

## Anemia, Transfusion, Surgery and the Kidney

Andrew Shaw FRCPC FRCA FFICM MMHC Professor and Chair Department of Anesthesiology and Pain Medicine University of Alberta



### **2019 Disclosures**

- Edwards Lifesciences
- FAST Biomedical
- Astellas
- No off label comments





# **Perioperative Transfusion Stewardship**





### Anesthesiology Performance Improvement and Reporting Exchange (ASPIRE)





### **Objectives**

- Discuss risks and outcomes associated with transfusion
- Describe ASPIRE transfusion measures
- Provide general recommendations based on American Society of Anesthesiologists (ASA) Transfusion Guidelines (2015)
- Review best practices when transfusion cannot be avoided
- Summarize ASPIRE recommendations based on literature presented





### **Risks Associated with Transfusion**

- Acute kidney injury
- Anaphylaxis
- Hemolytic transfusion reaction
- Transfusion-associated sepsis
- Transfusion-related acute lung injury (TRALI)
- Transfusion-associated circulatory overload
- Transfusion-associated graft-versushost disease





Goodnough & Shander. Anesthesiology. 2012;116(6):1367-1376. PMID: 22487863





## **Approximate Risk Per-Unit Transfusion of RBCs**

Adverse Event	Approximate Risk Per-Unit Transfusion of RBCs	
Febrile reaction <sup>11</sup>	1:60ª	
Transfusion-associated circulatory overload <sup>12,13</sup>	1:100 <sup>b</sup>	
Allergic reaction <sup>14</sup>	1:250	
Transfusion-related acute lung injury <sup>15</sup>	1:12 000	
Hepatitis C virus infection <sup>16</sup>	1:1 149 000	
Hepatitis B virus infection <sup>17</sup>	1:1 208 000 to 1:843 000 <sup>c</sup>	
Human immunodeficiency virus infection <sup>16</sup>	1:1 467 000	
Fatal hemolysis <sup>18</sup>	1:1972000	

Carson et al. JAMA. 2016;316(19):2025-2035. PMID: 27732721

Table 1 Approximate Disk Per-Unit Transfusion of Ped Blood Colls (PBCs)

<sup>a</sup> Estimated to be 1:91 with prestorage leukoreduction and 1:46 with poststorage leukoreduction.

- <sup>b</sup> Indicates the estimated risk per recipient rather than unit.
- <sup>c</sup> The estimate is variable depending on the length of the infectious period.





#### **Risks of Transfusion for Noncardiac Surgery**

Table 3. Impact of Intraoperative Transfusion on 30-Day Mortality and 30-Day Complications

Outcome	Transfusion Group, Outcome Rate (%)	No Transfusion Group, Outcome Rate (%)	Unadj OR Txf vs. No Txf (95% Cl)	Adj OR Txf <i>vs.</i> No Txf (95% Cl)	Adj OR Txf <i>vs.</i> No Txf (PS Method) (95% Cl)
Mortality	6.44	4.26	1.55 (1.24, 1.90)	1.29 (1.03, 1.62)	1.21 (0.96, 1.52)
Cardiac complications	2.08	1.40	1.50 (1.06, 2.12)	1.40 (0.97, 2.03)	1.31 (0.88, 1.95)
Pulmonary complications	12.6	6.03	2.24 (1.92, 2.63)	1.76 (1.48, 2.09)	1.75 (1.47, 2.08)
Renal complications	2.69	1.85	1.46 (1.08, 1.99)	1.32 (0.93, 1.88)	1.29 (0.91, 1.84)
CNS complications	0.69	0.58	1.20 (0.67, 2.15)	0.84 (0.43, 1.64)	0.68 (0.34, 1.38)
Sepsis complications	16.4	9.81	1.81 (1.58, 2.07)	1.43 (1.21, 1.68)	1.46 (1.24, 1.72)
Wound complications	9.17	4.65	2.07 (1.73, 2.48)	1.87 (1.47, 2.37)	1.89 (1.49, 2.41)
Thromboembolic	4.07	1.89	2.20 (1.69, 2.88)	1.77 (1.32, 2.38)	1.81 (1.34, 2.45)

Adj = adjusted; CI = confidence interval; CNS = central nervous system; OR = odds ratio; PS method = propensity score method; Txf = transfusion; Unadj = unadjusted.

Glance et al. Anesthesiology. 2011;114(2):283-292. PMID: 21239971





#### Outcomes Associated with Perioperative Blood Transfusion

- Transfusion based on a liberal trigger is associated with worse patient outcomes and increased institutional cost compared with a restrictive trigger.<sup>1</sup>
- Patients who received one or two units of rbcs had a 29% increased odds of death and a 40-90% increased odds of pulmonary, sepsis, wound, and thromboembolism complications.<sup>2</sup>
- 30-day mortality rate for patients who were transfused was 6.44% versus 4.26% for patients who were not transfused.<sup>2</sup>
- Restricting blood transfusions using a restrictive trigger of ≤ 7 g/dL results in a significant reduction in total mortality, acute coronary syndrome, pulmonary edema, re-bleeding, and bacterial infection compared with more liberal transfusion strategy.<sup>3</sup>

<sup>1</sup>Ejaz et al. *JAMA surgery*. 2015;150(7):625-630. PMID: 25946411
 <sup>2</sup>Glance et al. *Anesthesiology*. 2011;114(2):283-292. PMID: 21239971
 <sup>3</sup>Salpeter et al. *The American journal of medicine*. 2014;127(2):124-131.e123.PMID: 24331453





# Financial Impact: Total cost of a single unit of PRBCs

- Actual institutional acquisition costs approximately \$220 per unit
- Estimated mean activity-based cost of transfusion: \$760 per unit (\$522-\$1183) takes into account acquiring, delivering, administering, and monitoring each transfusion





Ejaz et al. JAMA surgery. 2015;150(7):625-630. PMID: 25946411



# Transfusion Recommendations & Guidelines



M•TQIP













# ASA Practice Guidelines for Perioperative Blood Management

- Preoperative Evaluation
- Preadmission Patient Preparation
- Pre-procedure Preparation
- Intraoperative and Postoperative Management of Blood Loss

Anesthesiology. 2015;122(2):241-275. PMID: 25545654





### **Preoperative Evaluation**

Perform several days to weeks in advance, if possible.

- Review Previous Medical Records & conduct a Patient/Family
  Interview
  - ✓ Previous blood transfusion?
  - ✓ History of drug-induced coagulopathy?
  - Presence of congenital coagulopathy?
  - ✓ Risk factors for organ ischemia?
  - ✓ History of thrombotic events?
- Review existing lab results (hemoglobin, hematocrit, coagulation profiles)
- Order additional lab tests based on patient's condition (anemia, coagulopathy)
- Conduct physical exam (ecchymosis, petechiae, pallor)

Prior to surgery, inform patient of potential risks vs. benefit of blood transfusion and identify patient preferences.





# **Preadmission Patient Prep Recommendations<sup>2</sup>**

- Prevention or reduction of perioperative anemia
  - Administration of erythropoietin can reduce need for RBC transfusions in patients with perioperative hemoglobin 10-13 g/dL who are at high risk for perioperative blood loss from elective, non-cardiac, non-vascular surgery <sup>1</sup>
  - Iron (IV infusion or daily oral administration)
- Discontinue anticoagulants/antithrombotic agents (Consider patient condition and risk factors)
  - Warfarin: 5 days before surgery; check PT/INR day of surgery.
  - Clopidogrel or other thienopyridines: Discontinue 5 days before surgery.
  - Aspirin: Discontinue 7-10 days before surgery (but not all do)
- Preadmission autologous blood donation (PAD)
  - Though autologous blood donation can reduce the use of allogenic blood transfusion by 40-52%, PAD is not found to be cost-effective as compared to other blood sparing strategies.<sup>3</sup>
     <sup>1</sup> Micromedex. Epoetin Alpha indications.
     <sup>2</sup> Anesthesiology. 2015;122(2):241-275. PMID: 25545654

<sup>a</sup> Birkmeyer et al. *Transfusion*. 1993;33(7):544-551. PMID: 8333017





### **Pre-procedure Preparation Recommendations**

#### **Adopt Blood Management Protocols**

- Multimodal protocol or algorithm
- Restrictive vs liberal transfusion protocol
- Non-transfusion protocol (bloodless surgery)
- Massive transfusion protocol
- Maximum surgical blood ordering schedule for elective procedures

#### **Reversal of anticoagulants**

- Vitamin K
- Prothrombin Complex Concentrates

#### Antifibrinolytics for prophylaxis of excessive blood loss

- Aminocaproic acid
- Tranexamic acid

#### Acute Normovolemic Hemodilution: Consider for cardiac and ortho procedures<sup>2</sup> <sup>1</sup>Anesthesiology. 2015;122(2):241-275. PMID: 25545654 <sup>2</sup>Shander & Rijhwani, *Transfusion*, 2004;44:26S-34S, PMID: 15585002





# Intraoperative and Postoperative Management of Blood Loss

- Allogenic Red Blood Cell Transfusion
  - Age of Stored Blood (controversial no firm conclusions)
  - Leukocyte reduction: reduces complications associated with transfusion
- Reinfusion of recovered red blood cell transfusion (cell saver administration supported)
- Intraoperative and postoperative patient monitoring
  - Monitor blood loss
  - Perfusion of vital organs
  - Anemia
  - Coagulopathy
- Treatment of excessive bleeding

Anesthesiology. 2015;122(2):241-275. PMID: 25545654





### **Treatment of Excessive Bleeding**

- ASA Practice Guidelines for Perioperative Blood Management
  - Transfusion of Platelets: Obtain platelet count before transfusion
  - Transfusion of FFP: Obtain coagulation tests (INR or PT and aPTT) before transfusing FFP
  - Transfusion of Cryoprecipitate: Assess fibrinogen levels before giving cryo
  - Pharmacologic Treatment of bleeding
    - -DDAVP (0.3u/kg)
    - -Antifibrinolytics (tranexamic acid, aminocaproic acid)
    - -Topical hemostatics (fibrin glue, thrombin gel)
    - -PCCs and rVIIa (careful if vascular anastomoses)

-Treatments for hypofibrinogenemia (cryoprecipitate, rec fibrinogen Anesthesiology. 2015;122(2):241-275. PMID: 25545654

### **Transfusion Triggers: Literature Review**

Clinical Practice Guidelines from AABB (American Association of Blood Banks)

- Recommendation #1: Transfusion is not indicated until hemoglobin level is 7 g/dL for hospitalized adult patients who are hemodynamically stable, including critically ill patients.\*
- Recommendation #2: Transfusion threshold of 7-8 g/dL is indicated for patients undergoing orthopedic or cardiac surgery, and those with preexisting cardiovascular disease.\*
- Recommendation #3: Patients, including neonates, should receive RBC units selected at any point within their licensed dating period rather than limiting patients to transfusion of only fresh (≤10 days) RBC units.

\*Recommendations do not apply to patients with Acute Coronary Syndrome, severe thrombocytopenia, and chronic transfusion-dependent anemia.

Carson et al. Jama. 2016;316(19):2025-2035. PMID: 27732721

Mueller et al. Jama. 2019; 321(10), 983-997. PMID: 30860564





# **Transfusion Triggers: Literature Review**

#### **Red Cross Transfusion Guidelines:**

- RBCs should be administered based on signs and symptoms, Hgb level, and hematologic results
- In the absence of acute hemorrhage, RBCs should be administered as single units, followed by appropriate evaluation to justify additional units.
- Complete administration of a single unit within 4 hours

#### **Post-transfusion Considerations:**

- In a non-bleeding, non-hemolyzing adult, the hemoglobin should equilibrate within 15 minutes after transfusion of RBCs.
- It is estimated that one RBC unit should increase Hgb by approximately 1g/dL or Hct by 3%.

American Red Cross. A compendium of transfusion practice guidelines. 2017.





# **Transfusion Triggers: Literature Review**

#### National Institute for Health and Care Excellence (NICE) Guidelines:

- Use Restrictive RBC Hgb Thresholds (7 g/dL) for patients who need RBC transfusions but do not have:
  - Major hemorrhage
  - Acute Coronary Syndrome
  - A need for regular blood transfusions for chronic anemia
- Post-transfusion Hgb target (goal) for restrictive therapy: 7-9 g/dL
- In patients with acute coronary syndrome, consider transfusion threshold of Hgb: 8 g/dL and target of 8-10 g/dL
- Set individual thresholds and targets for patients with chronic anemia
- Consider single unit red blood cell transfusions for adults who do not have active bleeding
- After each single unit of RBC transfusion, clinically reassess and check Hgb levels before administering additional units. National Institute for Health and Care Excellence. Blood transfusion. 2015.





#### 37<sup>th</sup> Vicenza Course on AKI & CRRT – May 28-30, 2019

Mueller et al. Jama. 2019; 321(10), 983-997. PMID: 30860564

# Transfusion Trigger Considerations in Cardiac Surgery





#### Percentage of Cardiac Cases Receiving a Transfusion per ASPIRE Measure Criteria



### **Transfusion Literature: Cardiac Surgery**

**Conflicting definitions of restrictive transfusion presented in the literature:** 

- In one review, there was no significant increase in rates of myocardial infarction, stroke, acute renal failure, or mortality using restrictive transfusion thresholds (Hgb: 7-9 g/dL) in patients undergoing cardiovascular surgery.<sup>1</sup>
- Low Hgb (<7) values are associated with increased operative mortality, increased likelihood of prolonged intensive care stay and greater likelihood of postoperative hospitalization of 9 or more days.<sup>2</sup>
- Restrictive transfusion thresholds (Hgb: 7-8 g/dL) are associated with higher rates of acute coronary syndrome in anemic patients compared with more liberal transfusion thresholds (9-10 g/dL).<sup>3</sup>

<sup>1</sup>Curley et al. *Critical care medicine*. 2014;42(12):2611-2624. PMID: 25167086 <sup>2</sup>Habib et al. *The Journal of thoracic and cardiovascular surgery*. 2003;125(6):1438-1450. PMID: 12830066 <sup>3</sup>Docherty et al. *BMJ (Clinical research ed)*. 2016;352:i1351. PMID: 27026510



### Liberal vs. Restrictive Transfusion Strategy in Death Cardiac Patients



Carson et al. American heart journal. 2013;165(6):964-971.e961. PMID: 23708168

ERSITY OF

- 110 Patients
- Restrictive: <8 g/dL</li>
- Liberal: <10 g/dL
- Restrictive transfusion strategy resulted in increased rate of death (18.5% vs. 12.7%).

---- Restrictive

P value: 0.032



# **Transfusion Recommendations: Cardiac Surgery**

#### **Cell Saver**

- Transfusion through cell saver is safe and results in a significant reduction in homologous transfusion.. Pts who receive intraoperative cell saver transfusion (ICT) also have decreased mediastinal drainage 12 hours postoperatively <sup>1</sup>
- Hgb levels fell significantly in patients on day 1 post-op.<sup>2</sup>
- Major concerns regarding the use of cell saver include:
  - $\checkmark$  Possible increase in the systemic inflammatory response  $^{3,\,4}$
  - ✓ Coagulopathy postoperatively <sup>5</sup>
  - ✓ An increased risk of fat and air emboli <sup>6</sup>

✓ Organ Failure <sup>7,8</sup>

<sup>1</sup>Cote et al. Canadian journal of surgery Journal canadien de chirurgie. 2016;59(5):330-336. PMID: 27668331
<sup>2</sup>Niranjan et al. European journal of cardio-thoracic surgery 2006;30(2):271-277. PMID: 16829083
<sup>3</sup>Sandoval et al. The heart surgery forum. 2001;4(2):113-117; discussion 117-119. PMID: 11544618
<sup>4</sup>Amand et al. Perfusion. 2002;17(2):117-123. PMID: 11958302
<sup>5</sup>Daane et al.. Perfusion. 2003;18(2):115-121.PMID: 12868789
<sup>6</sup>Engelhardt & Blumenberg D. Beitrage zur Infusionstherapie = Contributions to infusion therapy. 1991;28:317-321. PMID: 1725646
<sup>7</sup>Casey. The Annals of thoracic surgery. 1993;56(5 Suppl):S92-96. PMID: 8239845
<sup>8</sup>Reents et al. Thoracic surgery. 1999; 68(1): 58-62. PMID: 10421115



# TRICS III

- Mazer et al (2017) NEJM
- RCT of 5743 mod-high risk heart surgery patients: restrictive (7.5 g/dl) vs liberal (9.5 g/dl)
- Good group separation
- No difference death
- Slightly longer ICU LOS in restrictive group



• No difference AKI rates, but less blood given to restrictive group

Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery





#### **Optimizing Perfusion: Anemia Tolerance & Transfusion**

- Transfusion Trigger during CPB was 22%
- %△Cr = The peak postoperative change in serum creatinine level relative to pre-CPB values.
- Acute renal injury and failure (ARF) after cardiopulmonary bypass (CPB) has been linked to low on-pump hematocrit.



Increasing rates of AKI are seen as the HCT dips below 20-21% during CPB. Occurs whether the patient is transfused or not. Transfusion itself also increases the risk of AKI.



Habib et al.; Crit Care Med 2005;33:1749-1756

### Anemia and Hypotension: Co-Occurrence during CPB

• The likelihood of acute kidney injury with CPB-anemia does not change with different blood pressure values as measured at the time when the lowest CPB hematocrit occurred. Hypotension, Anemia Tolerance during CPB and

Postoperative Acute Kidney Injury





Haase et al Nephrol Dial Transplant 2012;27:153-160 Sickeler et al Ann Thor Surg 2014; 97; 865-71

# **Hemodilution and Transfusion**



Minimizing hemodilution and avoiding unnecessary transfusion is best practice.

- STS Guideline Recommendations
  - Multidisciplinary and multi modality:
    - Mini-circuits
    - Microplegia
    - Modified ultrafiltration
    - Blood salvage



Ann Thorac Surg 2011;91:944-82



### Cardiopulmonary Bypass: Anemia, Hypotension, and AKI



Patients with both anemia and hypotension during CPB did not differ in rates of AKI with those of anemia alone but did differ from patients with hypotension alone and patients with neither anemia or hypotension.



Sickeler et al Ann Thor Surg 2014; 97; 865-71

### **Massive Transfusion Protocols**

### Develop with multi-disciplinary committee that includes:

- Transfusion service/blood bank
- Emergency department
- Anesthesia
- Trauma Service

#### **Massive Transfusion Protocol should address:**

- Triggers for initiating massive transfusion in trauma
- Resuscitation in the trauma bay
  - MTP Product Availability
  - MTP Product Delivery
  - MTP Blood Product Transfusion
- Continuing MTP in OR, Angiography suite, ICU
- Transfusion service processes for delivery of blood products
- Transfusion targets
- Use of adjuncts for massive transfusion patients
- Termination of MTP
- Performance Improvement Monitoring



For more information: <u>American College of Surgeons</u>



### **Obstetric Hemorrhage Protocol**

American College of Obstetrics and Gynecology (ACOG) released the Safe Motherhood Initiative in 2013.

- Blood transfusion or cross-matching should not be used as a negative quality marker and is warranted for certain obstetric events.
- In cases of severe obstetric hemorrhage, ≥4 units of blood products may be necessary to save the life of a maternity patient.
- Hospitals are encouraged to coordinate efforts with their laboratories, blood banks, and quality
  improvement departments to determine the appropriateness of transfusion and quantity of blood
  products necessary for these patients.

For more information and resources, please visit the ACOG website: <u>ACOG Obstetric Hemorrhage</u> <u>Bundle</u>





### **Obstetric Hemorrhage Protocol Pocket Card**



# **ASPIRE (MPOG) Recommendations**

- Use the literature to develop evidence-based institution transfusion protocols and guidelines
- Restrictive transfusion protocols should be considered for asymptomatic patients
- There is rarely an indication to transfuse any patient with a Hgb >10g/dL
- Decision to transfuse should be based on objective assessment of the patient, including Hgb/Hct
- In the absence of acute hemorrhage, transfuse one unit at a time
- Reassess post-transfusion to determine if additional units are required







