**Hypoalbuminemia: Relationship with Length of Hospital Stay and Acute Adverse Outcomes after Myocardial Infarction**

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**Albumin Functions**

- **Transportation of molecules**
  - FFA
  - Calcium
  - Steroid hormones
  - Thyroxin
  - Bilirubin
  - Drugs such as aspirin, NSAIDs, warfarin, sulfonamides, penicillin, and digoxin
- **Oncotic pressure**
- **Negative acute phase protein**
- **Antioxidant**

- **Inhibits key components of atherogenesis and ischemia**
  - Endothelial apoptosis
  - Platelet aggregation
  - TNF-α-induced upregulation of VCAM-1 expression
- **Modulates arachidonic acid release and membrane fluidity**
- **Decreases blood viscosity**
- **Promotes vasodilation by providing a reservoir for nitric oxide**
- **Promotes wound healing**
Control of Albumin Level

- Hypoalbuminemia seen in:
  - Kidney disease: ↑excretion + dilution
  - Heart failure: ↓synthesis + dilution
  - Liver disease: ↓synthesis
  - Malnutrition: ↓dietary intake (hypoalbuminemia only in severe cases)\textsuperscript{12,13}
  - Inflammation: ↑catabolism + sequesters at site\textsuperscript{1}

Established Literature

- Hypoalbuminemia associated with adverse outcomes in kidney disease, chronic heart failure, wound repair, and acute coronary syndromes\textsuperscript{2, 11, 14-19}
Purpose of Our Study

• Examine the relationship between albumin levels and acute outcomes after MI
  • Length of hospital stay
  • Acute heart failure
  • Cardiogenic shock
  • Reinfarction
  • Death

• Study association of hypoalbuminemia with several patient characteristics (lab values, diagnoses, etc)

Methods

• Based on framework used in Hartopo, AB 2010
• Study type
  • Retrospective analysis

• Study Population
  • Men and women ages 35 – 75 presenting with an acute myocardial infarction
Methods

• Criteria
  • Men and Women aged 35 through 75
  • Measured serum albumin measured within 24 hours of admission
  • Acute myocardial infarction ICD-9 410
• Exclusions
  • CKD stages III-V, cirrhosis, CID, cancer, venous thromboembolism
  • Patients with acute conditions such as stroke, infection, sepsis
• Variables
  • Age, gender, zipcode, significant tobacco use history, BMI, systolic and diastolic BP, Pulse, BUN, Cr, Hgb, Hct, AST, ALT, glucose
  • Previous diagnosis of HTN, DM, AMI
  • ST or non ST elevation, albumin, adverse outcomes within 30 days (acute heart failure, cardiogenic shock, reMI, death), and length of stay

Methods

• Analysis
  • SAS software V9.2 (SAS institute, Cary, NC, USA)
  • Means (standard deviations) or median (range) for skewed distribution
  • Chi-square tests or Fischer’s exact tests were used to analyze differences between groups for categorical variables
  • Wilcoxon signed-rank test for continuous variables
  • P-values < 0.05 were considered significant
Results

- **Cases**: 200 patients were eligible
- 39 patients hypoalbuminemic

| Table I. Characteristics of Patients According to Serum Albumin Level |
|-------------------------------------------------|-----------------|-----------------|-----------------|---|
| Characteristic                                   | All patients (n=200) | Hypoalbuminemia (n=39, 20%) | Normoalbuminemia (n=161, 80%) | P  |
| Sex, n (%)                                       |                  |                          |                             |   |
| Male                                             | 143 (71.5)       | 24 (62)                  | 119 (74)                   | 0.12 |
| Female                                           | 57 (28.5)        | 15 (38)                  | 42 (26)                    |     |
| Age, year, mean ± SD                             | 60.4 (9.4)       | 61.8 ± 8.6               | 60 ± 9.6                   | 0.42 |
| Residence, n (%)                                 | 62 (31)          | 8 (21)                   | 54 (34)                    | 0.11 |
| Urban                                            |                  |                          |                             |     |
| Rural                                            | 138 (69)         | 31 (80)                  | 107 (67)                   |     |
### Table I. Characteristics of Patients According to Serum Albumin Level

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All patients (n=200)</th>
<th>Hypoalbuminemia (n=39, 20%)</th>
<th>Normoalbuminemia (n=161, 80%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical history n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>64 (32)</td>
<td>16 (41)</td>
<td>48 (30)</td>
<td>0.18</td>
</tr>
<tr>
<td>Hypertension</td>
<td>146 (73)</td>
<td>34 (87)</td>
<td>112 (70)</td>
<td>0.03</td>
</tr>
<tr>
<td>Previous MI</td>
<td>35 (17.5)</td>
<td>9 (23)</td>
<td>26 (16)</td>
<td>0.31</td>
</tr>
<tr>
<td>Smoker</td>
<td>132 (66)</td>
<td>26 (67)</td>
<td>106 (66)</td>
<td>0.92</td>
</tr>
<tr>
<td>BMI, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.77</td>
</tr>
<tr>
<td>Normal</td>
<td>36 (18.5)</td>
<td>6 (16)</td>
<td>30 (19)</td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>63 (32.3)</td>
<td>14 (37)</td>
<td>49 (31)</td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>96 (49.2)</td>
<td>18 (47)</td>
<td>78 (50)</td>
<td></td>
</tr>
<tr>
<td>Clinical, mean ± SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP</td>
<td>133.1 ± 26.4</td>
<td>130.0 ± 24.3</td>
<td>133.9 ± 26.9</td>
<td>0.35</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>77.5 ± 16.0</td>
<td>74.0 ± 17.9</td>
<td>78.3 ± 15.4</td>
<td>0.11</td>
</tr>
<tr>
<td>Heart rate</td>
<td>79.8 ± 21.8</td>
<td>79.3 ± 22.2</td>
<td>80.0 ± 21.7</td>
<td>0.98</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>14.0 ± 2.3</td>
<td>16.7 ± 26.6</td>
<td>16.6 ± 15.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>41.0 ± 6.5</td>
<td>37.3 ± 7.0</td>
<td>41.9 ± 6.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>3.8 ± 0.5</td>
<td>3.1 ± 0.3</td>
<td>4.0 ± 0.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Creatinine mg/dL</td>
<td>1.1 ± 1.0</td>
<td>1.1 ± 0.4</td>
<td>1.1 ± 1.1</td>
<td>0.057</td>
</tr>
<tr>
<td>BUN, g/dL</td>
<td>18.6 ± 10.2</td>
<td>23.0 ± 15.5</td>
<td>17.6 ± 8.2</td>
<td>0.04</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>162.0 ± 83.4</td>
<td>170.3 ± 84.5</td>
<td>160.0 ± 83.2</td>
<td>0.55</td>
</tr>
<tr>
<td>Laboratory, median (range)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT</td>
<td>34 (3897)</td>
<td>26.5 (3896)</td>
<td>34.0 (1092)</td>
<td>0.56</td>
</tr>
<tr>
<td>AST</td>
<td>40 (1567)</td>
<td>31.0 (175)</td>
<td>41.0 (1561)</td>
<td>0.35</td>
</tr>
<tr>
<td>Diagnosis, n(%)</td>
<td></td>
<td></td>
<td></td>
<td>0.46</td>
</tr>
<tr>
<td>STEMI</td>
<td>87 (42.5)</td>
<td>19 (49)</td>
<td>68 (42)</td>
<td></td>
</tr>
<tr>
<td>NSTEMI</td>
<td>113 (56.5)</td>
<td>20 (51)</td>
<td>93 (58)</td>
<td></td>
</tr>
</tbody>
</table>
Table II. Adverse Outcomes within 30 days According to Serum Albumin Level

<table>
<thead>
<tr>
<th>Adverse Outcome</th>
<th>Hypoalbuminemia (n=39, 20%)</th>
<th>Normoalbuminemia (n=161, 80%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, n (%)</td>
<td>2 (5)</td>
<td>6 (4)</td>
<td>0.66</td>
</tr>
<tr>
<td>Non-fatal outcomes, n (%)</td>
<td>19 (49)</td>
<td>37 (23)</td>
<td></td>
</tr>
<tr>
<td>Acute heart failure</td>
<td>13 (34)</td>
<td>26 (16)</td>
<td>0.01</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>5 (13)</td>
<td>10 (6)</td>
<td>0.11</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>1 (3)</td>
<td>1 (1)</td>
<td>0.23</td>
</tr>
<tr>
<td>Total adverse outcomes, n (%)</td>
<td>21 (54)</td>
<td>43 (27)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Chart 1. Adverse outcomes according to serum albumin level

- Hypoalbuminemia
- Normoalbuminemia
Table III. Length of Stay According to Serum Albumin Level

<table>
<thead>
<tr>
<th></th>
<th>Hypoalbuminemia (n=39, 20%)</th>
<th>Normoalbuminemia (n=161, 80%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of Stay (days), mean ± SD</td>
<td>5.9 ± 2.56</td>
<td>4.8 ± 7.8</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Chart II. Length of hospital stay according to serum albumin level

- Hypoalbuminemia
- Normoalbuminemia

Length of Stay (mean)
Discussion

• Patients with low serum albumin on admission for AMI were significantly more likely to experience adverse outcomes
  • Same results as Hartopo et al found in 2010
  • Acute heart failure being most significant adverse outcome
  • Length of stay significantly increased – rising cost of healthcare

• Albumin’s role is so diverse
  • Difficult to say whether decrease due to advanced disease (inflammation, malnutrition) or another process

Discussion

• Hypertension
  • Mechanical endothelial damage – extravasation of albumin?
  • Inflammatory State
  • Dilutional?

• Hct/Hgb
  • Proinflammatory cytokines affect multiple stages of erythroid development
  • Dilutional?

• BUN and Cr (not statistically significant)
  • Dilutional – somewhat expected
Discussion

• BMI
  • No significant relationship
  • Expect increased adverse outcomes with higher BMI
  • Aronson et al demonstrated U shaped curve with AMI 26.5-27.9 having lowest mortality
  • We combined both overweight and obese groups

Limitations

• Small sample size – cannot draw any universal conclusions
• Predominantly Caucasian and relatively rural population
• Retrospective study; causal relationship cannot be assumed
  • Many confounding variables that still remain even after exclusions
  • Hypoalbuminemia may simply be marker for underlying pathologic process leading to these adverse outcomes and longer length of hospital stay
• Both hypoalbuminemia and MI are common occurrences – it is challenging to conclude a meaningful correlation
• Extreme values in our data uncorrected due to time constraints
**Future Studies and Implications**

- Larger sample size and a more diverse population
- Examine the differences between different ethnicities
- Prospective study
- Exclude patients with elevated BUN and Creatinine eliminating renal causes for hypoalbuminemia, hypertension, and low hemoglobin and hematocrit
- Study relationship between hypoalbuminemia and adverse outcomes/length of hospital stay according to which treatment was utilized
- Studies have shown that treatment of hypoalbuminemia with albumin supplementation does not prevent these adverse outcomes – further research is needed to find possible treatment options

**Conclusions**

- Hypoalbuminemia upon admission for AMI associated with:
  - Adverse outcomes (acute heart failure), length of hospital stay
  - HTN
  - Increased BUN
  - Decreased Hgb/Hct
- Predictor of short term complications – not mortality
- Useful as costs of healthcare rise to help predict those patients that will require increased resources
Acknowledgements

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Questions?
References


22. Granger DN, Senchenkova E. 2010; .


