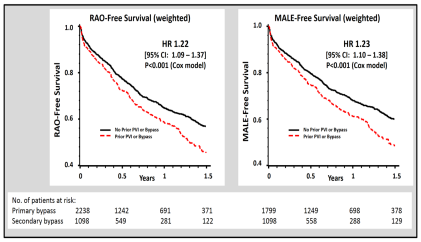
New Subanalysis Findings From The BEST-CLI RCT Are Critically Important To The Treatment Of CLTI Patients: Open Surgical Bypass Operations Still Have A Critical Role: Open Versus Endo Treatment Of Infrapopliteal Disease: **Does Endo Treatment Burn Bridges?**

Matthew Menard, MD

Disclosures:

- ***Novo Nordisk Foundation***
  - ***Grant Recipient***
- ***Janssen, Inc***
  - ***Advisory Board***
- ***Anges, Inc***
  - ***DSMB***

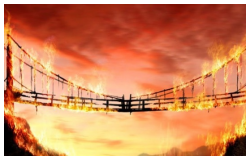
Secondary bypass works, but its inferior



Jones DW et al. J Am Heart Assoc. 2013 1

Questions:

- How does infrainguinal bypass after failed Endo compare with bypass performed as first-line therapy?
- **Does Endo-first treatment "burn bridges" for a secondary bypass?**



Potential causes for "burned bridges":

- Disruption of vulnerable plaque
- Wire injury
- Compromise to collateral vessels
- **Damage to runoff vessels**
- Compromise of a bypass target
- Progression of tissue loss and loss of optimal window for intervention
- Marker for a higher risk patient or disease pattern

Objectives:

- **Compare Primary Bypass (PB) and Secondary Bypass (SB) after failed Endo in the BEST-CLI dataset**
- BEST-CLI compared PB and Endo in patients with CLTI who were candidates for both treatment strategies
  - Cohort 1 (adequate SSGSV) – 1434 patients, 2.7 yrs median fu
  - Cohort 2 (no SSGSV) – 396 patients, 1.6 yrs median fu

Methods:

- Definitions
  - **PB defined as bypass performed at time of randomization**
  - **SB defined as bypass performed in the index limb in patients who were initially treated with Endo**
- Groups
  - All patients
  - Cohort 1 and Cohort 2
  - Patients who had technically successful Endo
  - Early SB (<30 days) and Late SB

Methods:

- Outcomes
  - **Primary:** Ipsilateral major (above ankle) amputation with death as a competing risk
  - **Secondary:** Major amputation or all-cause death
- Univariable, Multivariable, Matched Analyses based on Propensity Scores
  - age, gender, race, WIfI Stage, randomization strata, diabetes, ESRD, previous index infrainguinal reconstruction and smoking history

Results:

- Cohort 1 - 665 PB and 158 SB
- Cohort 2 - 192 PB and 45 SB
- Demographics, comorbidities, and medications were similar between groups in each cohort

Results:

- Cohort 1
  - **SSGSV used in 88% of PB**
  - PB - Tibial target in 56%
  - SB - Tibial Endo target in 29%
- Cohort 2
  - **SSGSV used in 20% of PB**
  - PB - Tibial target in 49%
  - SB - Tibial Endo target in 36%

Results:

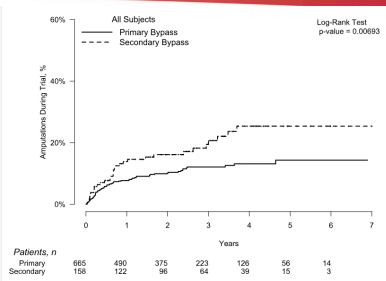
Time to SB after Endo

- 28 days in all patients
- 210 days with technically successful initial Endo

Unadjusted Outcomes at 1 year:

Outcomes	Primary Bypass	Secondary Bypass	P-Value
All Cohorts			
Major Amputation	***8.6%***	***14.4%***	***.006***
Maj Amputation with Death as Competing Risk	***8.1%***	***14%***	***.002***
Major Amputation or Death	19.1%	17.5%	.587
Cohort 1			
Major Amputation	***7.7%***	***13.9%***	***.008***
Maj Amputation with Death as Competing Risk	***7.4%***	***13.5%***	***.003***
Major Amputation or Death	16.8%	17.3%	.884
Cohort 2			
Major Amputation	11.8%	16.2%	.483
Maj Amputation with Death as Competing Risk	10.9%	15.9%	.28
Major Amputation or Death	27.9%	18.3%	.311

Kaplan-Meier Analysis – Cohort 1:



Risk-adjusted Outcomes – Cohort 1:

Outcome	HR	95% CI	P-value
Major Amputation			
Multivariable	***1.72***	***1.08 – 2.73***	***.02***
Propensity Matched	***1.62***	***1.04 – 2.54***	***.034***
Major Amputation – ENDO Technical Success only			
Multivariable	***2.21***	***1.26 – 3.86***	***.005***
Propensity Matched	***3.1***	***1.74 – 5.54***	***<.001***
Amputation/Death			
Multivariable	.92	.68 – 1.24	.57
Propensity Matched	.98	.74 – 1.31	.9
Amputation/Death - ENDO Technical Success only			
Multivariable	.87	.56 – 1.33	.51
Propensity Matched	.85	.56 – 1.28	.44

Early vs Late Secondary Bypass – Both Cohorts:

Major Amputation at 1-year

- 8.1 % for **primary bypass**
- 10.1% for **late secondary bypass** (> 30 days)
- 17.7 % for **early secondary bypass** (< 30 days)

- Early SB was associated with major amputation (HR 2.01, 95% CI 1.22 – 3.31, P=.006)

Summary

- **Secondary bypass was associated with a higher major amputation risk**
  - Observed when SSGSV was deemed available (Cohort 1)
  - Findings hold true when restricted to patients with initial Endo technical success (removing those with early Endo failures)
  - Patients with early SB after Endo had worse outcomes

Limitations:

- **BEST-CLI trial was not powered for analysis of SB**
- Survival bias favored those undergoing SB
- Anatomy and conduit details for SB not collected
- Selection bias in BEST-CLI - needed equipoise to enroll
- Procedural heterogeneity in BEST-CLI
- Primary outcome of the BEST-CLI trial, MALE/death was not used because SB, by definition, meets the criterion

Conclusions:

- Initial Endo in patients with CLTI and adequate SSGSV
  - Is not a "free shot"
  - May "burn bridges"
- PB for CLTI performs better than SB overall – even after technically successful Endo
- **Our current mandate as a community of vascular specialists is to figure out who should get endo and who should get surgery as a first step.**


BEST-CLI
Thank you very much