Anticoagulation Management in the Pre- and Postoperative Cardiac Surgical Patient

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- AstraZeneca: advisory board
- Haemonetics: advisory board
- CMEology grant supported by Baxter Healthcare
Blood Transfusion in the Operating Room Is Bad!

- Cardiac surgery
- Thoracic operations
- Vascular operations
- Cancer procedures
- General surgery
Transfusion and Serious Morbidity in 4445 Cardiac Surgical Patients

<table>
<thead>
<tr>
<th>Donor units transfused</th>
<th>Fraction with serious morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 thru 5</td>
<td>0.079</td>
</tr>
<tr>
<td>6 thru 10</td>
<td>0.171</td>
</tr>
<tr>
<td>11 thru 15</td>
<td>0.289</td>
</tr>
<tr>
<td>16 thru 20</td>
<td>0.305</td>
</tr>
<tr>
<td>21 thru 25</td>
<td>0.46</td>
</tr>
<tr>
<td>26 thru 30</td>
<td>0.571</td>
</tr>
<tr>
<td>31 thru 35</td>
<td>0.438</td>
</tr>
<tr>
<td>36 thru 40</td>
<td>0.625</td>
</tr>
<tr>
<td>41 thru 45</td>
<td>0.695</td>
</tr>
</tbody>
</table>

Serious morbidity and mortality increase with the amount transfused.

Blood Transfusion in General Surgical Population

Intraoperative Blood Transfusion and NSQIP Surgical Outcomes in 941,496 Patients

Hospital Cost and Outcomes

What Should We Do to Decrease Complications of Blood Transfusion?

♥ Avoid transfusion!
♥ Identify risk before operation
♥ Intervene to limit bleeding and transfusion - especially in high-risk patients
   ♥ Devices
   ♥ Drugs
   ♥ Process of care
What Works for Blood Conservation?

- Multiple interventions are better than a few ‘favorite’ interventions
- TQM approach – ‘Measurement and Management’
- ‘Outcome greater than sum of parts’
- Examples from cardiac operations
  - ANH, RAP, mini-circuits, biocompatible circuits, ultrafiltration, etc. have variable evidence but taken together they may have synergistic effect.
  - What does not work – PEEP, chest tube reinfusion.
4445 patients having cardiac procedures with CPB over 4 years

- More than 50% do not get transfusion
- Patients who receive > 10 units of blood are in 90th percentile
- 10%-20% of patients consume 80% of blood products

Predictors of Postoperative Bleeding and Blood Transfusion

2011 STS Guidelines

1. Advanced age
2. RBC volume
   a) Small body size or preop anemia
3. Drugs
   a) Anti-platelet or anti-coagulant drugs
4. Co-morbidities
5. Emergent operations
6. Complex operations

Managing Preoperative Risk Factors

- Preoperative risk assessment
  - Age, drugs, co-morbidities, anemia, low BMI, urgency, complexity

- What can we modify before operation?
  - Blood volume – erythropoietin/FeSO₄.
  - Limit anti-platelet & anti-coagulant drugs.
Do Anti-platelet Drugs Cause Increased Postoperative Bleeding?

Yes!
- Aspirin
- Clopidogrel
- 2b/3a inhibitors (short and long-acting)
- Prasugrel
- Ticagrelor
- Cangrelor

Preoperative drug usage is one of the few modifiable risk factors that can impact bleeding and blood transfusion.

Anti-platelet Guidelines - 2012

- Preoperative intervention
  - Point of care testing
    - Good negative predictive value.
  - Stop P2Y12 inhibitors 5-7 days, if possible
    - Even 1-3 day delay helps.
    - Anti-fibrinolytics may help.
  - Continue aspirin unless very high risk (e.g. Jehovah’s Witnesses)
    - Benefit outweighs risk for most patients.

The influence of baseline hemoglobin concentration on tolerance of anemia in cardiac surgery

Transfusion, 2008;48:666-672

Keyvan Karkoui, Duminda N. Wijeysundera, Terrence M. Yau, Stuart A. McCluskey, Adriaan van Rensburg, and W. Scott Beattie

- ≥10,000 patients with normal HGB undergoing CPB.
- Relationships between maximum decrease in HGB (from baseline) and the incidence of mortality, renal failure, and stroke.
- Greater than 50% decrease in HGB was associated with a 50% chance of suffering adverse events.
Preserving RBC Volume

- **RBC Volume**
  - HCT * Blood volume
  - Measure of amount of blood patient can afford to lose.

- **Perioperative EPO.**
- **Mini-circuits.**
- **Ultrafiltration.**
- **Pump salvage (centrifugation).**
- **Microplegia.**
- **Retrograde autologous priming (RAP).**
Class IIa

1. With **hemoglobin levels below 6 g/dL**, red blood cell transfusion can be lifesaving. Transfusion is reasonable in most **postoperative patients whose hemoglobin is less than 7 g/dL**, but no high-level evidence supports this recommendation. (Level of evidence C)

2. Transfuse **non–red cell hemostatic blood products based on clinical evidence of bleeding** and preferably guided by point-of-care tests that assess hemostatic function in a timely and accurate manner. (Level of evidence C)

Virginia Cardiac Surgery Quality Improvement Project (VCSQIP)

No Blood Products Used by Hospital: CAB Only, Calendar Year 2010

- Virginia Cardiac Surgery Quality Improvement Project (VCSQIP)
- Perioperative Anticoagulation
Inova Institutional Transfusion Protocol*

- Optimize preoperative anti-platelet therapy.
- Multidisciplinary evidence-based algorithm
- Modification in Perfusion techniques: RAP/ANH
- Indications for transfusion driven by Protocol

Transfusion administered only after approval by Cardiac Surgeon

* Courtesy of Alan Spier
# VCSQIP - Factors Related to Mortality

<table>
<thead>
<tr>
<th>Factor</th>
<th>Wald X²</th>
<th>OR</th>
<th>95% C.I.</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>63.30</td>
<td>1.05</td>
<td>1.04, 1.06</td>
<td>&lt;0.0001</td>
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<tr>
<td>Gender (Female)</td>
<td>11.10</td>
<td>1.51</td>
<td>1.19, 1.93</td>
<td>0.00</td>
</tr>
<tr>
<td>PAD</td>
<td>12.86</td>
<td>1.62</td>
<td>1.24, 2.10</td>
<td>&lt;0.0001</td>
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<tr>
<td>Stroke</td>
<td>6.79</td>
<td>1.67</td>
<td>1.14, 2.45</td>
<td>0.01</td>
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<tr>
<td>Diabetes</td>
<td>5.40</td>
<td>1.32</td>
<td>1.04, 1.66</td>
<td>0.02</td>
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<tr>
<td>Hypertension</td>
<td>1.85</td>
<td>1.30</td>
<td>0.89, 1.90</td>
<td>0.17</td>
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<tr>
<td>Endocarditis</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Renal Failure</td>
<td>6.89</td>
<td>2.07</td>
<td>1.20, 3.55</td>
<td>0.01</td>
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<tr>
<td>Ejection Fraction</td>
<td>83.00</td>
<td>0.96</td>
<td>0.95, 0.97</td>
<td>&lt;0.0001</td>
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<td>Left Main Disease</td>
<td>1.60</td>
<td>1.17</td>
<td>0.92, 1.48</td>
<td>0.21</td>
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<tr>
<td>Previous PCI</td>
<td>2.65</td>
<td>1.24</td>
<td>0.96, 1.61</td>
<td>0.10</td>
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<tr>
<td>CPB Utilization</td>
<td>4.23</td>
<td>0.68</td>
<td>0.47, 0.98</td>
<td>0.04</td>
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<tr>
<td>Pre-Guideline Transfusion Era</td>
<td>21.97</td>
<td>1.76</td>
<td>1.39, 2.23</td>
<td>&lt;0.0001</td>
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<tr>
<td>Intra-operative Blood Products</td>
<td>40.55</td>
<td>2.23</td>
<td>1.74, 2.85</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

AUC = 0.78; Hosmer-Lemeshow p = 0.05 with 14 degrees of freedom
VCSQIP - Differences Between Transfusion & No Transfusion

Complications of Blood Use: CABG Only, Non-Emergent, First CV Surgery, July 2008 - June 2010

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>OpMortality</td>
<td>3.2%</td>
<td>0.4%</td>
<td>3.8%</td>
<td>1.1%</td>
<td>3.6%</td>
<td>0.5%</td>
<td>1.6%</td>
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<tr>
<td>Prolong Vent</td>
<td>17.7%</td>
<td>3.4%</td>
<td>18.0%</td>
<td>7.1%</td>
<td>19.0%</td>
<td>3.8%</td>
<td>9.0%</td>
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<tr>
<td>Pneumonia</td>
<td>4.4%</td>
<td>0.8%</td>
<td>3.7%</td>
<td>1.9%</td>
<td>5.1%</td>
<td>0.8%</td>
<td>2.2%</td>
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<tr>
<td>Renal Failure</td>
<td>7.1%</td>
<td>1.0%</td>
<td>6.7%</td>
<td>2.6%</td>
<td>7.8%</td>
<td>1.2%</td>
<td>3.4%</td>
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<tr>
<td>Stroke Perm</td>
<td>2.5%</td>
<td>0.6%</td>
<td>1.8%</td>
<td>1.3%</td>
<td>2.6%</td>
<td>0.6%</td>
<td>1.4%</td>
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<tr>
<td>Readmission*</td>
<td>10.3%</td>
<td>7.3%</td>
<td>10.8%</td>
<td>7.9%</td>
<td>10.5%</td>
<td>7.4%</td>
<td>8.4%</td>
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<tr>
<td>Mediastinitis</td>
<td>0.7%</td>
<td>0.3%</td>
<td>0.8%</td>
<td>0.4%</td>
<td>0.8%</td>
<td>0.3%</td>
<td>0.5%</td>
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<tr>
<td>AFib</td>
<td>25.1%</td>
<td>15.8%</td>
<td>23.9%</td>
<td>18.4%</td>
<td>26.0%</td>
<td>16.1%</td>
<td>19.4%</td>
</tr>
<tr>
<td>Any Re-Op</td>
<td>7.1%</td>
<td>0.9%</td>
<td>6.8%</td>
<td>2.6%</td>
<td>8.2%</td>
<td>0.9%</td>
<td>3.3%</td>
</tr>
<tr>
<td>No Complications or Mortality</td>
<td>53.2%</td>
<td>76.6%</td>
<td>54.9%</td>
<td>70.1%</td>
<td>50.7%</td>
<td>75.7%</td>
<td>67.4%</td>
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<tr>
<td>All Patients</td>
<td>2,750</td>
<td>4,272</td>
<td>1,247</td>
<td>5,775</td>
<td>2,335</td>
<td>4,688</td>
<td>7,023</td>
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</table>

* <=30 Days from DOP

* p<0.001  ** p=0.02

Perioperative Anticoagulation
VCSQIP - Cost of CABG Complications

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>OpMortality</td>
<td>$98,827</td>
<td>$46,964</td>
<td>$98,981</td>
<td>$93,075</td>
<td>$102,557</td>
<td>$47,026</td>
<td>$89,703</td>
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<td>Proing Vent</td>
<td>$91,509</td>
<td>$56,261</td>
<td>$94,171</td>
<td>$77,462</td>
<td>$92,996</td>
<td>$58,274</td>
<td>$83,317</td>
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<td>Pneumonia</td>
<td>$113,725</td>
<td>$60,230</td>
<td>$112,494</td>
<td>$97,705</td>
<td>$115,289</td>
<td>$61,004</td>
<td>$102,066</td>
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<td>Renal Failure</td>
<td>$95,349</td>
<td>$45,505</td>
<td>$95,487</td>
<td>$81,591</td>
<td>$98,887</td>
<td>$46,531</td>
<td>$86,516</td>
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<td>Stroke Perm</td>
<td>$96,074</td>
<td>$44,381</td>
<td>$88,393</td>
<td>$80,195</td>
<td>$96,486</td>
<td>$50,366</td>
<td>$82,074</td>
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<tr>
<td>Readmission*</td>
<td>$39,894</td>
<td>$31,485</td>
<td>$40,951</td>
<td>$33,873</td>
<td>$40,300</td>
<td>$32,046</td>
<td>$35,484</td>
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<tr>
<td>Mediastinitis</td>
<td>$102,683</td>
<td>$45,437</td>
<td>$76,279</td>
<td>$82,598</td>
<td>$107,008</td>
<td>$43,518</td>
<td>$81,215</td>
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<td>AFib</td>
<td>$55,713</td>
<td>$34,769</td>
<td>$61,197</td>
<td>$40,924</td>
<td>$57,259</td>
<td>$35,771</td>
<td>$46,356</td>
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<td>Any Re-Op</td>
<td>$106,763</td>
<td>$73,540</td>
<td>$122,098</td>
<td>$89,542</td>
<td>$106,818</td>
<td>$76,452</td>
<td>$101,368</td>
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<td>No Complications or Mortality</td>
<td>$34,990</td>
<td>$29,016</td>
<td>$36,533</td>
<td>$29,903</td>
<td>$35,134</td>
<td>$29,434</td>
<td>$30,861</td>
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<tr>
<td>All Patients</td>
<td>$47,242</td>
<td>$31,167</td>
<td>$49,151</td>
<td>$34,938</td>
<td>$48,820</td>
<td>$31,805</td>
<td>$37,462</td>
</tr>
</tbody>
</table>

* <=30 Days from DOP

Cost of Complications of Blood Use: CABG Only, Non-Emergent, First CV Surgery, July 2008 - June 2010

* p<0.001
Difference in Cost Between Transfused and Non-transfused Groups 2008-2010

$44,000,000
How Do You Measure Quality in Blood Management?

- Domains of performance in cardiac surgery
  - Preoperative medical care
  - Operative care
    - Perfusion interventions
    - Hemostatic drugs
  - Outcome measures
Performance Measure - Preoperative Medical Care

- Multidisciplinary protocols
- Treat preoperative anemia (EPO/Fe)
- Continue aspirin
- Stop P2Y12 inhibitors
- Use point-of-care tests
Perioperative Anticoagulation

Performance Measure – Operative Care

♥ Choice of operation
  ♥ Minimally invasive procedures

♥ Perfusion interventions
  ♥ Mini-circuits
  ♥ Microplegia
  ♥ Modified ultrafiltration
  ♥ Pump salvage
  ♥ Biocompatible circuits

♥ Intraoperative drugs
  ♥ Anti-fibrinolytic drugs
  ♥ Topical hemostatic agents
Performance Measure - Blood Conservation Outcome Measures

- Any intraoperative blood transfusion.
- Any transfusion within 72 hours of operation.
- Any non-PRBC transfusion.
- Unusual blood derivatives (rFVIIa, factor IX, etc.).
- Reoperation for bleeding.
What Do You Think?

Are these reasonable measures of performance?
Would you like to be rated on these measures?

It’s coming!
Conclusions

- Bleeding and blood transfusion predict high cost and adverse outcome.
- Evidence-based interventions limit bleeding-related complications.
- Bleeding-related outcomes are prime targets for quality indicators.
Q29. All of the following have some evidence-base to support use for blood conservation during cardiac procedures except:

a. Acute normovolemic hemodilution.
b. Cell salvage.
c. Modified ultrafiltration.
d. PEEP.
e. Transfusion algorithm supplemented with point-of-care testing.
Questions?
Questions Remain

❤️ How do we measure physiologic indicator of need for transfusion?
❤️ No readily available point-of-care measure of O2 delivery/consumption.

❤️ What is the best option for blood replacement to control bleeding?
❤️ Whole blood, new blood fractions (PCC, rFVIIa, etc.)
Oxygen Delivery vs. HCT At Different Flow Rates

\[ \text{DO}_2 = \text{Q(indexed)} \times 10 \times (\text{HGB} \times 1.36 \times \text{SaO}_2 + \text{PO}_2 \times 0.003) \]

Cardiac Index
- 2.0
- 2.4
- 2.8

O₂ Delivery (ml/min/m²)

272 ml/min/m²

HCT (%)
It’s Not Just About Transfusion!

Components of blood management:

1. Managing anemia
   - Preoperative assessment
   - Preserving RBC volume
2. Optimizing coagulation status
   - Anti-platelet drugs
4. Focus on patient centered decision making.
STS Blood Conservation Guidelines
68 Recommendations

♥ 2011 recommendations
♥ 11 Class I
♥ 49 Class II
  ♥ 21 Class IIa
  ♥ 28 Class IIb
♥ 8 Class III

Evidence-Based Blood Conservation Strategies

- 2011 STS Guidelines
  - Preoperative risk assessment
    - Anti-platelet drugs
    - Blood volume - EPO
  - Intraoperative
    - Blood derivatives
    - Blood salvage
    - Heparin/protamine management
    - Minimally invasive techniques
    - Topical hemostats
- Process of care
  - Multidisciplinary algorithm
  - Point of care

Preserving RBC Volume

- **RBC Volume**
  - **HCT *blood volume**
  - **Measure of amount of blood patient can afford to lose**

- **Perioperative EPO**
- **Mini-circuits**
- **Ultrafiltration**
- **Pump salvage (centrifugation)**
- **Microplegia**
- **Autologous normovolemic hemodilution**
Impact of 2007 Blood Conservation Guidelines – Anesthesia Survey

- Wide variation in clinical practice.
- Survey of 1,061 cardiac programs.
  - 32% response rate.
  - 70% of respondents were familiar with guidelines.
  - 26% changed blood conservation practice.
  - Of 38 guideline recommendations, only 4 of 38 changed by > 5% of respondents.

Likosky, et al. 2010
USA Allogeneic RBC Transfusions from NBCUS Data

RBC Transfusions (millions)


10.6M 40.3 RBC/1,000
14.9M 48.9 RBC/1,000
13.8M 44.2 RBC/1000

Benjamin, private communication.
Point-of-Care Testing

- Fibrinolysis and fibrinogen
  - TEG, MCA 210, TAS system
- Coagulation factors
  - Whole blood aPTT and PT
- Platelets
  - Bleeding time, PFA-100, TEG, RPFA

75 y/o, 55 kg, women, with preop HCT = 35%

Alternative Anticoagulants for CPB

**Indications**
- HIT

**Results**
- Variable
- Slow disappearance.

**Options**
- Hirudin
- Bivalrudin
- Prostaglandin
- Lepirudin
- Argatroban
Does Blood Conservation Cause Better Outcome?

7 RCTs tested transfusion algorithms with point-of-care testing to reduce transfusion

6 of 7 RCTs showed reduced transfusion or re-exploration rates

Didn’t matter what type of POC testing

Various algorithms used

Transfusion Algorithms and POC Testing - An Example

<table>
<thead>
<tr>
<th>Study</th>
<th>Pts</th>
<th>Algorithm</th>
<th>POC tests</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avidan, 2004</td>
<td>210</td>
<td>• Transfuse PRBC for Hb ≤ 8.0</td>
<td>• TEG</td>
<td>Decreased transfusion of heme and non-heme blood</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• DDAVP for abnormal PFA-100 followed by platelets if no response to DDAVP</td>
<td>• PFA-100</td>
<td>products</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Aprotinin for abnormal TEG amplitude</td>
<td>• Hepcon</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Explore for failure to respond and continued bleeding</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Adverse effects of low hematocrit during cardiopulmonary bypass in the adult: Should current practice be changed?

Robert H. Habib, PhDα,β,γ
Anoar Zacharias, MDα,β,γ
Thomas A. Schwann, MDα,β,γ
Christopher J. Riordan, MDα,β,γ
Samuel J. Durham, MDα,β,γ
Aamir Shah, MDα,β,γ

Blood Salvage and Collaboration

- Pump salvage (Class IIa Level of evidence C)
- Centrifugation instead of direct infusion (Class IIa Level of evidence A)
- Modified ultrafiltration (MUF) (Class I Level of evidence A)
- Multidisciplinary blood management teams (Class IIa Level of evidence B)
Anticoagulation Management in the Pre- and Postoperative Cardiac Surgical Patient

Victor A. Ferraris, MD, PhD
University of Kentucky
Linda and Jack Gill Heart Institute
Lexington, Kentucky
The Virginia Cardiac Surgery Quality Initiative was formed in 1994.
Do Thienopyridines Cause Postoperative Bleeding?

- Evidence is more compelling than for aspirin
- 15 studies with clopidogrel and CABG
- Almost all studies show increased bleeding when clopidogrel given within 5 days of CABG – some with increased mortality
- AHA/ACC and STS guidelines recommend stop clopidogrel for 5-7 days before operation, if possible. Even 1 or 2 days helps.

Introoperative Strategies to Minimize Hemodilution

- Minicircuits (Class I Level of evidence A)
- Vacuum-assisted venous drainage (Class IIb Level of evidence C)
- Retrograde autologous priming (Class IIb Level B)
- Biocompatible CPB circuits (Class IIb Level of evidence A)
Retrograde and Antegrade Autologous Priming

- Passive displacement of crystalloid solution from the CPB circuit using the patient’s blood volume via the arterial and venous lines of the CPB circuit.

- Potential benefits:
  - Less hemodilution during CPB
  - ↑ Hemoglobin, COP, plasma and platelets
  - ↓ Dilution of circulating pharmacologic agent
  - Reduced blood transfusions on CPB
  - Inexpensive

Retrograde Autologous Priming –
Class IIb Recommendation

❤ 5 prospective studies
   ❤ 3 showed no benefit
   ❤ 2 showed benefit
   ❤ Not possible to do meta-analysis

❤ Contraindications
   ❤ Urgent operation
   ❤ Anemia
   ❤ Sepsis

❤ May be beneficial when used as part of a multimodality approach
**Class IIb**

- For *longer CPB times* (> 2 to 3 hours), consider maintenance of higher or patient-specific heparin concentrations during CPB.
- May reduce hemostatic system activation, reduce consumption of platelets and coagulation proteins, and reduce blood transfusion. (Level of evidence B)
Protamine Titration

♥ Class IIb

♥ Lower total protamine dose may reduce bleeding and blood transfusion requirements.

♥ Either protamine titration or empiric low-dose regimens (e.g., >50% of total heparin dose)

♥ Monitoring protocols can markedly influence protamine doses used to neutralize heparin.

Topical Hemostatic Agents - 2011 - Mostly Class IIb

Anastomotic sealants
- Cellulose and collagen
- Fibrin sealants
- Thrombin/gelfoam
- Synthetic
  - Cyanoacrylate
  - Polyethylene glycol
- Albumin/glutaraldehyde
- Chitin and polysaccharides

Anti-fibrinolytic solutions
- Aprotinin-based topical solutions
- Lysine analog solutions

Perioperative Anticoagulation