How can statins and other medical treatment decrease the amputation and major adverse limb event rates after revascularizations for CLI

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Disclosures
• None

Critical Limb Ischemia (CLI)
• Most advanced form of PAD
• Defined by presence of ischemic rest pain, non-healing wounds/ulcerations or tissue loss/gangrene
• CLI is only seen in a small percentage of PAD patients
• But overall mortality is near 50% at 5 years and 70% at 10 years

Guideline Recommended Therapies
• American College of Cardiology (ACC) and American Heart Association (AHA) guidelines for PAD management (2012):
  ▫ Tobacco cessation
  ▫ Aspirin
  ▫ Statins
  ▫ Angiotensin-converting enzyme (ACE) inhibitors

Background
• A previous study by Armstrong et al (2014) looked at 739 patients with PAD who received diagnostic or interventional lower-extremity angiography
• The study found that patients who received all 4 guideline driven therapies had decreased major adverse cardiovascular events (MACE) and major adverse limb events (MALE) at 3 years post angiogram compared to patients with less than 4 guideline therapies

Study Rationale
• CLI patients are at an increased risk of mortality, myocardial infarction and stroke
• The extent to which guideline-driven therapies decreases the risk of these adverse events is not well defined in patients with CLI
Objective

- To determine the rates of ACC/AHA guideline adherence in patients with CLI at CAMC
- To determine the effect of guideline driven therapy on rates of MACE (MI, stroke and death) and amputation at 30 days and 1 year in CLI patients

Methods

- Retrospective study
- Inclusion criteria:
  - Patients 18 years old and older, whose CLI was managed by CAMC’s Vascular Center of Excellence (VCOE) or received a diagnostic or interventional procedure at CAMC’s Circulatory Dynamics Lab (CDL) between 1/1/2010 and 12/31/2014
  - Had an ICD 9 diagnosis code for rest pain, ulcer, or gangrene
  - Had medication records in chart
  - Had a minimum follow-up of 1 year

Methods-Data Collection

- Subject characteristics
  - Demographics
  - BMI
  - Comorbidities
  - Disease classification
  - Rutherford classification
  - ABI
- Lower extremity vascular procedures performed
- Guideline recommended therapies at discharge
  - Aspirin/antiplatelet
  - Plavix
  - Statin
  - ACE inhibitor
  - Tobacco use
- Date of last follow-up with CAMC

Methods

- Outcomes examined at 30 days and 1 year following initial CDL or VCOE visit:
  - MI
  - Stroke
  - All cause mortality
  - Amputation
    - Minor: below the ankle
    - Major: above the ankle

Data Analysis

- Performed using SPSS version 19.0
- Descriptive statistics were performed
- Continuous variables were compared using t-test
- Categorical variables were compared using Chi-square or Fisher’s exact test, when appropriate
- A p-value < 0.05 was considered statistically significant

Methods

- Due to time constraints, we examined consecutive patients with CLI receiving procedures in CAMC’s CDL from 1/1/2010 to 11/3/2011
- 255 patient charts were reviewed, 62 excluded

<table>
<thead>
<tr>
<th>Reason for Exclusion</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower extremity procedure not performed</td>
<td>15</td>
</tr>
<tr>
<td>Not classified as CLI</td>
<td>18</td>
</tr>
<tr>
<td>No medication list on record</td>
<td>3</td>
</tr>
<tr>
<td>No follow-up</td>
<td>17</td>
</tr>
<tr>
<td>Death/palliative care prior to discharge</td>
<td>9</td>
</tr>
</tbody>
</table>

- 193 patients included in analyses
Patient Demographics

- Gender
  - Male: 102, 52.8%
  - Female: 91, 47.2%
- Age
  - Mean: 67.77 ± 12.80
  - Pre-procedure ABI
    - Median: 0.53 [IQR: 0.35-0.74]
    - N = 156

Rutherford Classification:

- Stage 5 - Major Tissue Loss 75%
- Stage 4 - Minor Tissue Loss 25%

Comorbidities

- Percent of Patients
  - Obese: 37%
  - MI: 14%
  - Stroke: 30%
  - CAD: 58%
  - COPD: 24%
  - CKD: 19%
  - CHF: 0%

Guideline Driven Therapies

- Therapy Type
  - Aspirin/Anti-platelet: 61%
  - Statin: 61%
  - ACEi/ARB: 28%

- Number of Therapies
  - 0: 12%
  - 1: 10%
  - 2: 26%
  - 3: 18%
  - 4: 20%

Major Adverse Cardiovascular Events (MACE) at 30 Days

- All patients
  - MACE: 5.7%
  - MI: 1.0%
  - Stroke/TIA: 1.6%
  - Death: 3.1%

- Less than 4 guideline-driven therapies
  - MACE: 5.7%
  - MI: 1.3%
  - Stroke/TIA: 1.3%
  - Death: 3.2%

- 4 guideline-driven therapies
  - MACE: 5.7%
  - MI: 0%
  - Stroke/TIA: 2.9%
  - Death: 2.9%

- P values
  - MACE: 1.00
  - MI: 1.00
  - Stroke/TIA: 0.45
  - Death: 1.00

MACE vs. Number of Guideline-driven Therapies

- MACE at 30 days
  - P = 0.35

- No MACE
  - MACE=5 days
  - % of patients
    - 0: 11%
    - 1: 9%
    - 2: 15%
    - 3: 75%

- MACE at 1 year

<table>
<thead>
<tr>
<th>Total</th>
<th>Less than 4 guideline-driven therapies</th>
<th>4 guideline-driven therapies</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE</td>
<td>27.2%</td>
<td>27.5%</td>
<td>28.6%</td>
</tr>
<tr>
<td>MI</td>
<td>5.7%</td>
<td>5.1%</td>
<td>8.6%</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>4.1%</td>
<td>3.8%</td>
<td>5.7%</td>
</tr>
<tr>
<td>Death</td>
<td>20.7%</td>
<td>21.5%</td>
<td>17.1%</td>
</tr>
</tbody>
</table>
MACE vs. Number of Guideline-driven Therapies

<table>
<thead>
<tr>
<th>Number of Therapies</th>
<th>MACE at 1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>No MACE</td>
<td>18%</td>
</tr>
<tr>
<td>1 guideline therapy</td>
<td>44%</td>
</tr>
<tr>
<td>2 guideline therapies</td>
<td>19%</td>
</tr>
<tr>
<td>3 guideline therapies</td>
<td>36%</td>
</tr>
<tr>
<td>4 guideline therapies</td>
<td>5%</td>
</tr>
</tbody>
</table>

\[ p = 0.68 \]

Amputations at 30 days

<table>
<thead>
<tr>
<th>Category</th>
<th>Total</th>
<th>Less than 4 guideline-driven therapies</th>
<th>4 guideline-driven therapies</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Amputations</td>
<td>5.7%</td>
<td>6.3%</td>
<td>2.9%</td>
<td>0.69</td>
</tr>
<tr>
<td>Major Amputations (ankle or above)</td>
<td>2.5%</td>
<td>0%</td>
<td>2.1%</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Amputations at 1 year

<table>
<thead>
<tr>
<th>Category</th>
<th>Total</th>
<th>Less than 4 guideline-driven therapies</th>
<th>4 guideline-driven therapies</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Amputations</td>
<td>27.5%</td>
<td>27.2%</td>
<td>28.6%</td>
<td>1.00</td>
</tr>
<tr>
<td>Major Amputations (ankle or above)</td>
<td>15.2%</td>
<td>14.3%</td>
<td>15.0%</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Discussion

- Less than 20% of the study patients adhered to all 4 guideline-driven therapies
- No significant difference in MACE or amputation rates at 30 days and 1 year were seen between patients following all 4 guideline-driven therapies vs. those who followed less than 4 therapies

Our study’s findings did not agree with those of Armstrong et al showing a therapy benefit
- This may be due to:
  - The previous study looked at patients with PAD where our study focused on patients with the more severe disease state of CLI
  - Our study also looked at outcomes at 1 year post procedure rather than 3 years
  - The Armstrong study had 32% of patients receiving all 4 guidelines whereas our cohort had 18%. The low percentage of patients adhering all 4 guideline also made the sample size of that cohort small
  - Our study also only looked at discharge medications while Armstrong required both patient reporting pre-procedure and physician prescribing for adherence
  - We also excluded patients who died during their hospital stay

Limitations

- Retrospective study
- Small sample size, especially in the all 4 Guideline Therapies cohort
- Narrow study window
  - Viewing outcomes further than 1 year may provide a better understanding of the long-term effects of following guideline therapies
- Medication compliance
  - Patients may have been discharged with certain medications but lack of compliance could have altered the results
- Medication compliance
- Used discharge medications vs. home medications at time of admission.
- Excluded patients who died during admission of procedure
- Selection bias
  - Patients with severe coronary disease are more likely to already be on all 4 guideline-driven therapies
Conclusion

• No significant benefit on MACE and amputation rates was seen with using all 4 guideline-driven therapies at 1 year in patients with CLI.

• However, we still believe that following the guideline-driven therapies (aspirin, statins, ACE inhibitors, and smoking cessation) would be the best option for the patients who have developed such a severe form of PAD.