Low Dose versus High Dose Heparinization during Post Cardiotomy ECMO: A Case Control Study

Vanessa Arnold, BS
Mindy M Blackwell, MS, CCP
Perfusion Technology Program
College of Health Sciences
Rush University

Disclosures

I have no relevant financial relationships to disclose.

Introduction

- The use of ECMO is associated with several risks
- Patient related adverse events:
  - Hemorrhage or extremity thrombosis
- Circuit related adverse events:
  - Pump failure, oxygenator failure, or circuit thrombosis
Introduction

Post Cardiotomy ECMO Patients Are Exposed To Two Discrete Non-biological Surfaces

- Initial Assault Occurs On CPB
- Continues while on ECMO
  - SIRS
  - DIC

It is proposed that thromboembolic events in this ECMO population is grossly underestimated (Rastan et al, 2006)

Introduction

- ELSO Recommended Anticoagulation Protocols
  - Bolus 50-100 IU /kg
  - When ACT reaches 300 or below, heparin initiated at 7.5-20 U/kg/hr
  - aPTT 1.5 – 2.5x baseline

ELSO anticoagulation guidelines; 2014
Introduction

- Muehrcke et al (1996) n=23 Males, VA ECMO, 58.4 +/- 35 hrs on ECMO
- 5000 IU heparin at initiation and during low flow
- 30% survival
- Lamarche et al (2010), n=32 Postcardiotomy / eCPR VA ECMO,
- Heparin reversed 1:1 in postcardiotomy patients
- No heparin while on ECMO
- 58% of postcardiotomy patients were weaned from ECMO
- Conclusion: Quadrox D Oxygenator may have mitigated activation of the coagulation cascade

Introduction

- Iwashita et al (2015) 45 postcardiotomy and eCPR patients
- 3000 IU heparin at initiation
- 3 out of 32 fatal bleeding
- 28% survival
- Yeo et al (2015) n = 71 VA ECMO,
- ACT maintained at 140-160sec vs. 180-220sec
- Significantly lower blood product use in the low dose group

Materials & Methods

An Institutional Review Board (IRB) approved, retrospective record review was performed on all status postcardiotomy patients who were placed on extracorporeal membrane oxygenation (ECMO) between the years 2012 and 2015 at Rush University Medical Center.
Materials & Methods

- Heparin was completely reversed with protamine in both groups
- Anticoagulation was measured using the Activated Partial Thromboplastin Time (aPTT)
- Low Dose Group (LD)
  - Patients treated with 5,000 IU heparin bolus during low flow periods
- Conventional Dose Group (CD)
  - Heparin titrated to maintain an aPTT at 1.5 – 2.5 times the baseline, as recommended by ELSO
  - Heparin turned off per MD preferences

Inclusion Criteria
- Age: Adult Patients older than 20 years
- Placed on ECMO within 24 hours of Cardiopulmonary Bypass (CPBP) Procedure

Exclusion Criteria
- V-V ECMO
- Cardiac Surgeries Performed after ECMO Initiation
- Less than 24 hours on ECMO

Lab Values
- Activated Partial Thromboplastin Time (aPTT)
- Blood Urea Nitrogen (BUN)
- Serum Creatinine (sCRT)
- Glomerular Filtration Rate (GFR)
- Aspartate Aminotransferase (AST)
- Alanine Transaminase (ALT)
Materials & Methods

Miscellaneous
- Chest XRAY / Computed Tomography Positive for Thrombus
- Significant Circuit Thrombosis
- Hemofiltration
- Hemodialysis
- Hours on ECMO
- Survival to Decannulation
- Survival to Discharge

Materials & Methods
- Maquet Quadrox Oxygenator
- Centrimag Centrifugal Pump & Revolution Centrifugal Pump (post September 2015)
- Carmeda Coated Tubing
- Cannulation: Central or Peripheral

Statistical Analysis
- A retrospective chart review was undertaken as an exploratory pilot without a priorn sample size calculation based on a primary endpoint
- Both groups were divided and sorted by:
  1. Gender
  2. BSA
  3. Hours on ECMO
- Matched Cases were analyzed utilizing the Student’s t test
Null Hypothesis

\( H_0: \) Patients treated with low dose heparin therapy during ECMO for post cardiotomy failure will have the same risk for developing thrombotic organ dysfunction as those patients treated with conventional heparin therapy.

\( H_A: \) Patients treated with low dose heparin therapy during ECMO for post cardiotomy failure will have an increased risk for developing thrombotic organ dysfunction as those patients treated with conventional heparin therapy.

Results

Demographic Variables

<table>
<thead>
<tr>
<th></th>
<th>Conventional Dose (19)</th>
<th>Low Dose (16)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age yrs Mean ± SD</td>
<td>60 ± 14</td>
<td>62 ± 12</td>
<td>0.421</td>
</tr>
<tr>
<td>BSA m² Mean ± SD</td>
<td>2.0 ± 0.2</td>
<td>2.1 ± 0.2</td>
<td>0.237</td>
</tr>
<tr>
<td>Female n(%)</td>
<td>9 (47%)</td>
<td>5 (31%)</td>
<td>0.332</td>
</tr>
<tr>
<td>Surgery Type n(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>6 (32%)</td>
<td>1 (6%)</td>
<td></td>
</tr>
<tr>
<td>VALVE</td>
<td>6 (32%)</td>
<td>9 (56%)</td>
<td></td>
</tr>
<tr>
<td>CABG / VALVE</td>
<td>2 (11%)</td>
<td>2 (13%)</td>
<td></td>
</tr>
<tr>
<td>HeartTransplant</td>
<td>2 (11%)</td>
<td>1 (6%)</td>
<td></td>
</tr>
<tr>
<td>OTHER</td>
<td>3 (16%)</td>
<td>3 (19%)</td>
<td></td>
</tr>
</tbody>
</table>

ECMO Events

- Discharged: 4 (19), 5 (16)
- Detach Lines: 5, 3
- Cath Change: 8, 7
- O2 in Circuit: 16, 14
- Neo-Cath Need: 30, 29
- HeartBiff: 14, 9
- Mechanical: 7, 7

There were no significant differences in ECMO Events.
Results

There was a significant difference in time spent on ECMO \( p < 0.05 \)

Paired Samples T Test

<table>
<thead>
<tr>
<th>Change in</th>
<th>Conventional Dose</th>
<th>Low Dose</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs) Mean ±SD</td>
<td>53 ± 11</td>
<td>54 ± 11</td>
<td>0.93</td>
</tr>
<tr>
<td>BSA (m(^2)) Mean ±SD</td>
<td>2.1 ± 0.25</td>
<td>2.1 ± 0.25</td>
<td>0.783</td>
</tr>
<tr>
<td>Hours on ECMO Mean ±SD</td>
<td>174 ± 96</td>
<td>123 ± 112</td>
<td>0.024</td>
</tr>
<tr>
<td>sCRT (mg/dL) Mean ±SD</td>
<td>-0.23 ± 0.49</td>
<td>-0.21 ± 1.37</td>
<td>0.951</td>
</tr>
<tr>
<td>BUN (U/L) Mean ±SD</td>
<td>8.89 ± 24.51</td>
<td>4.44 ± 17.13</td>
<td>0.549</td>
</tr>
<tr>
<td>tBilirubin (U/L) Mean ±SD</td>
<td>4.42 ± 8.80</td>
<td>4.83 ± 13.99</td>
<td>0.949</td>
</tr>
<tr>
<td>AST (mg/dL) Mdn±SD</td>
<td>-1333 ± 5492</td>
<td>1201 ± 3642</td>
<td>0.268</td>
</tr>
<tr>
<td>ALT (mg/dL) Mdn±SD</td>
<td>-177 ± 357 mg/dL</td>
<td>356 ± 1076 mg/dL</td>
<td>0.316</td>
</tr>
<tr>
<td>GFR Mean ±SD</td>
<td>0.00 ± 0.866</td>
<td>-0.33 ± 1</td>
<td>0.282</td>
</tr>
</tbody>
</table>

Results

![Graph showing change in sCRT and BUN](image)
### Results

<table>
<thead>
<tr>
<th>Change in tBilirubin (U/L)</th>
<th>Change in AST (mg/dL)</th>
<th>Change in ALT (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.9</td>
<td>4.83</td>
<td>1201</td>
</tr>
<tr>
<td>4.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Conventional Dose
- Low Dose

### Conclusions

- No significant difference in organ function
- Small Sample Size
- Use of Hemoconcentration and Hemodialysis may have effected the outcomes
- Heparin start time varied from 0 - 93 hours and heparin titration was adjusted throughout the treatment

### Sources


Sources


