Inclusion Criteria
- Pediatric congenital heart patients undergoing cardiac surgery on cardiopulmonary bypass

Exclusion Criteria
- None

Background
Bleeding is a known risk factor for cardiac surgery. Traditional methods of monitoring coagulation in the operating room require multiple laboratory tests with an approximate turn-around time of 45 - 60 minutes.\(^1\) Rotational thromboelastometry (ROTEM) and thromboelastography (TEG) are promising new tools utilized in adult cardiac surgery to monitor clot formation. ROTEM and TEG offer timely graphic and numerical results detailing the assessment of the patient’s whole blood coagulation profile.\(^2-4\) Although utilized in adult cardiac surgery, there is limited knowledge on the effectiveness of ROTEM directed transfusion pathways in children.

Critically Analyze the Evidence
The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. The table below defines how the quality of evidence is rated and how a strong versus a weak recommendation is established.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>STRONG</td>
<td>Desirable effects clearly outweigh undesirable effects or vice versa</td>
</tr>
<tr>
<td>WEAK</td>
<td>Desirable effects closely balanced with undesirable effects</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quality</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td>Moderate</td>
<td>Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td>Low</td>
<td>Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence</td>
</tr>
<tr>
<td>Very Low</td>
<td>Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence</td>
</tr>
</tbody>
</table>

PICO Question 1: In pediatric patients with congenital heart disease that are at high risk for post-cardiopulmonary bypass coagulopathy, does the use of a goal-directed transfusion pathway to guide intra-operative blood transfusions decrease the transfusion of blood products post-cardiopulmonary bypass?

Recommendation(s): Strong recommendation with low quality evidence that the use of a goal-directed transfusion algorithm decreases the amount of blood products given after separation from cardiopulmonary bypass. In addition, a ROTEM-guided algorithm can be employed successfully to decrease blood product administration.\(^2,5-13\)

It is well documented that blood transfusion is associated with increased morbidity, increased length of stay, increased post-operative ventilator days and increased hospital costs after cardiac surgery.\(^7\) There are no existing clinical guidelines or recommendations for the treatment of post-bypass bleeding in pediatric patients. A review of the literature found five studies reporting on the use of transfusion algorithms to treat post-bypass coagulopathy in pediatric cardiac surgery patients. In a prospective study using ROTEM to guide treatment of post-bypass bleeding, Romlin 2011 used a ROTEM-guided algorithm for transfusion. This study confirmed that significantly fewer blood products were administered to patients who received the intervention compared with the control group (44% vs. 80%, p<0.001).\(^5\) As a quality improvement initiative, Whitney 2013 measured the impact of a standardized goal-directed transfusion algorithm based on laboratory coagulation tests in pediatric cardiac surgery patients and demonstrated significant reductions in transfusion of packed red blood cells (PRBCs), cryoprecipitate, and total blood products after the algorithm was implemented.\(^8\) A 2015 randomized control trial to determine if a ROTEM-based blood transfusion pathway reduced postoperative bleeding in pediatric patients undergoing heart surgery found that patients randomized to the ROTEM-pathway had a decreased amount of postoperative transfusions and no difference noted in intraoperative red blood cell transfusions than the control group; however there was significantly more fresh frozen plasma (FFP) and platelet concentrate administered intraoperatively.\(^2\)
evaluated the use of TEG in pediatric patients undergoing cardiac surgery with cardiopulmonary bypass. The researchers found that patients that underwent cardiopulmonary bypass after the implementation of TEG had a reduction in the use of platelets (1 versus 2.2 units; p<0.0001) and cryoprecipitate (0.7 versus 1.7 units; p<0.0001) units transfused. (9) However, a 2010 non-blinded randomized controlled trial of 31 children undergoing surgery for transposition of the great artery or double outlet right ventricle with the use of TEG found no significant difference in the total platelet and total red blood cell usage between groups (p=0.984 and p=0.109, respectively). (10) Faraoni 2015 reported their experience in the development of a ROTEM-based algorithm. The study retrospectively reviewed the transfusion history of 150 children who underwent elective cardiac surgery with cardiopulmonary bypass in order to refine the algorithm reported in Romlin 2011. (11)

Hass 2014 retrospectively reviewed the effects of a ROTEM-assisted transfusion/coagulation management algorithm in pediatric patients undergoing major craniofacial surgery. Implementation of the algorithm resulted in decreased number of intraoperative transfusions of platelet concentrate (pre-algorithm group 25% compared to post-algorithm group 9%) and total avoidance of FFP transfusions; however the number of transfusions of fibrinogen concentrate increased over time (pre-algorithm group 61% and post-algorithm group 100%). (12) A 2015 retrospective review documented the implementation of a protocol involving a blood sparing technique and the use of TEG in 80 pediatric patients receiving craniofacial surgery. The study concluded that the use of this type of protocol results in decreased intraoperative blood product administration without an effect on postoperative administration. (13) The use of TEG- or ROTEM-guided transfusions in adult and pediatric patients with bleeding was found to reduce the proportion of patients in need of pooled red blood cells (RR 0.86, 95% CI 0.79-0.94; I²=0%;10 studies) and FFP transfusion (RR 0.57, 95% CI 0.33-0.96; I²=86%; 10 studies) in a recent meta-analysis. (6)

Critical Points of Evidence

Evidence Supports

- Use of a goal-directed transfusion algorithm decreases the amount of blood products given after separation from cardiopulmonary bypass. In addition, a ROTEM-guided algorithm can be employed successfully to decrease blood product administration. (2,5-13) — Strong recommendation, low quality evidence
TCH Evidence-Based Outcomes Center
Clinical Algorithm for ROTEM-guided Goal Directed Therapy for Bleeding after Cardiopulmonary Bypass (CPB) in Pediatric Heart Surgery

Begin

Patient with congenital heart disease at risk for post-bypass coagulopathy?
- Yes
  - Confirm availability of all blood products and pharmacologic factors
  - Send baseline ROTEM prior to induction of anesthesia
  - Send ROTEM® upon rewarming to guide post-bypass factor replacement
  - Significant bleeding after protamine?
    - Yes
      - Consider the use of recombinant Factor VIIa 50 mcg/kg unless prothrombin complex concentrate has been given due to high risk of thrombosis
    - No
      - Normal ROTEM®?
        - Yes
          - No treatment
        - No
          - Surgical Reevaluation

- No
  - Low risk for acquired Von Willebrand Syndrome?
    - Yes
      - Test for Von Willebrand Syndrome preoperatively
      - If disease found preoperatively, should plan for Antihemophilic Factor/Von Willebrand Factor Complex (Humate) administration with procedure
    - No
      - Confirm availability of all blood products and pharmacologic factors
      - Age > 6 months and PTT Hepzyme > 50 sec?
        - Yes
          - Send baseline ROTEM prior to induction of anesthesia
          - If Patient > 5kg, fibrinogen concentrate 70 mg/kg
          - If Patient < 5kg, 1 unit cryoprecipitate
        - No
          - If Patient > 5kg, FIBTEM MCF < 9 mm?
            - Yes
              - Administer fibrinogen concentrate or cryoprecipitate
            - No
              - HEPTEM MCF < 50 mm?
                - Yes
                  - Administer 15 mL/kg FFP
                - No
                  - HEPTEM CT > 240 seconds?
                    - Yes
                      - Administer prothrombin complex concentrate (kcentra) 25 units/kg or FFP 15-30 mL/kg
                    - No
                      - Continued Bleeding?
                        - Yes
                          - OFF Algorithm
                        - No
                          - Repeat ROTEM® and follow algorithm steps again

- No
  - OFF algorithm
    - Low risk of post CPB bleeding
      - No ROTEM® needed
References
6. Wikkelso, A., Wetterslev, J., Møller, A., & Afshari, A. Thromboelastography (TEG) or thromboelastometry (ROTEM) to monitor haemostatic treatment versus usual care in adults or children with bleeding. Cochrane Database of Systematic Reviews, 2016(8), CD007871.
Clinical Standards Preparation
This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

ROTEM-Guided Goal Directed Therapy for Bleeding after Cardiopulmonary Bypass in Pediatric Heart Surgery Content Expert Team
Recommendation vetted through Perioperative Blood Transfusion Content Expert Team
Rahul Baijal, MD
Nicole Crews, NP
Frances Garza, RN
Frank Gerow, MD
Lisa Hensch, MD
Lauren Kane, MD
Helena Karlberg, MD
Sandi Lam, MD
Monica Lopez, MD
Vincent Orion, RN
Nihar Patel, MD
Kerri Phelps, RN
Audra Rushing, RN
Jun Teruya, MD
Adam Vogel, MD
Amber Yates, MD

EBP Course Participant and EB OC Support
Erin Gottlieb, MD
Julie Nicholson, RN
Andrea Jackson, MBA, RN, Research Specialist
Charles Macias, MD, MPH, Medical Director

Additional EB OC Support
Tom Burke, Research Assistant
Sherin Titus, Research Assistant
Karen Gibbs, MSN/MPH, RN, Research Specialist
Betsy Lewis, MSN, RN, Research Specialist
Jennifer Loveless, MPH, Research Specialist
Sheesha Porter, MS, RN, Research Specialist
Ellis Arjmand, MD, PhD, MMM, Associate Medical Director
Christina Davidson, MD, MFM, Associate Medical Director
Anne Dykes, MSN, RN, Assistant Director
Kathy Carberry, MPH, RN, Director

No relevant financial or intellectual conflicts to report.

Development Process
This clinical standard was prepared using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:
1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
   - N/A
3. Literature Review of Relevant Evidence
   - Searched: PubMed, Medline, Cochrane Collaborative
4. Critically Analyze the Evidence
   - 1 meta-analysis, 2 randomized controlled trials, and 6 nonrandomized studies
5. Summarize the Evidence
   - Materials used in the development of the guideline, evidence summary, and order sets are maintained in a ROTEM-Guided Goal Directed Therapy for Bleeding after Cardiopulmonary Bypass in Pediatric Heart Surgery evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence
Published clinical guidelines were evaluated for this review using the AGREE II criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate the quality of the evidence.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Quality</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>STRONG</td>
<td>High</td>
<td>Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td>WEAK</td>
<td>Moderate</td>
<td>Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence</td>
</tr>
<tr>
<td></td>
<td>Very Low</td>
<td>Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence</td>
</tr>
</tbody>
</table>

Recommendations
Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the existing evidence.

Approval Process
Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children’s Hospital. Content Expert Teams are involved with every review and update.

Disclaimer
Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the context of the patient’s specific case.
judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient’s family, to make the ultimate judgment regarding care.

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jun 2017</td>
<td>Originally completed</td>
<td></td>
</tr>
</tbody>
</table>