Improving Outcomes of Cardiac Surgery with a Point-of-Care Based Transfusion Algorithm

Summer Syed (local PI)

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Institute of Health Policy, Management and
Transfusions at TGH

Highest in Ontario

Graph showing transfusions in 2012 with categories RBC, FFP, Platelet, and ≥4 U Tx.
Transfusions at TGH

- Highest in Ontario
- One of the Highest in Ontario

Graph showing transfusions at TGH with categories RBC, FFP, Platelet, and ≥4 U Tx.
Cardiac surgery with cardiopulmonary bypass impairs coagulation
Coagulation

TF-Bearing Cell

TF

VIIa

Xa

Va

Platelet

VIII/vWF

V

VIIa

Va

XIa

Fibrinogen

Fibrin Monomers

Fibrin Matrix

Activated Platelet

IXa

IX

Platelet

VIIa

Xa

Va

Xa

IIa

X

Xa

IIa

X

Xa

IIa

X

XIIa

XIIIa
Coagulation

Clot
Coagulation

Thrombin

Clot
Coagulation
Coagulation

- Thrombin
- Fibrinogen
- Clot
Coagulation
Coagulation

- Thrombin
- Fibrinogen
- Platelets
- Clot
- Fibrinolysis
Conventional coagulation tests are not very informative
Coagulation

Conventional coagulation tests are not very informative
Conventional coagulation tests are not very informative.
Coagulation

Conventional coagulation tests are not very informative
Coagulation

Conventional coagulation tests are not very informative
Coagulation

Conventional coagulation tests are not very informative
We do not know when to initiate treatment
Rewarmed

Protamine (1.1 mg / mg initial heparin dose) post-CPB

ACT normalized (± 25% of baseline if normal at baseline)

Measure Blood Loss (Must use 5-minute packing method)

Collect blood for POC tests ROTEM and Platelet Function (x2 blue top tubes)

 Measure ACT, POC INR. Send samples for PTT, PT, INR, Fibrinogen

If ACT elevated, give additional protamine and repeat ACT

Sponges Weigh < 60 gm (or no sponges weighed)

No Blood Products

(MCF-AFTEM) / (MCF-EXTEM) > 1.5 or LI30 < 95%

Tranexamic acid 2 – 4 gm

Sponges Weigh > 60 gm

MCF-EXTEM <40 & MCF-FIBTEM >7 mm or <75% or <75,000 Functioning Platelets (PhWrk Coll) or Clopidogrel* within 5 days of surgery

Platelets 1 pool

CT-EXTEM > 100 s or POC INR > 2.0

FFP 15 ml/kg† (3 – 6 U); Consider PCC if RV failure, volume overload, or on coumadin

MCF-FIBTEM ≤ 7 mm

Cryoprecipitate 10 U or Fib Conc 50 mg/kg†

If meet criteria for more than one blood product type:
- Sponges 60 – 120 gm, must treat in order of steps that meet criteria (1 – 4), one at a time
- Sponges > 120 gm, can combine steps and give products together

* New antiplatelet drugs may require more than 1 pool of platelets for reversal
† Use ideal body weight to calculate dosing
oscillating axis (+- 4.75°)

mirror

counterforce spring

ball bearing
data processor

detector

LED light source

cuvette + sample

temperature controlled

cuvette holder

clot formation

sensor pin
Normal clotting

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<th>MCF: 57mm</th>
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Low Platelet Count or Function

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<th>EXTEM</th>
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<td>CFT: 444s</td>
<td>CT: 200s</td>
<td>CFT: 448s</td>
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<tr>
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<td>A10: 23mm</td>
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<tr>
<td></td>
<td></td>
<td>α: 80°</td>
<td>α: 72°</td>
<td></td>
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<tr>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>FIBTEM</td>
<td></td>
<td>ATEM</td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>67s</td>
<td>CFT: -s</td>
<td>CT: 52s</td>
<td>CFT: 398s</td>
</tr>
<tr>
<td>A10</td>
<td>15mm</td>
<td>MCF: 16mm</td>
<td>A10: 25mm</td>
<td>MCF: 36mm</td>
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<tr>
<td></td>
<td></td>
<td>ML: -%</td>
<td>ML: -%</td>
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Low Fibrinogen
Hyperfibrinolysis

<table>
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<td>CFT</td>
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<tr>
<td>ML</td>
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<td></td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>α</td>
<td>65°</td>
<td></td>
<td>74°</td>
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</table>

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</thead>
<tbody>
<tr>
<td>CT</td>
<td>51s</td>
<td>CFT</td>
<td>52s</td>
<td></td>
</tr>
<tr>
<td>A10</td>
<td>7mm</td>
<td>MCF</td>
<td>55mm</td>
<td></td>
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<tr>
<td>ML</td>
<td>94%</td>
<td></td>
<td>0%</td>
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</tr>
<tr>
<td>α</td>
<td>-°</td>
<td></td>
<td>64°</td>
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</tbody>
</table>
Plateletworks
Plateletworks

- Uses a standard cell counter
- Tube 1: EDTA → CBC
- Tube 2: Activators (e.g., collagen, ADP)
  - Shake, then wait 4 minutes
  - Functioning platelets clump → No longer counted
  - Therefore measuring non-functioning platelets

- Calculate functional platelet count:
  - Functional platelet count = (# plt tube 1 – # plt tube 2)
  - Functional platelet % = (# plt tube 1 – # plt tube 2) / (# plt tube 1)
We do not know when to initiate treatment

Patient is oozy!
Institute an POC-based Algorithm

- Non-selective
  - All CVS patients

- Enforcement
  - All transfusions audited

- Multidisciplinary
  - Anesthesia, Surgery, Perfusion, Blood bank, Hematology, Nursing
Rewarmed

Protamine (1.1 mg / mg initial heparin dose) post-CPB

ACT normalized (± 25% of baseline if normal at baseline)

Measure Blood Loss (Must use 5-minute packing method)

Collect blood for POC tests ROTEM and Platelet Function (x2 blue top tubes)

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If ACT elevated, give additional protamine and repeat ACT

Sponges Weigh < 60 gm (or no sponges weighed)

No Blood Products

(MCF-AFTEM) / (MCF-EXTTEM) > 1.5

LI30 < 95%

Tranexamic acid 2 – 4 gm

Sponges Weigh > 60 gm

MCF-EXTTEM <40 & MCF-FIBTEM >7 mm or

< 75% or < 75,000 Functioning Platelets (PhWrk ColI) or

Clopidigrel* within 5 days of surgery

Platelets 1 pool

FFP 15 ml/kg† (3 – 6 U); Consider PCC if RV failure, volume overload, or on coumadin

CT-EXTTEM > 100 s or

MCF-FIBTEM ≤ 7 mm

Cryoprecipitate 10 U or

Fib Conc 50 mg/kg†

If meet criteria for more than one blood product type:
- Sponges 60 – 120 gm, must treat in order of steps that meet criteria (1 – 4), one at a time
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† Use ideal body weight to calculate dosing
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Sponges Weigh < 60 gm (or no sponges weighed)

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- (MCF-AFTEM) / (MCF-EXTEM) > 1.5 or LI30 < 95%
  - Tranexamic acid 2 – 4 gm

Sponges Weigh > 60 gm

- MCF-EXTEM <40 & MCF-FIBTEM >7 mm or < 75% or < 75,000 Functioning Platelets (PltWk Coll) or Clopidogrel* within 5 days of surgery
  - Platelets 1 pool

- CT-EXTEM > 100 s or POC INR > 2.0
  - FFP 15 ml/kg† (3 – 6 U); Consider PCC if RV failure, volume overload, or on coumadin

- MCF-FIBTEM ≤ 7 mm
  - Cryoprecipitate 10 U or Fib Conc 50 mg/kg†

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Sponges Weight > 60 gm

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## Transfusion Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Pre-program (2012; n = 1303)</th>
<th>Post-program (2013; n = 632)</th>
<th>P-value</th>
<th>Relative Risk Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC %</td>
<td>52%</td>
<td>40%</td>
<td>&lt; 0.0001</td>
<td>0.79 (0.72 – 0.87)</td>
</tr>
<tr>
<td>Platelets %</td>
<td>34%</td>
<td>19%</td>
<td>&lt; 0.0001</td>
<td>0.56 (0.48 – 0.66)</td>
</tr>
<tr>
<td>Plasma %</td>
<td>34%</td>
<td>13%</td>
<td>&lt; 0.0001</td>
<td>0.37 (0.30 – 0.45)</td>
</tr>
</tbody>
</table>
## Other Clinical Outcomes

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pre-program (2012; n = 1303)</th>
<th>Post-program (2013; n = 632)</th>
<th>P-value</th>
<th>Relative Risk Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-exploration</td>
<td>6.5%</td>
<td>2.9%</td>
<td>0.001</td>
<td>0.48 (0.30 – 0.79)</td>
</tr>
<tr>
<td>Massive bleeding (&gt; 4 units RBC)</td>
<td>20%</td>
<td>11%</td>
<td>&lt; 0.0001</td>
<td>0.51 (0.40 – 0.64)</td>
</tr>
<tr>
<td>Refractory bleeding (rFVIIa use)</td>
<td>3.4%</td>
<td>1.1%</td>
<td>0.002</td>
<td>0.28 (0.12 – 0.60)</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>6.1%</td>
<td>3.3%</td>
<td>0.008</td>
<td>0.48 (0.30 – 0.77)</td>
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</tbody>
</table>
Transfusions at TGH

Highest in Ontario

One of the Highest in Ontario

- RBC
- FFP
- Platelet
- ≥4 U Tx

2012
Transfusions at TGH

One of the Lowest in Ontario
# Program Operating Expenses

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
<th>Unit Cost</th>
<th>Total (per year)</th>
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</thead>
<tbody>
<tr>
<td>Labour</td>
<td>1.2 FTE (9 – 5 coverage; after-hours testing to be provided by anesthesia)</td>
<td>$150,000</td>
<td>$150,000</td>
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<tr>
<td></td>
<td>POCT Staff time (1 hour per week)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disposables (Reagents and Supplies)</td>
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<td></td>
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<tr>
<td>ROTEM</td>
<td>2000 tests per year (1500 for cardiac; 500 for other – primarily lung and liver transplant)</td>
<td>$28</td>
<td>$56,000</td>
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<tr>
<td>PlateletWorks</td>
<td>2000 tests per year (1500 for cardiac; 500 for other – primarily lung and liver transplant)</td>
<td>$28</td>
<td>$56,000</td>
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<tr>
<td>Quality Control and Proficiency Testing</td>
<td>Cost per year</td>
<td>$13,000</td>
<td>Absorbed</td>
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<tr>
<td>Service Contracts</td>
<td>Rotem and Plateletworks service and preventative maintenance agreements</td>
<td>$7,000</td>
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<tr>
<td></td>
<td>Total operating costs per year</td>
<td>$269,000</td>
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### Annual Savings in Direct Transfusion Costs

<table>
<thead>
<tr>
<th>Product</th>
<th>Number saved (compared to 2012)</th>
<th>Cost per unit*</th>
<th>Total costs</th>
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</thead>
<tbody>
<tr>
<td>RBC (units)</td>
<td>1370</td>
<td>$840</td>
<td>$1,150,000</td>
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<tr>
<td>Platelet (doses)</td>
<td>400</td>
<td>$600</td>
<td>$240,000</td>
</tr>
<tr>
<td>Plasma (units)</td>
<td>1543</td>
<td>$80</td>
<td>$123,000</td>
</tr>
<tr>
<td>rFVIIa (doses)</td>
<td>30</td>
<td>$5000</td>
<td>$150,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td>~ 1,700,000†</td>
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</tbody>
</table>

* Costs: CBS production costs x 2 (activity based costing estimated to be 3-5 times production costs)
† Not including cost-savings due to reduced complications
Blood Conservation in Cardiac Surgery Using a Novel Transfusion Algorithm Based on Point-of-Care Testing: A Stepped-Wedge Cluster Randomized Controlled Trial

Does an integrated blood transfusion algorithm that employs POC coagulation tests applied across a network of hospitals reduce blood transfusions and associated adverse outcomes in cardiac surgery?
**Blood Transfusion Algorithm**

- **Rewarmed**
  - Protamine (≤1 mg/mg initial heparin dose) post-CPB
  - ACT normalized (= 10% of baseline if normal at baseline)
  - Measure Blood Loss (Must use 5-minute packing method)†
- **Sponges Weigh < 60 gm (or no sponges weighed)**
  - No Blood Products
- **Sponges Weigh ≥ 60 gm§**
  - Normal POC tests
    - Repeat POC tests, Consider Floseal, Pack and wait for results
  - Abnormal POC tests
    - Functioning platelets < 75,000 or A10-EXTEM < 35 + A10-FIBTEM > 7 mm
      - Platelets 1 pool
    - A10-FIBTEM ≤ 7 mm
      - Cryoprecipitate 10 U or Fibrinogen 4 g
    - CT-EXTEM > 90 s
      - Octaplex 20 IU/kg(BW) or Plasma 2 – 4 U
Randomization Schedule (10 hospitals) (Stepped wedge cluster randomization)
Details

- 11 hospitals
  - POC algorithm will become standard-of-care
    - Waive individual patient consent

- ~7000 patients will be operated on during study, ~ 4000 during intervention phase
  - Powered to detect an absolute 8% reduction in RBC transfusion rate before and after intervention
  - Greater reductions expected for other blood products
  - May also detect differences in other clinical outcomes
    - > 80% power to detect a 50% reduction in AKI
Current Status

- CIHR funded
- Multidisciplinary team at each hospital
- TEM and Helena will provide machines and disposables
- REB submission at UHN completed, at other sites in process
- Study group meeting in May
- Randomization in July/August
- Anticipated accrual September 2014 – March 2015
- Future: TBD at each site