Can low preoperative albumin levels predict heparin resistance?

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Conflicts of interest

- None to report
Outline

- Introduction
- Materials and Methods
- Results – Hospital A, Hospital B and Combined
- Discussion
- Limitations
- Acknowledgements
Introduction

- Incidence of Heparin Resistance (HR) reported at 15-20% \(^4\)
- HR is usually explained by ATIII deficiency but is often multifactorial \(^2\)
- Factors linked to acquired ATIII deficiency are malnutrition and heparin therapy \(^5\)
- Albumin levels, as well as total protein levels, are indicators of nutrition status \(^3\)
- Can a low preoperative albumin accurately predict heparin resistance?
Materials and Methods

- Prospective, controlled, observational study
- September 2016 – March 2017
- Comparison of patient populations at two large hospital centers
- Pre-bypass heparin anticoagulation administration and protocol
- Data collection included both categorical and continuous patient variables
Exclusion and Inclusion Criteria

Criteria excluded patient populations with existing anticoagulation complications

**Exclusion Criteria**
- Contraindication for heparin
- Documented clotting disorders
- Actively infected
- Deep Vein Thrombosis
- Heart and lung transplants
- Sickle cell disorder
- Hepatic disease

**Inclusion Criteria**
- Adults aged 25 years and older
- CABG, valve or combination
- Use of cardiopulmonary bypass
- Use of heparin therapy
### Categorical Variables

<table>
<thead>
<tr>
<th>Categorical Variables</th>
<th>Cardiovascular Disease</th>
<th>Medical Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Aortic Stenosis</td>
<td>ASA therapy</td>
</tr>
<tr>
<td></td>
<td>Mitral Regurgitation</td>
<td>clopidogrel therapy</td>
</tr>
<tr>
<td></td>
<td>Tricuspid Regurgitation</td>
<td>heparin therapy</td>
</tr>
<tr>
<td></td>
<td>Valvular disease</td>
<td>coumadin therapy</td>
</tr>
<tr>
<td></td>
<td>Pulmonary Hypertension</td>
<td>debatrigan therapy</td>
</tr>
<tr>
<td></td>
<td>Atrial dysrhythmia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Coronary Artery Disease</td>
<td></td>
</tr>
</tbody>
</table>

### Continuous Variables

<table>
<thead>
<tr>
<th>Continuous Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>BSA (m²)</td>
</tr>
<tr>
<td>WBC count, total (x 10⁹/L)</td>
</tr>
<tr>
<td>PLT (x 10⁹/L)</td>
</tr>
<tr>
<td>PT (sec)</td>
</tr>
<tr>
<td>PTT (sec)</td>
</tr>
<tr>
<td>PT-INR</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
</tr>
<tr>
<td>Protein (g/dL)</td>
</tr>
<tr>
<td>Cr (μmol/L)</td>
</tr>
</tbody>
</table>

Data collected was separated based on statistical variable.
Results – Hospital A

<table>
<thead>
<tr>
<th>Variable</th>
<th>NHR (n=25)</th>
<th>HR (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin, average (g/dL)</td>
<td>4.0</td>
<td>4.0</td>
</tr>
<tr>
<td>ACT, average (sec)</td>
<td>466</td>
<td>357</td>
</tr>
<tr>
<td>Initial heparin, average (units)</td>
<td>20280.0</td>
<td>18000.0</td>
</tr>
<tr>
<td>Total heparin, average (units)</td>
<td>30360.0</td>
<td>34208.3</td>
</tr>
</tbody>
</table>

NHR – non-Heparin Resistant; HR – Heparin Resistant; ACT – Activated Clotting Time

- On average, the HR population did not exhibit a low preoperative albumin level
- On average, the HR population did exhibit a suboptimal pre-bypass ACT and a higher total heparin dose
## Results – Hospital B

<table>
<thead>
<tr>
<th>Variable</th>
<th>NHR (n=16)</th>
<th>HR (n=1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin, average (g/dL)</td>
<td>4.4</td>
<td>4.4</td>
</tr>
<tr>
<td>ACT, average (sec)</td>
<td>515</td>
<td>315</td>
</tr>
<tr>
<td>Initial heparin, average (units)</td>
<td>25000.0</td>
<td>19000.0</td>
</tr>
<tr>
<td>Total heparin, average (units)</td>
<td>34750.0</td>
<td>35000.0</td>
</tr>
</tbody>
</table>

NHR – non-Heparin Resistant; HR – Heparin Resistant; ACT – Activated Clotting Time

- On average, the HR population did not exhibit a low preoperative albumin level.
- On average, the HR population did exhibit a suboptimal pre-bypass ACT and a higher total heparin dose.
Results – Comparative

Welch Two Sample t-test, Hospital A vs. B

<table>
<thead>
<tr>
<th>Variable</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB ACT</td>
<td>1.14970</td>
<td>0.00575</td>
</tr>
</tbody>
</table>

Average initial CPB ACT:
Hospital A – 411s
Hospital B – 415s

- Initial CPB ACT as the comparative variable in a Welch Two Sample t-test, significance was demonstrated
- Significance likely due to difference in anticoagulation protocols between Hospital A and Hospital B

*CPB – Cardiopulmonary Bypass; ACT – Activated Clotting Time; CI – Confidence Interval*
Results – Combined

Summary and comparison of statistically significant variables of combined hospital data.

<table>
<thead>
<tr>
<th>Significant Variables</th>
<th>NHR (n=41)</th>
<th>HR (n=13)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA therapy</td>
<td>54%</td>
<td>31%</td>
<td>0.014</td>
</tr>
<tr>
<td>WBC count, total (x 10^9/L)</td>
<td>8.22</td>
<td>6.75</td>
<td>0.023</td>
</tr>
<tr>
<td>Protein (g/dL)</td>
<td>7.0</td>
<td>6.7</td>
<td>0.008</td>
</tr>
<tr>
<td>Heparin (units), initial</td>
<td>20951.2</td>
<td>18076.9</td>
<td>0.006</td>
</tr>
<tr>
<td>Protamine (mg)</td>
<td>155</td>
<td>154</td>
<td>0.010</td>
</tr>
</tbody>
</table>

NHR – non-Heparin Resistant; HR – Heparin Resistant; ASA – aspirin; WBC – White Blood Count

Neither hospital center had statistically significant variables when analyzed separately, so populations were combined and analyzed. The result were five significant variables.
Discussion

- **Significant variables**
  - **ASA therapy**
    - most common anticoagulant therapy for both HR and NHR, as well as in cardiac surgical patient populations
  - **WBC count**
    - NHR > HR population; unexpected; averages were not in abnormal range
  - **Protamine**
    - HR received less on average, despite higher total heparin dose
  - **Protein level**
    - HR < NHR population; averages were not in abnormal range
  - **Initial heparin dose**
    - NHR > HR population; anticoagulation protocols
Discussion, continued

- Protein level emerged with significance
  - Role of globulin just as important as albumin in basic health of patient
  - Globulins $\rightarrow$ gammaglobulins $\rightarrow$ mostly immunoglobulins

- WBC count
  - Despite excluding endocarditis; WBC count still a factor

- Significant variables not reported in existing literature

- Variability in the study designs and exclusion criteria in existing literature
Limitations

- Small study population lacked statistical power
  - Focus on single hospital center performing high volume of CABG
- Utilize pump heparin as a variable independent of initial heparin dose
- High dimensional data set
  - Number of variables was greater than observational data set.
  - Small patient population and greater number of continuous and categorical variables limited statistical power.
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  Quinnipiac University
References


