Chronic Limb Threatening Ischemia and the BEST-CLI Trial

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Site PI, BEST-CLI Trial
Johns Hopkins University School of Medicine
Disclosures

- None

- BEST-CLI trial Site PI for JHUSOM
  - Trial supported by NHLBI: 1U01HL107407-01A1
Outlines

- Chronic limb-threatening ischemia
  - Definitions
  - Epidemiology
  - Natural History
  - Treatment Algorithms
  - Impediments to Optimal Management

- BEST-CLI trial

- Multidisciplinary approach to limb preservation
• Peripheral Arterial Disease (PAD)
  • a disorder causing lower extremity arterial obliteration that limits blood flow to the limbs and may lead to arterial insufficiency
Definitions

- Peripheral Arterial Disease (PAD)
  - a disorder causing lower extremity arterial obliteration that limits blood flow to the limbs and may lead to arterial insufficiency

- Chronic Limb Threatening Ischemia (CLI)
  - a state of arterial insufficiency manifested by chronic, inadequate tissue perfusion at rest
  - characterized by ischemic rest pain, ulcers or gangrene
  - presence of objective hemodynamic evidence of arterial insufficiency
Etiology of PAD

- Atherosclerosis
- Embolization
- Thrombosis
- Buerger’s Disease
- Vasculitis
- Arterial Trauma
- Popliteal Entrapment
- Popliteal Adventitial Cystic Disease
## Etiology of PAD

- Atherosclerosis
- Embolization
- Thrombosis
- Buerger’s Disease
- Vasculitis
- Arterial Trauma
- Popliteal Entrapment
- Popliteal Adventitial Cystic Disease
Peripheral Arterial Disease

- Prevalence: 25-30% patients > 80 years old in the US
  - > 200 million people worldwide

Hirsch AT. Circulation 2012;125 (110);1449-1472
Norgren L. Int Angiol 2007;6(2):81-157
Peripheral Arterial Disease

- Prevalence: 25-30% patients > 80 years old in The US
  - > 200 million people worldwide

Chronic Limb Threatening Ischemia (CLI)

- Prevalence: ~11% of patients with PAD
- Incidence: 500 – 3,500 cases/million/year

Hirsch AT. Circulation 2012;125 (110);1449-1472
Norgren L. Int Angiol 2007;6(2):81-157
Demographic Factors

- Male gender (cf female)
- Age (per 10 years)
- Diabetes
- Smoking
- Hypertension
- Dyslipidemia
- Hyperhomocysteinemia
- Race (Asian/hispanic/black vs. white)
- C-reactive protein
- Renal insufficiency

From 2000 to 2010 worldwide prevalence of PAD increased by 23.5%
Diagnosis

- CLI is suspected in patients with atherosclerotic risk factors who:
  - Burning, gnawing pain in distal foot at rest made worse by elevation and improved with dependency
  - Tissue loss usually affecting the distal extremity

- On Physical Exam
  - Ulceration or gangrene; dependent rubor; thin, shiny skin; absence of hair
  - No palpable pulses
Confirmation of CLI
Vascular Laboratory

- **Physiological Studies**
  - Ankle Brachial Index (ABI)
  - Toe pressures
  - Doppler waveforms
  - Pulse Volume Recordings (PVR)
  - Transcutaneous oximetry (TcPO$_2$)
### Hemodynamic Definitions of CLI

<table>
<thead>
<tr>
<th></th>
<th>Patients with Tissue Loss</th>
<th>Patients with Ischemic Rest Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankle pressure</td>
<td>&lt;70 mm Hg</td>
<td>&lt;50 mm Hg</td>
</tr>
<tr>
<td>Toe pressure</td>
<td>&lt;50 mm Hg</td>
<td>&lt;30 mm Hg</td>
</tr>
<tr>
<td>TcPO2</td>
<td>&lt;40 mm Hg</td>
<td>&lt;20 mm Hg</td>
</tr>
</tbody>
</table>

- **ABIs ≤ 0.4**
  - Anyone with ABI > 0.9 deserves further investigation

*Patel MR et al. PARC. J Am Coll Cardiol. 2015;65:931-41*
The natural history of untreated severe or critical limb ischemia

>1,500 patients in 13 studies at 1 year f/u

---22% major amputation rate

did not receive revascularization with a minimum follow-up of ≥1 year. Predefined outcomes of interest were mortality, major amputation, and wound healing. Random-effects meta-analysis was used to pool cumulative incidence across studies.

Results: We identified 13 studies enrolling 1527 patients. During a median follow-up of 12 months, all-cause mortality rate was 22% (confidence interval [CI], 12%-33%) and major amputation rate was 22% (CI, 2%-42%). Worsened wound or ulcer was found at 35% (CI, 10%-62%). There was a trend toward improvement in mortality and amputation rate in studies done after 1997. The quality of evidence was low because of increased risk of bias and inconsistency.

Conclusions: Mortality and major amputations are common in patients who have untreated CLI during a median follow-up of 1 year, although these outcomes have improved in recent times. (J Vasc Surg 2015;62:1642-51.)
Risk of Amputation is affected by

- Degree of ischemia
Risk of Amputation is affected by

- Degree of ischemia
- Extent and depth of tissue loss
Risk of Amputation is affected by

- Degree of ischemia
- Extent and depth of tissue loss
- Presence and extent of infection
Limb Issues Often Overlap

Tissue Loss Dominant

Ischemia Dominant

Infection Dominant

The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: Risk stratification based on Wound, Ischemia, and foot Infection (WIFI)

Joseph L. Mills, Sr, MD, Michael S. Conte, MD, David G. Armstrong, DPM, MD, PhD, Frank B. Pomposelli, MD, Andres Schanzer, MD, Anton N. Sidawy, MD, MPH, and George Andros, MD, on behalf of the Society for Vascular Surgery Lower Extremity Guidelines Committee, Tucson, Ariz; San Francisco and Van Nuys, Calif; Brighton and Worcester, Mass; and Washington, D.C.

Critical limb ischemia, first defined in 1982, was intended to delineate a subgroup of patients with a threatened lower extremity primarily because of chronic ischemia. It was the intent of the original authors that patients with diabetes be excluded or analyzed separately. The Fontaine and Rutherford Systems have been used to classify risk of amputation and likelihood of benefit from revascularization by subcategorizing patients into two groups: ischemic rest pain and tissue loss. Due to demographic shifts over the last 40 years, especially a dramatic rise in the incidence of diabetes mellitus and rapidly expanding techniques of revascularization, it has become increasingly difficult to perform meaningful outcomes analysis for patients with threatened limbs using these existing classification systems. Particularly in patients with diabetes, limb threat is part of a broad disease spectrum. Perfusion is only one determinant of outcome; wound extent and the presence and severity of infection also greatly impact the threat to a limb. Therefore, the Society for Vascular Surgery Lower Extremity Guidelines Committee undertook the task of creating a new classification of the threatened lower extremity that reflects these important considerations. We term this new framework, the Society for Vascular Surgery Lower Extremity Threatened Limb Classification System. Risk stratification is based on three major factors that impact amputation risk and clinical management: Wound, Ischemia, and foot Infection (WIFI). The implementation of this classification system is intended to permit more meaningful analysis of outcomes for various forms of therapy in this challenging, but heterogeneous population. (J Vasc Surg 2014;59:220-34.)

- Wound: extent and depth
- Ischemia: perfusion/flow
- Foot Infection: presence and extent
**WIfI Classification**

- Designed to be analogous to the TNM staging system for cancer
- Based upon existing validated systems or best available data with 4 point scales

### Wound – Clinical Category

<table>
<thead>
<tr>
<th>Grade</th>
<th>Clinical Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Ischemic rest pain; Pre-gangrenous skin changes; frank ulcer or gangrene (Pedis or UT Class 0)</td>
</tr>
<tr>
<td>1</td>
<td>Minor tissue loss: small shallow ulceration (&lt; 5 cm²) of distal leg (Pedis or UT Class 1); no exposed bone or limited to distal phalanx</td>
</tr>
<tr>
<td>2</td>
<td>Major tissue loss: deeper ulceration(s) with exposed joint or tendon, ulcer 5-10 cm² not involving calcaneus (Pedis or UT Classes 2 and 3); gangrenous changes to digits. Salvageable with multiple digital amputations; TMA + skin coverage</td>
</tr>
<tr>
<td>3</td>
<td>Extensive ulcer/gangrene &gt; 10 cm² involving forefoot (plantar or dorsal ulcers of the midfoot); full thickness heel ulcer &gt; 5 cm² + calcaneal involvement. Salvageable only with complex foot reconstruction, nontraditional TMA (Chopart/Lisfranc), soft tissue coverage or complex wound management needs</td>
</tr>
</tbody>
</table>

### Ischemia -

<table>
<thead>
<tr>
<th>Grade</th>
<th>ABI</th>
<th>Ankle SP</th>
<th>TP, TcPO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>≥ 0.80</td>
<td>≥ 100 mmHg</td>
<td>≥ 60 mmHg</td>
</tr>
<tr>
<td>1</td>
<td>0.60-0.79</td>
<td>70-99 mmHg</td>
<td>40-59 mmHg</td>
</tr>
<tr>
<td>2</td>
<td>0.40-0.59</td>
<td>50-69 mmHg</td>
<td>30-49 mmHg</td>
</tr>
<tr>
<td>3</td>
<td>&lt; 0.40</td>
<td>&lt; 50 mmHg</td>
<td>&lt; 30 mmHg</td>
</tr>
</tbody>
</table>

ABI=ankle brachial index; SP=systolic pressure; TP=toe pressure; TcPO2=transcutaneous oximetry

### Foot Infection - SVS Grades

<table>
<thead>
<tr>
<th>Grade</th>
<th>Clinical Description</th>
<th>IDSA Class</th>
<th>IWGDF Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Wound without purulence or manifestations of infection &gt;2 manifestations of infection (erythema or purulence, pain, tenderness, warmth or induration) any cellulitis or erythema extends &lt; 2cm around ulcer; infection is limited to skin or subcutaneous tissue; no local complications or systemic illness</td>
<td>uninfected</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>Any infection in patient who is systemically and metabolically stable but has ≥ 1 of the following: cellulitis extending 2cm, lymphangitis, spread beneath fascia; deep tissue abscess; gangrene; muscle, tendon, joint or bone involvement</td>
<td>mild</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>Infection in patient with systemic or metabolic toxicity</td>
<td>moderate</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>severe</td>
<td>4</td>
</tr>
</tbody>
</table>

IDSA = International Diabetes Federation; IWGDF = International Wound Management Guidelines for Diabetes Foundation
## Risk of Amputation vs WIfI Stage

<table>
<thead>
<tr>
<th>Study (year): # limbs at risk</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
<th>Stage 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cull (2014): 151</td>
<td>37 (3%)</td>
<td>63 (10%)</td>
<td>43 (23%)</td>
<td>8 (40%)</td>
</tr>
<tr>
<td>Zhan (2015): 201</td>
<td>39 (0%)</td>
<td>50 (0%)</td>
<td>53 (8%)</td>
<td>59 (37%)</td>
</tr>
<tr>
<td>Darling (2015): 551</td>
<td>5 (0%)</td>
<td>111 (10%)</td>
<td>222 (11%)</td>
<td>213 (24%)</td>
</tr>
<tr>
<td>Causey (2016): 160</td>
<td>21 (0%)</td>
<td>48 (25%)</td>
<td>42 (21%)</td>
<td>49 (31%)</td>
</tr>
<tr>
<td>Beropoulis (2016): 126</td>
<td>29 (13%)</td>
<td>42 (19%)</td>
<td>29 (19%)</td>
<td>26 (38%)</td>
</tr>
<tr>
<td>Ward (2016): 98</td>
<td>5 (0%)</td>
<td>21 (14%)</td>
<td>14 (21%)</td>
<td>58 (34%)</td>
</tr>
<tr>
<td>Darling (2016): 992</td>
<td>12 (0%)</td>
<td>293 (4%)</td>
<td>249 (4%)</td>
<td>438 (21%)</td>
</tr>
<tr>
<td>N = 2279 (weighted mean)</td>
<td>148 (3.4%)</td>
<td>628 (8.3%)</td>
<td>652 (10.3%)</td>
<td>851 (25%)</td>
</tr>
</tbody>
</table>

**Median (% 1 yr amputation)**

<table>
<thead>
<tr>
<th></th>
<th>0%</th>
<th>10%</th>
<th>19%</th>
<th>34%</th>
</tr>
</thead>
</table>

Courtesy of J Mills
Relative 5-Year Mortality Rates

![Graph showing relative 5-year mortality rates for various cancers.](image)

- Prostate Cancer*: 8%
- Hodgkin's Disease*: 18%
- Breast Cancer*: 23%
- PAD†: 32%
- Colorectal Cancer*: 39%
- Lung Cancer*: 86%

Goals Of Treatment

- Medical therapy to optimize cardiovascular risk
- Wound management
- Revascularization (measures to improve limb perfusion)

Hirsch AT et al. J Am Coll Cardiol 2006;47:1239-131
Conte MS and Farber A. BJS 2015;102:1007-1009
Medical Therapy

- Antiplatelet agents (ASA or clopidogrel)
- Tobacco cessation
- Statins
- Diabetes control
- Blood Pressure Reduction
  - < 130/85 mm Hg
  - preferably with ACE-I

*J Am Coll Cardiol. 2016 Mar 22;67(11):1338
Circ Res. 2015 Apr 24;116(9):1509*
Wound Management

- Antibiotics
- Debridement / Minor amputation
- Wound management & offloading
Revascularization

- Relieve pain
- Heal wounds
- Preserve a functional limb
- Avoid major amputation
- Maintain ambulatory status
Revascularization Options in CLI

A Surgical revascularization

Diffuse peripheral arterial disease

Occlusion

Superficial femoral artery

Infrapopliteal bypass with single-segment great saphenous vein graft

Anterior tibial artery

Posterior tibial artery

Gangrene

B Endovascular revascularization

Stent

Angioplasty
1906- Technique of vascular anastomosis described
(Carrel A, Guthrie CC. Surg Gynecol Obstet 2:266,1906)
1948- 1st successful femoral popliteal bypass using rGSV in a patient with PAD
(Kunlin J. Rev Chir Paris 70:206-236, 1951)

1906- Technique of vascular anastomosis described
(Carrel A, Guthrie CC. Surg Gynecol Obstet 2:266, 1906)
## Infrainguinal Bypass

<table>
<thead>
<tr>
<th>Study</th>
<th>Primary Graft Patency @ 5 years</th>
<th>Secondary Graft Patency @ 5 years</th>
<th>Limb Salvage @ 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taylor L. et al N=300</td>
<td>80%</td>
<td>84%</td>
<td>90%</td>
</tr>
<tr>
<td>Shah D. et al N=2,048</td>
<td>72%</td>
<td>81%</td>
<td>95%</td>
</tr>
<tr>
<td>Pomposelli FB. et al N=1,032</td>
<td>57%</td>
<td>63%</td>
<td>78%</td>
</tr>
</tbody>
</table>

**Perioperative mortality: 1-6%**
Infrainguinal Bypass

- Traditional treatment
- Durable outcomes
- Long follow up periods available

- Invasive
- Is associated with
  - blood loss
  - morbidity
  - mortality
  - wound complications
1964
Charles Dotter
Novel Technology
Figure 2. Trends in Diagnostic Angiography, Therapeutic Endovascular Interventions, and Lower Extremity Bypass Surgery, 1996-2010

- No. of diagnostic lower extremity angiographic procedures (RR, 1.65 [95% CI, 1.56-1.73])
- No. of endovascular interventions (RR, 4.23 [95% CI, 4.17-4.28])
- No. of lower extremity bypass surgical procedures (RR, 0.39 [95% CI, 0.38-0.41])
Endovascular Treatment Options

- Plain Balloon Angioplasty (PTA)
- Stenting
- Atherectomy
- Laser assisted PTA
- Brachytherapy
- Stent grafts
- Drug eluting stents
- Drug coated balloons
- Bioabsorbable stents
- ........
There is a lot of literature...

Publications reporting 1-yr patency following SFA stenting or stent-grafting from 2000-2009
courtesy L. Schwartz
Endovascular Therapy for CLI

- Minimally invasive
- No need for
  - general anesthesia
  - incisions
  - hospitalization
- Lower morbidity and mortality
- Decreased durability
  - Low patency rates in some vascular beds
- Expensive
- Driven by business interests
We have tools that work....

...but **which** tool works best for **whom** and **when**?
Current Status of Limb Revascularization?

1. Variability in Treatment
2. Absence of Value-driven Care
3. Insufficient Comparative Effectiveness Data
Variability of Intensity of Vascular Care Across Regions of the United States

Proportion of Patients Undergoing a Vascular Procedure In The Year Prior To Amputation

- Very Low Intensity Regions: 33%
- Low Intensity Regions: 41%
- Medium Intensity Regions: 46%
- High Intensity Regions: 50%
- Very High Intensity Regions: 58%

$p<0.001$

Goodney et al, Circulation CV Q+O 2012 (5) 94-102
% of Patients with CLI and PAD treated with Surgical Bypass (vs. Endovascular Therapy)

All VQI Centers Mean = 31%

Procedure Selection Variation
CLI is

Very Expensive
Americans pay much higher prices for healthcare services

<table>
<thead>
<tr>
<th></th>
<th>Total hospital and physician costs, 2013a</th>
<th>Diagnostic imaging prices, 2013a</th>
<th>Price comparison for in-patent pharmaceuticals, 2010 (U.S. set to 100)b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bypass surgery</td>
<td>Appendectomy</td>
<td>MRI</td>
</tr>
<tr>
<td>Australia</td>
<td>$42,130</td>
<td>$5,177</td>
<td>$350</td>
</tr>
<tr>
<td>Canada</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>France</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Germany</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Netherlands</td>
<td>$15,742</td>
<td>$4,995</td>
<td>$461</td>
</tr>
<tr>
<td>New Zealand</td>
<td>$40,368</td>
<td>$6,645</td>
<td>$1,005</td>
</tr>
<tr>
<td>Switzerland</td>
<td>$36,509</td>
<td>$9,845</td>
<td>$138</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>United States</td>
<td>$75,345</td>
<td>$13,910</td>
<td>$1,145</td>
</tr>
</tbody>
</table>

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
At the end of the day we need to know how to manage this patient...

- 75 year old diabetic woman with right forefoot gangrene
- PE: normal femoral but no distal pulses
- Rt ABI: 0.3
Which **FIRST** Revascularization **Option** in CLI Has the **BEST Value**?

**VS**

Bypass Surgery

**VS**

Endovascular Therapy
Limitations of Published Data

- Retrospective
- Poorly controlled
- Suboptimal endpoints
- Sponsor and Operator bias
- Patients with claudication and CLI are “lumped together”
- Short or incomplete follow up
Is There any Level I Evidence?
**BASIL Trial**

- **Aim:** To compare outcomes of surgery-first strategy with angioplasty first strategy in patients with CLI

- **Results:**
  - No significant difference in amputation-free survival at >5 year follow-up
  - Trend toward benefit for surgery noted in those patients who survived more than 2 years

- **Limitations:**
  - Underpowered
  - Endovascular therapy limited to angioplasty
  - Lack of lesion standardization

Bradbury A. J Vasc Surg 2010; 51(5 Suppl)5S-17S
% of Patients with CLI and PAD treated with Surgical Bypass (vs. Endovascular Therapy)

All VQI Centers Mean = 31%

Procedure Selection Variation

100% Bypass
Best Endovascular vs. Best Surgical Therapy in Patients with Critical Limb Ischemia

Sponsored by the National Heart Lung and Blood Institute
BEST-CLI Trial: Overview

- Prospective, randomized, multicenter, multispecialty, pragmatic, open-label superiority trial
- 2100 patients at 160 clinical sites
- Funded at level of $25 million
- Goal: to assess treatment efficacy, functional outcomes, cost and value in patients with CLI and infrainguinal PAD who are candidates for both open vascular and endovascular surgery
BEST Trial Organization

National Heart, Lung, and Blood Institute
  D. Bonds, D. Reid, X. Tian

Clinical Coordinating Center
  Trial Chairs
  Brigham and Women’s Hospital
  A. Farber, Boston Medical Center
  M. Menard, Brigham and Women’s Hospital*
  K. Rosenfield, Mass General Hospital
  * Awarded Institution

Executive Committee
  NHLBI, CCC, DCC, C-E Core +
  M. Conte, C. White (Co-Chairs)
  M. Creager, M. Dake, M. Jaff,
  J. Kaufman, R. Powell

Certified Clinical Centers
  US & Canada

Clinical Events Committee

Subcommittees

Cost-Effectiveness Core
  Brigham and Women’s Hospital
  J. Avorn, N. Choudhry

Data Coordinating Center
  New England Research Institutes, Inc.
  S. Assmann, S. Siami

DSMB
5 Active Sites Overseas
New Zealand
- Wellington Hospital
- Waikato Hospital
- Auckland City Hospital
Finland
- Helsinki University Hospital
Italy
- San Giovanni di Dio Hospital

Onboarding Germany
- St. Franziskus Hospital – Muenster

133 sites currently open for enrollment
BEST-CLI is a Pragmatic Trial

- Definition of “Best Treatment” is left to the investigator
- All commercially available endovascular therapies allowed as long as accepted as standard of care
- All surgical bypass techniques and conduits allowed
- Trial approximates “real world”
BEST-CLI Trial Design: Two Cohorts

- **Cohort #1** Patients with adequate single segment great saphenous vein (SSGSV) N=1620
  
  Open surgery vs. Endovascular treatment

- **Cohort #2** Patients without adequate SSGSV (if randomized to OPEN conduit may include arm vein, short saphenous vein, composite vein, cryopreserved vein, and prosthetic conduit) N=480
  
  Open surgery vs. Endovascular treatment
Novel Primary Endpoint

Major Adverse Limb Event (MALE) – free survival

**MALE defined as:**

- Above ankle amputation or
- **Major** re-intervention
  - new bypass graft
  - jump/interposition graft revision
  - thrombectomy/thrombolysis
Key Secondary Endpoints

- Re-intervention and Amputation-free Survival
- Amputation-free Survival
- MALE

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

- Functional status / quality of life measures
  - EQ5D as main measure; also SF-12

- All financial costs of care
  - Hospital care (index admission and all f/u)
  - Outpatient care
  - Rehabilitation
Collaboration within BEST-CLI

Inclusive of everyone who performs revascularization for CLI:

- Vascular Surgeons
- Interventional Cardiologists
- Interventional Radiologists

If our trial is going to define practice it has to involve everyone.

What about Podiatry???
72% sites are multidisciplinary

- VS alone: 28%
- VS + IR: 23%
- VS + IC: 32%
- VS + IR + IC: 13%
BEST Investigator Data

- Investigators by Specialty (n= 930)
  - 690 Vascular Surgeons
  - 114 Interventional Cardiologists
  - 111 Interventional Radiologists
  - 3 Vascular Medicine
  - 12 Other specialties
Enrollment Update

- As of March 26, 2019 -
  - 1657 subjects randomized (79% complete)
Patient Characteristics (as of 4/9/2018 data freeze)

- Strata
  - Rest pain, no tibial dz 8%
  - Rest pain and tibial dz 12%
  - Tissue loss, no tibial dz 24%
  - Tissue loss and tibial dz 56%
BEST-CLI is positioned

• Provide a treasure trove of relevant data about CLI and its management
What questions will BEST-CLI answer?

- How does *infrainguinal bypass with optimal conduit (SSGSV)* fare against *endovascular therapy*?
- How does *bypass with non-optimal conduit* fare against *endovascular therapy*?

Define an evidence-based standard of care for revascularization of CLI

- Will prospectively validate the *SVS WIfI* classification
- Will relate comparative *hemodynamic outcomes* of revascularization to *clinical outcomes*
What about the wounds???
Case Example

- 69 year old female
  - PMH: DM, HPL, CAD, obesity
- Underwent left partial ray amputation at OSH for wet gangrene
- Wound ischemia -> dry gangrene
- Recommended LLE AKA because foot not salvageable
Physical Exam
Randomized to Bypass

- Left common femoral endarterectomy with bovine pericardium patch angioplasty
- Left CFA to PTA bypass w Propaten and vein patch
TMA with rotational plantar flap (Podiatry)
Post-Op

- Intra-op Cx: E. cloacae, Proteus, MSSA
- ID: Zosyn x6 weeks (PICC)
- Discharged to Rehab
- Fu in Multi-D clinic
  - Sutures out/healed by 14 d post-op
A Multifactorial Problem Needs a Multidisciplinary Approach

Multidisciplinary care improves amputation-free survival in patients with chronic critical limb ischemia

Jayar Chung, MD, J. Gregory Modrall, MD, Chul Ahn, PhD, Lawrence A. Lavery, DPM, and R. James Valentine, MD, Dallas, Tex

![Amputation-Free Survival: Multi-disciplinary care versus Standard wound care](chart)

![Graph showing survival analysis](chart)

(J Vasc Surg 2015;61:162-9.)
Multidisciplinary Diabetic Foot & Wound Service

- Multidisciplinary team
  - Vascular surgery, surgical podiatry, endocrinology
    - Single clinic visit
    - Robust home health nursing group
  - Consultants
    - Ortho foot & ankle, plastic surgery, ID, PMNR
- Inpatient/outpatient
July 2012 – Dec 2015
290 Diabetic patients
412 wounds
  • 58% WIfI Stage 3 or 4
352 Debridments & minor amputations
118 revascularizations
- Major amputation at 1 year

\[ P = 0.56 \]
The Burden of Limb Salvage

Time spent

The Society for Vascular Surgery Wound, Ischemia, and foot Infection (WIfI) classification independently predicts wound healing in diabetic foot ulcers

Caitlin W. Hicks, MD, MS,a,b Joseph K. Canner, MHS,c Nestoras Mathioudakis, MD, MHS,a,d Ronald Sherman, DPM,a,b Mahmoud B. Malas, MD, MHS,c,d James H. Black III, MD,b and Christopher J. Abularrage, MD,a,b Baltimore, Md (J Vasc Surg 2018;1-8.)

**Table III.** One-year outcomes for diabetic foot ulcer (DFU) patients overall and by Wound, Ischemia, and foot Infection (WIfI) stage

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (N = 709)</th>
<th>Stage 1 (n = 230)</th>
<th>Stage 2 (n = 141)</th>
<th>Stage 3 (n = 179)</th>
<th>Stage 4 (n = 159)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHT, days</td>
<td>127.9 ± 4.8</td>
<td>96.9 ± 8.3</td>
<td>78.5 ± 6.4</td>
<td>146.9 ± 9.6</td>
<td>195.1 ± 10.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>12-month wound healed, %</td>
<td>84.9 ± 1.7</td>
<td>94.1 ± 2.0</td>
<td>96.3 ± 2.3</td>
<td>83.1 ± 3.4</td>
<td>67.4 ± 4.4</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

WHT, Wound healing time.
Values are reported as mean ± standard error of the mean.
## Overall costs of multidisciplinary care

### Table: Overall costs of multidisciplinary care by stage

<table>
<thead>
<tr>
<th>Inpt &amp; Outpt $$$</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
<th>Stage 4</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Revenue</td>
<td>13,205</td>
<td>16,406</td>
<td>42,470</td>
<td>58,374</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total Cost</td>
<td>12,577</td>
<td>14,692</td>
<td>38,141</td>
<td>52,733</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Variable Direct</td>
<td>5,698</td>
<td>6,534</td>
<td>16,849</td>
<td>24,564</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Variable Indirect</td>
<td>1,556</td>
<td>1,814</td>
<td>4,204</td>
<td>5,726</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Fixed Direct</td>
<td>1,572</td>
<td>1,752</td>
<td>4,699</td>
<td>6,083</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Fixed Indirect</td>
<td>3,751</td>
<td>4,593</td>
<td>12,389</td>
<td>16,359</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Variable Net Margin</td>
<td>6,122</td>
<td>9,176</td>
<td>22,623</td>
<td>26,635</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Overall Net Margin</td>
<td>2,176</td>
<td>3,270</td>
<td>6,466</td>
<td>7,980</td>
<td>.008</td>
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</tbody>
</table>
Diabetic foot ulcers in a multidisciplinary setting
An economic analysis of primary healing and healing with amputation

Multi-D teams decrease major amps & save $$$

<table>
<thead>
<tr>
<th></th>
<th>&lt; 70</th>
<th>≥ 70</th>
<th>Sex</th>
<th>Male</th>
<th>Female</th>
<th>Toe pressure ≤ 45 and/or ankle pressure &lt; 80 mmHg†</th>
<th>Toe pressure &gt; 45 and ankle pressure ≥ 80 mmHg†</th>
<th>Healing time</th>
<th>Minor amputations</th>
<th>Major amputations</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>27</td>
<td>50</td>
<td></td>
<td>43</td>
<td>34</td>
<td>314 (27–805)</td>
<td>316 (27–968)</td>
<td>8</td>
<td>27</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sex</td>
<td>60</td>
<td>31</td>
<td>360 (44–992)</td>
<td>379 (44–992)</td>
<td>30</td>
<td>254 (25–998)</td>
<td>238 (27–501)*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Toe pressure ≤ 45 and/or ankle pressure &lt; 80 mmHg†</td>
<td>14</td>
<td>267</td>
<td>267 (27–531)</td>
<td>267 (27–531)</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Toe pressure &gt; 45 and ankle pressure ≥ 80 mmHg†</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Healing time</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
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<td></td>
<td>≥ 8 months</td>
<td>22</td>
<td>356</td>
<td>356 (27–968)</td>
<td>356 (27–968)</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>≥ 9 months</td>
<td>30</td>
<td>312</td>
<td>312 (44–745)</td>
<td>312 (44–745)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>≥ 3 months</td>
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</tr>
</tbody>
</table>
Controlling Costs

Major vs. Minor amputations

Single Center Study examining Outcomes Pre/Post DFS

Decreased Amputations
Decreased Surgeries

Conclusion
Early referral to DFS=

1. Earlier presentation of disease
2. Reduced delays to treatment
3. Decreased costs of care
BEST-CLI, Podiatry, and CLI
An Important Relationship

- Podiatry
- Medical Management
- CLI
- Wound Management
- Revascularization Management

BEST-CLI
BEST-CLI, Podiatry, and CLI

Our Plea to You

- Continue to take excellent care of patients
- Be cognizant of CLI in patients who present with foot wounds
- Liaison with BEST-CLI investigators to optimize blood flow
- Aggressive and early debridement/minor amputation as needed
- Consider establishing/joining a multi-D limb preservation team

  - This is where CLI care is headed!
Thank You

Questions?

@CaitlinWHicks
@HopkinsSurgery
@BEST-CLI