P = 0.0005)				
Total (95% CI)			**100.0%**	**-102.99 [-149.88, -56.09]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 7.10$, df = 8 (P = 0.53); $I^2 = 0\%$				
Test for overall effect: Z = 4.30 (P < 0.0001)				
Test for subgroup differences: $Chi^2 = 0.18$, df = 1 (P = 0.67), $I^2 = 0\%$				



Corredor et al: Anaesthesia 2015;70:715-731

POC Algorithm vs. Control- RBC Transfusion

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
15.1.1 TEG/ROTEM only				
Ak 2009	-0.1791	0.1339	11.0%	0.84 [0.64, 1.09]
Girdauskas 2010	-0.046	0.0847	24.5%	0.96 [0.81, 1.13]
Shore-Lesserson 1999	-0.3624	0.1992	5.2%	0.70 [0.47, 1.03]
Subtotal (95% CI)			**40.6%**	**0.88 [0.75, 1.03]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.44$, df = 2 (P = 0.30); $I^2 = 18\%$				
Test for overall effect: Z = 1.64 (P = 0.10)				
15.1.2 TEG/ROTEM + PFT				
Agarwal 2014	-0.3425	0.1303	11.5%	0.71 [0.55, 0.92]
Avidan 2004	-0.0305	0.136	10.6%	0.97 [0.74, 1.27]
Weber 2012	-0.1543	0.0647	37.3%	0.86 [0.75, 0.97]
Subtotal (95% CI)			**59.4%**	**0.84 [0.73, 0.97]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 2.86$, df = 2 (P = 0.24); $I^2 = 30\%$				
Test for overall effect: Z = 2.40 (P = 0.02)				
Total (95% CI)			**100.0%**	**0.86 [0.79, 0.94]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.65$, df = 5 (P = 0.34); $I^2 = 11\%$				
Test for overall effect: Z = 3.24 (P = 0.001)				
Test for subgroup differences: $Chi^2 = 0.15$, df = 1 (P = 0.70), $I^2 = 0\%$				



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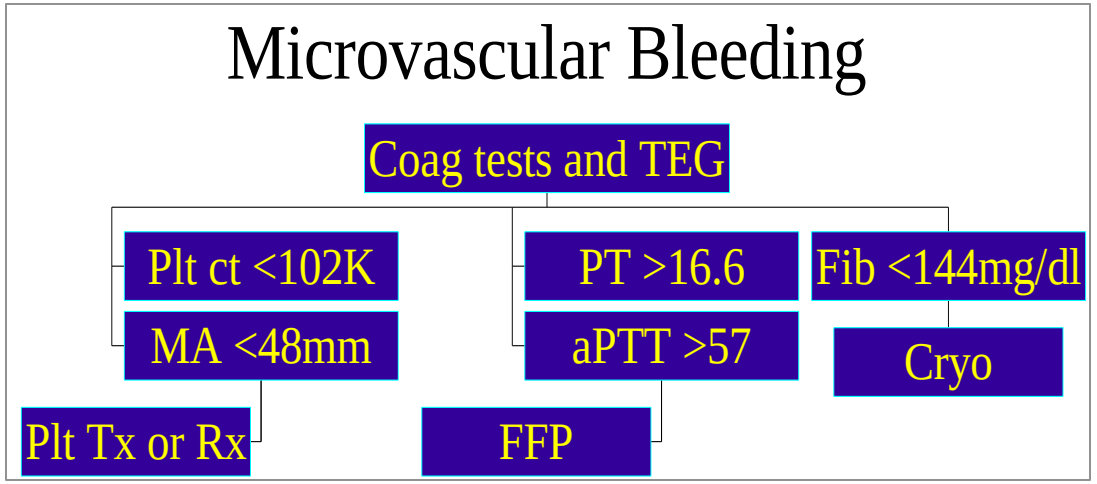
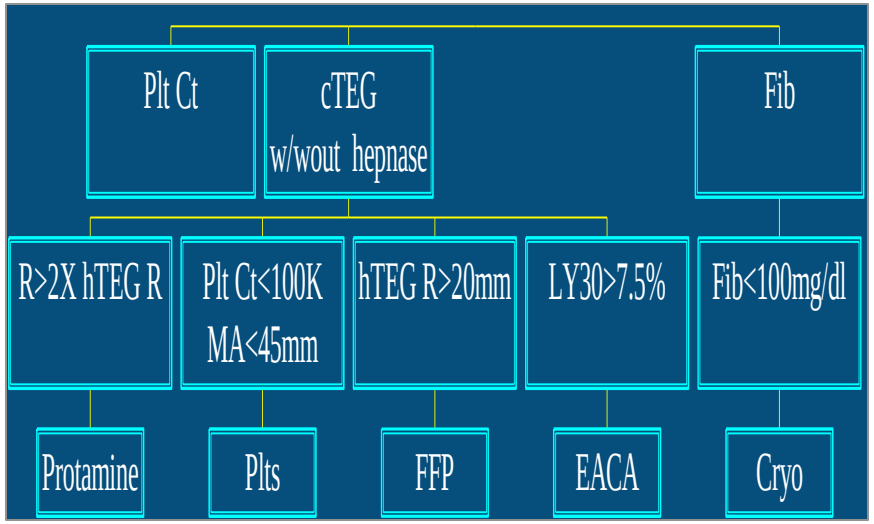
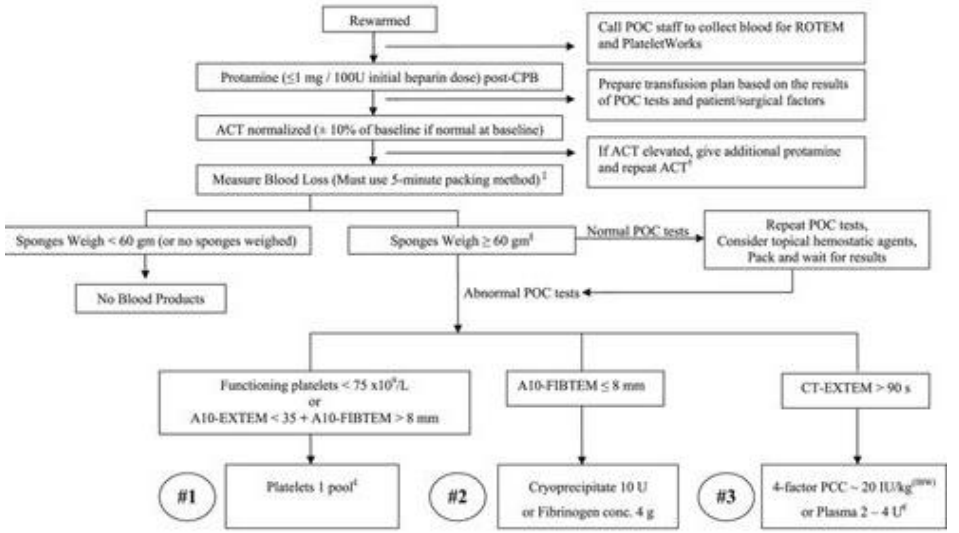
Microvascular Bleeding



TEG Variable	Implication	Therapy
14<R<21mm	↓Clot factors	1 FFP
21<R<28mm	↓↓Clot factors	2 FFP
R>28mm	↓↓↓Clot factors	4 FFP
MA<48mm	↓Plt number/fx	1 Plt pools
MA<40mm	↓↓Plt number/fx	2 Plt pools
LY30>7.5%	Fibrinolysis	Aprotinin



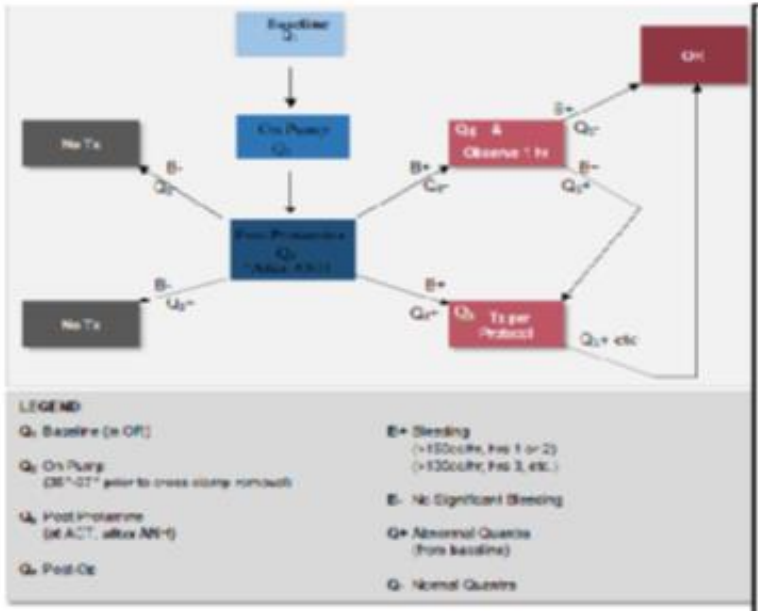
Cardiac Surgery Blood Transfusion Algorithm*



Protamine	• CTR ≥ 1.4 = Heparin Influence • Consider Protamine
Cryo	• CS < 13.7 hPa – Low Clot Stiffness • FCS < 1.4 hPa • Consider Fibrinogen
Platelets	• CS < 13.7 hPa – Low Clot Stiffness • FCS > 1.4 hPa and PCS < 11.8 hPa • Consider Platelets
FFP or PCC	• CT > 189 sec and CTR < 1.3 • Consider FFP or KCentra

Therapeutic Goals –
Reassess after intervention

Amicar or TXA	• Severely Low CS/FCS • Consider Antifibrinolytics if not given previously
Protamine	• CTR 1.4 to 2.0 give 25 mg • CTR >2.0 give 50 mg
Cryo	• FCS < 1.4 hPa give cryo or • Fibrinogen concentrate: • Calculate dose from deficit to target[1]
Platelets	• If Known DAPT consider DDAVP • PCS < 14.1 hPa 1pk platelets • PCS<11.2 hPa 2pk platelets
FFP or PCC	• CT > 189 give FFP or KCentra



YRMC Quantra Sampling Protocol and Algorithm

i. **Sampling Protocol:**

a. Baseline: At time of ANH draw from Cordis side port.
b. On Pump Rewarm: At 35-37 degrees prior to cross-clamp release and discontinuation from CPB machine.
c. Post Protamine: Same time as post protamine ACT. (NOTE: Usually done after protamine and ANH units transfused.)
d. Post Op: See ICU standing orders: if chest tube drainage is 150 cc's/hour or greater.

ii. **Algorithm:**

a. if the patient is bleeding and the *Quantra values have changed*, consider in the following order:

i. if CTR ≥ 1.4: Consider Protamine
ii. if CS is lower than the patient's baseline assess the following:

1. Fibrinogen: FCS lower than the patient's baseline:
   a. Slow to moderate bleeding: 1-2 5 packs of Cryoprecipitate
   b. Moderate to Active bleeding: 2-3 5 packs of Cryoprecipitate
2. Platelets: PCS lower than the patient's baseline:
   a. Slow to moderate bleeding: 1-2 units of platelets.
   b. Moderate to Active bleeding: 2-3 units of platelets.
3. Clotting Factors: if CT/CTH are both elevated and CTR < 1.3
   a. Slow to moderate bleeding: 1-2 units FFP or Kcentra
   b. Moderate to Active bleeding: 2-3 units FFP or Kcentra

NOTE: if more than one parameter has changed consider which parameter has changed most significantly and treat with that corresponding blood product. Active bleeding may require more than one type of blood product or treatment. With CT/CTH elevated (high value), and with low CS/PCS/FCS values the parameter will be reported in yellow.

b. if the patient is bleeding and the *Quantra values have not changed*, consider the following:

iii. DDAVP (desmopressin): Will increase platelets ability to adhere. Viscoelastic tests (VET) such as Quantra do not assess platelet adhesion.
iv. Calcium: VET will mask hypocalcemia. The tests utilize Calcium to neutralize citrate from the blue top tube.
v. Platelets if platelet inhibition is suspected or known due to preop testing with Verify Now.

For references and more information regarding the algorithms in the previous slides, please contact Scott Firestone and/or Kalie Kissoon:

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Key Takeaway 4:

Prophylactic use of plasma in cardiac operations in the absence of coagulopathy is not indicated, does not reduce blood loss and exposes patients to unnecessary risks and complications of allogeneic blood component transfusion.

Class III: Harm, Level A

Key Takeaway 5:

In order to reduce bleeding in patients requiring elective cardiac surgery, ticagrelor should be withdrawn preoperatively for a minimum of 3 days, clopidogrel for 5 days and prasugrel for 7 days

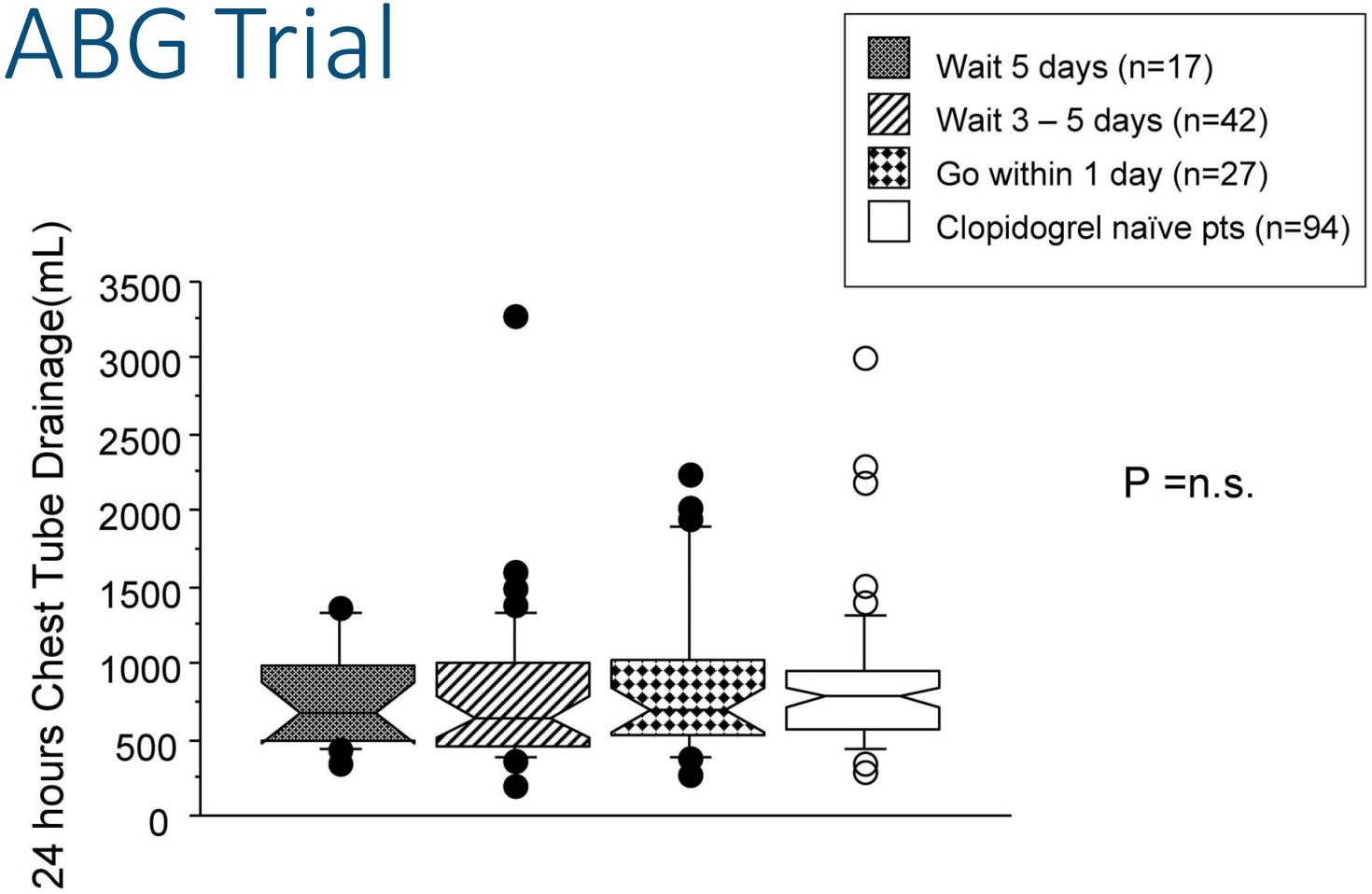
Class I, Level B-NR

TARGET-CABG Trial

- Prospective single-center, non-blinded (n=180)
- Primary CABG w CPB, age 18-85, ASA
  - Clopidogrel treated: load dose or ≤ 5 days
  - Clopidogrel naïve
- MA-ADP measured at least 8 hr after load
  - MA-ADP>50 mm: surgery within 1 day
  - MA-ADP 35-50 mm: surgery 3-5 days
  - MA-ADP <35 mm: surgery > 5 days

Mahla E et al: Circ Cardiovasc Interv. 2012;5:261-269

TARGET-CABG Trial



Mahla E et al: Circ Cardiovasc Interv. 2012;5:261-269

Key Takeaway 6:

Reduced priming volume in the CPB circuit reduces hemodilution and is indicated for blood conservation.

Class I, Level B-NR

Effects of Reduced Priming Volume

- Sun et el 2017 47,000 patients
- ↑ prime volume/est blood volume= ↑ transfusions

- Dickenson 2019 21,000 patients
- Larger prime volumes= independent predictor of blood transfusions

Key Takeaway 7:

Routine use of red cell salvage using centrifugation is helpful for blood conservation in cardiac operations using CPB.

Class I, Level A

Key Takeaway 8:

Allogeneic RBC transfusion is unlikely to improve oxygen transport when the hemoglobin concentration is greater than 10 g/dL and is not recommended.

Class III: No Benefit, Level B-R

Important Recommendation that holds from the 2011 Guidelines

- The Golden "10/30" Rule is an Unproven Historical & Empirical Practice
  - Transfuse RBCs to maintain a Hgb concentration of 10 g/dL and a hematocrit above 30% **regardless of symptoms!**
  - The rationale was based on physiologic evidence that cardiac output increases when hemoglobin falls below 10 g/dL.
  - In the face of cardiac disease, the ability to increase cardiac output may be compromised
  - To reduce strain on the heart, Hgb levels were historically kept higher to improved oxygen delivery
- The "10/30" rule has not been proven to be a beneficial practice strategy and is not supported by the available evidence

In contradistinction

- There is voluminous clinical and physiological data within the medical literature to support the premise that patients can tolerate Hgb levels that are <10g/dL or a hematocrit < 30% without adverse events in the perioperative period.

- The best available evidence suggests not to transfuse if Hgb >10g/dL

Key Takeaway 9:

The concept of patient blood management informs the recommendations in this document and stresses the importance of an evidence-based, multimodal, and multidisciplinary approach to not just conserving blood resources, but optimizing outcomes in patients who are high risk for transfusion.

Key Takeaway 10:

The four major tenets of PBM are 1) managing anemia, 2) optimizing coagulation, 3)interdisciplinary blood conservation modalities and 4) patient centered decision making in order to achieve improved patient outcomes.

- **Multidisciplinary approach** has proven benefit in conserving blood resources and optimizing outcomes.
- **Well-established evidence for blood conservation**
- **Proven efficacy** in reducing bleeding and associated transfusion-related risks, especially in **high-risk patients**.
- Very strong implication that bleeding and transfusion are **modifiable risks**
- Each single component of blood conservation intervention may have limited or obscure results if used alone, but **the optimal outcome results from the summation of multiple steps and interventions,** not just a few 'favorites'**.**
- Focus is '**patient centered**' aimed at optimizing surgical outcomes.

Clinical Scenarios

Clinical Scenario 1

- A 72 y/o gentleman with a history of CABG surgery 10 years earlier presents with recurrent angina. Repeat cardiac catheterization revealed 99% occlusion of all 4 of his saphenous vein grafts. Left ventricular function was normal. After unsuccessful attempts at stent placement, he is scheduled for reop CABG. He is placed on an infusion of heparin 1000U/hr and an infusion of tirofiban 0.1ug/kg/min. He was given a single dose of abciximab (Reopro®) during the catheterization procedure. He is scheduled for repeat CABG . Medications: Atenolol 50 mg po qday, Plavix 75 mg qday, ASA 80 mg qday
- Currently his hemoglobin/hematocrit is 11.5/35. In preparation for surgery, the anesthesiologist informed him that during repeat open heart surgery he may receive a blood transfusion. The patient refused to accept the possibility of receiving blood for fear of blood-born infection. He now wishes to cancel his surgery.

Clinical Scenario 2

Patient is an 83 year old female who had a surgical AVR 8 years ago presents to the cath lab with a STEMI. Cardiac cath shows severe 3 vessel coronary artery disease with a greater than 95% L main stenosis. Current meds include Apixaban, yet she does not know why she is on it. Cardiologist calls and says that he placed an IABP because she was having pain and she needs urgent/emergent surgery. Her Hct is 32g/dL. As the cardiologist walks away, he says “Oh! I forgot, by the way she is a JW”.

Intraoperative Recommendations

- Acute Normovolemic Hemodilution (ANH) (Class IIA, Level A), Retrograde Autologous Priming (RAP) (Class I,Level B-R), Reduced Priming Volume (Class I, Level B-NR)
- Use of Antifibrinolytic Agents: Intravenous (Class I, Level A), Topical (Class IIA, Level B-R), POC Viscoelastic Testing (Class I, Level B-R), Intraoperative Red Cell Salvage (Class I, Level A)
- Use of the above strategies along with meticulous hemostasis can limit blood loss to a minimum, and this patient can recover at a relatively low morbidity and mortality

MiECC

- The adoption of a combined strategy of surgical approach, anesthesia, and perfusion management along with CPB circuit features designed to minimize hemodilution and optimize biocompatibility, has been termed minimally invasive extracorporeal circulation (MiECC). Configuration of the circuit components for MiECC have been defined by consensus to include a combination of multiple techniques (including a closed CPB circuit; biologically inert blood contact surfaces; reduced priming volume; a centrifugal pump; a membrane oxygenator; a heat exchanger; a cardioplegia system; a venous bubble trap/venous air removing device and a shed blood management system)

Many thanks to our authors, and especially our panelists. Please find the full text online.

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PATIENT BLOOD MANAGEMENT GUIDELINES

STS/SCA/AmSECT/SABM Update to the Clinical Practice Guidelines on Patient Blood Management

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