Transcatheter Arterialization of Deep Veins in Chronic Limb-Threatening Ischemia

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Disclosures

- NIH R21AG077310 Federal Award
- I hate unnecessary amputations
• **2.1 million people** living with limb loss in USA - expected to **double** by 2050

• **300-500** amputations are performed **every day**

• Of persons with diabetes, **up to 55%** will require amputation of the second leg within 2-3 years

• Amputations caused by diabetes **increased by 24%** from 1988 to 2009.
Why do current therapies fail?

Microvascular decimation:

- High prevalence of medial artery calcification and small artery disease
- Presence of a wound changes perfusion requirements
- Flow to ankle ≠ wound healing
- **No-option CLTI patients** do not respond to any traditional interventions

*Need for new tools in the below-knee toolbox*

The “200” day rule
## Existing below knee toolbox

**FDA Approved Therapies**
designed to open arteries

<table>
<thead>
<tr>
<th></th>
<th>Angioplasty</th>
<th>Atherectomy</th>
<th>Stents</th>
<th>Covered Stents</th>
<th>Drug Coated Balloons</th>
<th>Drug Eluting Stents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Above the Knee</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Below the Knee</strong></td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
</tbody>
</table>

**Standard ATK technologies have failed to demonstrate long-term efficacy in BTK**
So what do we offer these no-option pts???
Enter DVA!!!
Deep Venous Arterialization is...

- shunting arterial blood to the deep veins to *arterialize* the vein
- not a new concept (1881)
- plagued by incorrect patient selection, lack of technology until now!
Who is the *Perfect Candidate*...
Edmonds et al. raised the question if ischemic foot disease could be explained by one disease (atherosclerosis), or by the occurrence of 2 diseases (diabetic macroangiopathy [SAD] and classical atherosclerosis [BAD]). They concluded that “the detailed nature of PAD in diabetes has not been fully defined. Of course, in a diabetic patient, particularly a patient who develops arterial disease in later life, both diseases may co-exist”.

Diabetic Peripheral Arteriopathy: A Tale of Two Diseases

Michael E. Edmonds\textsuperscript{a} • C. Shanahan\textsuperscript{b} • Nina L. Petrova\textsuperscript{a}
DVA options include open surgical bypass, hybrid, percutaneous
Percutaneous Trans-Venous Deep-Vein Arterialization

Pedal Access

AV Alignment

AV Crossing

Valvulotomy

Straight Extension

Stent Deployment

Tapered Crossing Stent Deployment

Venous Arterialization Achieved
Percutaneous Trans-Venous Deep-Vein Arterialization

Serial angiogram images courtesy of Dr. Roberto Ferraresi
Lateral Plantar Vein Anatomy
Pneumatic Tourniquet & Table Position

• Single cuff technique
• Table in reverse-Trendelenburg

• Two cuff technique
• Table in reverse-Trendelenburg
• R TMA
Posterior Tibial Artery to Posterior Tibial Vein DVA

56 y/o, R5 non-healing surgical wound. Former smoker, hypertension, insulin dependent DM2

Baseline

Toe pressure: 0

4 Months

Toe pressure: 64
**US Pivotal Trial**

Multicenter, prospective pivotal study of the LimFlow System

**NATIONAL PIs**
- Dr. Dan Clair
  Vanderbilt University
- Dr. Mehdi Shishehbor
  University Hosp. Cleveland

**ENROLLMENT**
- 105 patients
- 20 sites in US

**KEY CRITERIA**

**Inclusion**
- No-Option CLTI
- Rutherford 5/6
- Stable Dialysis allowed

**Exclusion**
- Life expectancy <12M
- Severe heart failure
- Hepatic Insufficiency

**PRIMARY ENDPOINT**
Bayesian Amputation Free Survival (AFS) at 6M
Pre-specified literature-based PG of 54%

**SECONDARY ENDPOINT**
Technical Success
Wound Healing
Rutherford Class Pain

Published in The NEW ENGLAND JOURNAL of MEDICINE
Patient Demographics

**BASELINE CHARACTERISTICS (n=105)**

- Age (Avg, years) 69 (38-89)
- Gender (% Male) 69%
- African American 15%
- Hispanic or Latino 28%

**COMORBIDITIES**

- Diabetes 77%
- Hypertension 91%
- Dialysis 18%
- CKD 39%
- Rutherford 5 65%
- Rutherford 6 35%

**Crossing Artery**

- PTA 75%
- Peroneal 19%
- TPT 6%

**PROCEDURAL RESULTS**

*Technical Success* 99%

Primary Endpoint
6 Month AFS, Limb Salvage, Survival

Survival = 87%
Limb Salvage = 76%
AFS = 66%

Time after Index Procedure (days)
ORIGINAL ARTICLE

Transcatheter Arterialization of Deep Veins in Chronic Limb-Threatening Ischemia

Mehdi H. Shishehbor, D.O., M.P.H., Ph.D., Richard J. Powell, M.D., Miguel F. Montero-Baker, M.D., Anahita Dua, M.D., Jorge L. Martinez-Trabal, M.D., Matthew C. Bunte, M.D., Arthur C. Lee, M.D., Andrew S. Mugglin, Ph.D., Joseph L. Mills, M.D., Alik Farber, M.D., and Daniel G. Clair, M.D., for the PROMISE II Investigators

DVA
Dr. Anahita Dua
Vascular Surgeon, Mass General

Enrollment

180 Per-protocol patients
22 Sites in US

Primary Endpoint

Amputation Free Survival (AFS) at 12M
Subjects who underwent a major amputation continued to be followed for co-morbidities and mortality

Study Design & Objective

A prospective, single-arm, observational registry to track the clinical progression of CLTI and incidence of death, amputation, and revascularization attempts over a one-year period

Inclusion: Rutherford 5/6 CLTI

No-Option
• No option for conventional endovascular or surgical intervention
• No-option status determined by treating physician

Multiple Revasc Fails
• 2+ revascularization attempts in previous 6 months without resolution of symptoms

Exclusion: Subject participating in the PROMISE II Clinical Trial of TADV
Participating Centers

CURRENT LANDSCAPE

> 150K annual amputations\(^1\)

> Primary amputation\(^2\)

  73% NO diagnostic angio

  54% NO revasc attempts

> CLariTI Registry

  22 sites participated, mix of academic centers and community hospitals

  Vascular Surgeons

  Interventional Cardiologists

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\(^1\) Creager, AHA, 2021; \(^2\) Mustapha, CLI Journal, 2021; \(^3\) Goodney et al, JVS, 2013
## Baseline Clinical Characteristics (n=180)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median Age (range)</strong></td>
<td>70 (60-78)</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>120 (66.6%)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>99 (55.0%)</td>
</tr>
<tr>
<td>Black or African Descent</td>
<td>65 (36.1%)</td>
</tr>
<tr>
<td>Asian</td>
<td>4 (2.2%)</td>
</tr>
<tr>
<td>Unknown/Declined to State</td>
<td>11 (6.1%)</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>156 (86.7%)</td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>19 (10.6%)</td>
</tr>
<tr>
<td>Unknown/Declined to State</td>
<td>5 (2.8%)</td>
</tr>
<tr>
<td><strong>History of Smoking</strong></td>
<td>108 (60.0%)</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td></td>
</tr>
<tr>
<td>Heart Failure</td>
<td>59 (32.8%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>141 (78.3%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>166 (92.2%)</td>
</tr>
</tbody>
</table>

### NO-OPTION STATUS
- 2+ Revasc Fails: 34%
- No Option: 66%

### DIABETES
- Not diabetic: 25%
- Type I: 4%
- Type II: 71%

### RACE
- Caucasian: 55%
- Black or African Descent: 36%
- Asian: 2%
- Unknown: 6%

### RENAL DISEASE
- None: 49%
- CKD: 25%
- ESRD: 23%
- RI: 3%
12 Month Results, No-Option Cohort

- Survival = 66.6%
- Limb Salvage = 48.4%
- AFS = 32.6%

Graph showing survival, limb salvage, and AFS over time after index procedure.
12 Month Results, No-Option Cohort

- Survival = 66.6%
- Limb Salvage = 48.4%
- AFS = 32.6%

Graph: 12M Pooled Results

- Survival = 86%
- Limb Salvage = 73%
- AFS = 63%

Time After Index Procedure (days)
### Comparison of Transcatheter Arterialization of Deep Veins to Standard of Care in Patients with No-Option Chronic Limb Threatening Ischemia

**Title:** Comparison of Transcatheter Arterialization of Deep Veins to Standard of Care in Patients with No-Option Chronic Limb Threatening Ischemia

**Authors:** Richard J Powell, Christopher M Mullin, Daniel G Clair, Mehdi H Shishehbor, Anahita Dua

**Affiliations:**

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2.可能存在
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**PMID:** 3785666

**DOI:** 10.1016/j.avsg.2023.08.010

**Abstract**

**Background:** Patients with no-option chronic limb-threatening ischemia (no-option CLTI) have limited therapeutic options. The PROMISE II study evaluated transcatheter arterialization of deep veins (TADV) as a treatment option for no-option CLTI. In the current study, patients from PROMISE II were...
HELLO
I AM...
HERE TO STAY!