Update on the BEST-CLI Trial

Matthew T. Menard, M.D
Brigham & Women’s Hospital
Boston, Massachusetts
Disclosure

Speaker name: Matthew T. Menard

☐ I do not have any potential conflict of interest
A Growing Problem

- Diabetes
- Obesity
- Metabolic Syndrome
- Elderly
- PAD/CLI
Medicare expenditure on CLI > $4 billion

(CHF = $3.9B, Cerebrovascular disease = $3.7B)

- 90% inpatient care

- $1,700 per patient (>2X avg beneficiary)

- 3% of total Medicare budget (THR = 0.9%, TKR 1.7%)
The Exponential Rise in Health Care Expenditures

Federal Spending on Medicare and Medicaid
As budget negotiations continue, lawmakers and White House officials are considering ways to slow the growth of federal spending on Medicare and Medicaid, which is projected to continue rising at a rapid pace.

Endovascular-first approach is not associated with worse amputation-free survival in appropriately selected patients with critical limb ischemia.

Karan Garg, MD, Patrick A. Kaszubs, BS, Rameen Moridzadeh, BS, Caron B. Rockman, MD, Mark A. Adelman, MD, Thomas S. Maldonado, MD, Frank J. Veith, MD, and Firas F. Mussa, MS, MD, New York, NY.
Medicare & Medicaid Is Talking About “Value”

CENTERS FOR MEDICARE & MEDICAID SERVICES

Roadmap for Implementing Value Driven Healthcare in the Traditional Medicare Fee-for-Service Program
Insurers Are Talking About “Value”

Value-Based Benefits

Because your plan includes Value-Based Benefits, if you are at risk for cardiovascular disease (taking high blood pressure medications in combination with high cholesterol medications) or have asthma, diabetes, or coronary artery disease (CAD), or depression associated with any of these conditions, your coverage can help you more affordably manage your care. Also, if you are a current smoker and are ready to quit, your Value-Based Benefits coverage gives you access to no-cost smoking cessation programs and medications (when prescribed by your doctor).

Fill your prescriptions through our convenient, low-cost mail service pharmacy, and you’ll pay the same copayment for a three-month supply of certain Tier 1 and Tier 2 medications as you would for a one-month supply from a retail pharmacy. This is a savings of up to eight copayments per year for each medication.

Your spouse and covered dependents are also eligible for these savings.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Value-Based Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>Pay less for a three-month supply of certain antiasthmatic medications through the mail service pharmacy. This will help you afford your medications and stay out of the emergency room.</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Pay less for a three-month supply of certain medications and supplies to help manage blood sugar when you use the mail service pharmacy to fill prescriptions. There are no copayments for the first two office visits in each calendar year for certain diabetic monitoring care. You can use those two office visits for diabetes evaluation and management, diabetic foot care, and diabetic eye exams.</td>
</tr>
</tbody>
</table>
Employers (as Payers) Are Talking About “Value”

The Leapfrog Group
Informing Choices. Rewarding Excellence.
Getting Health Care Right.

About Us

Mission Statement
To trigger giant leaps forward in the safety, quality and affordability of health care by:
- Supporting informed healthcare decisions by those who use and pay for health care; and,
- Promoting high-value health care through incentives and rewards.

The Leapfrog Group is a voluntary program aimed at mobilizing employer purchasing power to alert America’s health industry that big leaps in health care safety, quality and customer value will be recognized and rewarded. Among other initiatives, Leapfrog works with its employer members to encourage transparency and easy access to health care information as well as rewards for hospitals that have a proven record of high quality care.
What Is “Value” in Health Care?

Value = dollars spent per health-related outcome

Which **FIRST** Revascularization **Option** in CLI Has the BEST **Value**?

VS

Bypass Surgery

VS

Endovascular Therapy (Endo)
What is current state of evidence
SPECIAL ARTICLE

THE USE OF ANGIOPLASTY, BYPASS SURGERY, AND AMPUTATION IN THE MANAGEMENT OF PERIPHERAL VASCULAR DISEASE

SEAN R. TUNIS, M.D., M.S.C., ERIC B. BASS, M.D., M.P.H., AND EARL P. STEINBERG, M.D., M.P.P.

Abstract  Background. Percutaneous transluminal angioplasty has been adopted widely as a treatment for patients with peripheral vascular disease of the lower extremities. However, the effect of this procedure on the overall management of peripheral vascular disease and on the outcomes of patients has not been clearly delineated. In particular, it is not known whether angioplasty has replaced other treatments for peripheral vascular disease.

Methods. To assess the extent to which angioplasty is used and the associated changes in the surgical management of peripheral vascular disease of the lower extremities, we used data on hospital discharges in Maryland to identify all angioplasty procedures, peripheral bypass operations, and lower-extremity amputations performed for peripheral vascular disease in Maryland hospitals between 1979 and 1989.

Results. We estimate that from 1979 to 1989 the annual rate of percutaneous transluminal angioplasty for peripheral vascular disease of the lower extremities, adjusted for age and sex, rose from 1 to 24 per 100,000 Maryland residents (P<0.0001 by linear regression). Despite this increase in the use of angioplasty, the adjusted annual rate of peripheral bypass surgery also rose substantially, from 32 to 65 per 100,000 (P<0.001), whereas the adjusted annual rate of lower-extremity amputation remained stable at about 30 per 100,000. Total charges for hospitalizations during which a peripheral revascularization procedure was performed increased from $14.7 million in 1979 (in 1989 dollars) to $30.5 million in 1989.

Conclusions. In Maryland, the adoption of percutaneous transluminal angioplasty for peripheral vascular disease of the lower extremities has been associated with an increase in the use of peripheral bypass surgery and with no decline in lower-extremity amputations. These results could be due to increased diagnosis of peripheral vascular disease, expanded indications for procedural interventions, or an increased number of repeat procedures performed in patients with peripheral vascular disease of the lower extremities. (N Engl J Med 1991; 325:556-62.)
Peripheral Vascular Disease

Comparative effectiveness of endovascular and surgical revascularization for patients with peripheral artery disease and critical limb ischemia: Systematic review of revascularization in critical limb ischemia

W. Schuyler Jones, MD, Rowena J. Dolor, MD, Vic Hasselblad, PhD, Sreekanth Vemulpalli, MD, Sumeet Subherwal, MD, Kristine Schmit, MD, Brooke Heidenfelder, PhD, and Manesh R. Patel, MD
Durham, NC

Background For patients with critical limb ischemia (CLI), the optimal treatment to enhance limb preservation, prevent death, and improve functional status is unknown. We performed a systematic review and meta-analysis to assess the comparative effectiveness of endovascular revascularization and surgical revascularization in patients with CLI.

Methods We systematically searched PubMed, Embase, and the Cochrane Database of Systematic Reviews for relevant English-language studies published from January 1995 to August 2012. Two investigators screened each abstract and full-text article for inclusion, abstracted the data, and performed quality ratings and evidence grading. Random-effects models were used to compute summary estimates of effects, with endovascular treatment as the control group.

Results We identified a total of 23 studies, including 1 randomized controlled trial, which reported no difference in...
Variation in LE Revascularization

Typical CLI patient

- 86 y.o. F with debilitating BL rest pain

- CABG: 2/2017
Case Presentation

• PE:
  – Diminished femoral pulses
  – Non-palpable distal pulses

• ABIs: .31/.35

• TBIs: 0/0
Critical Limb Ischemia: % Treated by Bypass (vs. PVI)

All VQI Centers Mean = 31%

Procedure Selection Variation

100% Bypass
BEST-CLI

Best Endovascular versus Best Surgical Therapy in Patients with Critical Limb Ischemia
BEST-CLI Trial: Overview

- **NIH-funded**, prospective, randomized, multicenter, open-label superiority trial

- **2100 patients** at 160 clinical sites in United States and Canada
  - Minimum 2-year follow up each patient
  - Finland, New Zealand, Italy, Germany, France

**Goal:** *to assess outcomes, quality of life and cost in patients who are candidates for both open and endovascular surgery*
Why Is BEST-CLI Important?

Uniquely positioned to provide level I data for CLI

- Well-powered and designed
- Real-world pragmatic trial
- Multidisciplinary – everyone involved
  - CLI Teams

Novel primary endpoint

- Major Adverse Limb Event (MALE) - free survival
  - Death,
  - Amputations AND
  - Major re-interventions
Key Secondary Endpoints

- Re-intervention and Amputation-free Survival (RAS)
- Amputation-free Survival
- MALE-POD

Additional Secondary Endpoints

- Freedom from hemodynamic failure
- Freedom from clinical failure
- Freedom from critical limb ischemia
- Number of re-interventions per limb salvaged
- Freedom from re-interventions (major and minor) in index limb
Robust Cost-Effectiveness Analysis

Target Population

Randomize

Intervention

Control

Trial Completion

Lifetime

MEASUREMENT MODELING
Quality Adjusted Life Years (QALYs) will be calculated based on area under the curve of quality of life for each patient. The average QALYs in two intervention arms then will be compared as outcomes.
Optimal Medical Therapy

**BEST-CLI Trial Optimal Medical Therapy (OMT) Report Cards**

**Overview of Site 1005 Optimal Medical Therapy Performance Metrics**

<table>
<thead>
<tr>
<th>Site</th>
<th>Site Name</th>
<th>Date of Data Freeze</th>
<th># Randomized</th>
<th>HTN Control</th>
<th>DM Control</th>
<th>Statin Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>1005</td>
<td>Brigham and Women’s Hosp.</td>
<td>11/1/2017</td>
<td>17</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Summary of Performance Metrics on Page 3*

**Explanation of Performance Metrics.**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Grade</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (HTN) Control</td>
<td>Excellent</td>
<td>Greater than 80% of patient visits with subjects either meeting age-specific targets for both SBP and DBP or at least one anti-hypertensive medication reported</td>
</tr>
<tr>
<td></td>
<td>Fair</td>
<td>Between 60% and 80% of patient visits with subjects either meeting age-specific targets for both SBP and DBP or at least one anti-hypertensive medication reported</td>
</tr>
<tr>
<td></td>
<td>Poor</td>
<td>Less than 60% of patient visits with subjects either meeting age-specific targets for both SBP and DBP or at least one anti-hypertensive medication reported</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>Your site did not have any patient visits with data available for this metric</td>
</tr>
<tr>
<td>Diabetes (DM) Control</td>
<td>Excellent</td>
<td>Greater than 80% of patient visits with Hemoglobin A1c &lt;8%</td>
</tr>
<tr>
<td></td>
<td>Fair</td>
<td>Between 60% and 80% of patient visits with Hemoglobin A1c &lt;8%</td>
</tr>
<tr>
<td></td>
<td>Poor</td>
<td>Less than 60% of patient visits with Hemoglobin A1c &lt;8%</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>Your site did not have any patient visits with data available for this metric</td>
</tr>
<tr>
<td>Statin Use</td>
<td>Excellent</td>
<td>Greater than 80% of patient visits with statin use reported</td>
</tr>
<tr>
<td></td>
<td>Fair</td>
<td>Between 60% and 80% of patient visits with statin use reported</td>
</tr>
<tr>
<td></td>
<td>Poor</td>
<td>Less than 60% of patient visits with statin use reported</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>Your site did not have any patient visits with data available for this metric</td>
</tr>
</tbody>
</table>

- Based on percentage of post-baseline visits at which targets are met
- Baseline visits are not considered because they reflect care the subject received before the subject was enrolled in BEST
- One patient can contribute data at more than one visit
- Grades are based on accepted, defined standards and not on comparison with other trial sites
BEST Investigators

Investigators by Specialty (n= 986)

• 563 Vascular Surgeons
• 126 Interventional Cardiologists
• 115 Interventional Radiologists
• 7 Vascular Medicine Specialists

81% sites are multi-disciplinary
Typical CLI Team
Enrollment Update

- 1st patient randomized 28/Aug/2014
- As of 1/30/2018
- 133 active sites
- 1183 subjects randomized (917 to go)
Trial Conduct

- Trial compliance is excellent
  - Low rate of lost to follow up
  - Low crossover rate
Investigator Specialty in BEST-CLI

865 physicians credentialed at 136 centers
Comparison of Endovascular Investigator Specialty

BEST-CLI vs National Medicare Claims

Percent

<table>
<thead>
<tr>
<th>VS</th>
<th>IC</th>
<th>IR</th>
<th>other</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>15</td>
<td>15</td>
<td>5</td>
</tr>
</tbody>
</table>

BEST-CLI

Medicare Claims
Conclusions

- There is an exceptional knowledge deficit in CLI management cf other areas of clinical therapy.

- Largely unproven, expensive care has filled the void.

- RCTs are imperfect ... but are the best tool we have!

- **BEST-CLI** will provide powerful, Level I data that will help begin the process of developing a much-needed evidence-based approach to CLI.
Update on the BEST-CLI Trial

Matthew T. Menard, M.D
Brigham & Women’s Hospital
Boston, Massachusetts