HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

How Do Prior Endovascular Interventions Affect Future Lower Extremity Bypass Outcomes For CLTI: Why Do The Results Of The BEST-CLI Trial Make This More Important

Kenneth Rosenfield, MD, MHCDS
Mass General Hospital
Boston MA

MASSACHUSETTS GENERAL HOSPITAL
FIREMAN VASCULAR CENTER

DISCLOSURES

'No Disclosures'

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Redefining the Treatment of Peripheral Artery Disease

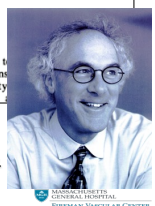
Role of Percutaneous Revascularization

Jeffrey M. Isner, MD, and Kenneth Rosenfield, MD

The times, they are a changin'.
Bob Dylan

The application of a catheter-based approach to the treatment of arterial occlusion of the lower extremities was proposed by Dotter and Judkins[1] nearly 30 years ago; 13 years later, Gruentzig[2] widespread basis to convert t tal or less lengthy occlusions with less technical difficulty efficacy. Plain old balloon

Isner and Rosenfield; Circulation; 1993



Jeffrey Michael Isner, M.D.
1947-2001

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Peripheral Artery Disease
Paradigm Shift (1989-2024)

- Effective percutaneous revascularization strategies available
  - Less invasive, lower "cost" to patient, repeatable
  - More Endo "tools"
- Transition from ***Open*** **to** ***Endovascular***
- New paradigm: ***"Endo First"*** … If anatomy amenable to percutaneous Rx, then should be attempted first
- BUT are there data to support this???
- *NB: Rapidly changing field – moving target with novel devices and evolving physician skill sets – has presented a challenge to develop evidence base*

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"Endo First" Concern – possible Penalty

- **If Endo fails and, in the process, "Burns a Bridge", negatively affecting subsequent surgical "rescue" and related clinical outcomes, that is problematic.**
- **QUESTIONS: How relevant is this concern, how often does it occur and what is the impact?**

NB: What about failed surgery? Can this also lead to less favorable subsequent endo (or repeat surgical) outcomes?
In practice, failed ANYTHING often compromises the next "rescue" procedure… And may be a marker of poor patient/vessel/limb substrate, rather than a bridge burned.

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Potential causes for "burned bridges"

- Compromise of bypass target
  - what would initially have been above-knee is now below-knee
- Compromise of collateral vessels
- Damage to runoff vessels
  - Wire injury
  - Disruption of vulnerable plaques → distal embolization
- Progression of tissue loss→ loss of optimal window for intervention

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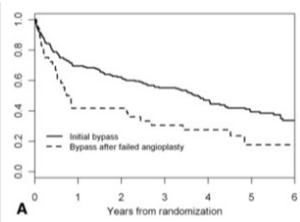
Surgery after Failed Endo – BASIL I Trial



Amputation free survival in patients undergoing primary bypass vs. bypass surgery after failed balloon angioplasty

Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: Analysis of amputation free and overall survival by treatment received

Andrew W. Bradbury, BSc, MD, MBA, FRCSEd,* Donald J. Adam, MD, FRCSEd,† Jocelyn Bell, PhD,* John P. Forbes, PhD,‡ T. Gerry R. Fowkes, PhD, FRCPE,§ Ian Gillespie, MD, FRCR,‖ Charles Vaughan Ruckley, ChM, FRCSEd, CBE,† and Gillian M. Raab, PhD,‡ on behalf of the BASIL trial Participants,* Birmingham and Edinburgh, United Kingdom

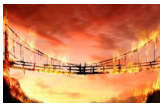
Background: An intention-to-treat analysis of randomized Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial data showed that initial randomization to a bypass surgery (BSX) first strategy was associated with improved amputation free survival (AFS) and overall survival (OS) at 5 years. The aim of BASIL was to inform treatment received. We also compare vein with prosthetic BSX and transluminal with subintimal balloon angioplasty (BAP) and examine outcomes from BSX after failed BAP.

Methods: We randomly assigned 452 patients with IS-2 due to infrapopliteal disease to 2[1] United Kingdom hospitals to a BSX first (n = 224) or BAP first (n = 228) strategy. Patients were followed up for a minimum of 2 years (median, 4 years) and more than half for >5 years. We prospectively collected data on every procedure, major amputation, and death.

Results: Patients randomized to BAP were more likely to have their assigned treatment first (94% vs 85%, $P = .01$, χ^2 test). Of 228 BAP patients, 108 (47%) required a BSX (median, 14 days; IQR, 3–42 days). Of 224 BSX patients, 15 (7%) had a BAP (4 in 15 BSX (10%) patients had vein angioplasty, 4 had transluminal stenting, 3 BAP (1.3%) vs 13 BSX (5.8%) had undergone the opposite treatment first), and 10 BAP (2.6%) and 2 (0.9%) BSX had received the assigned treatment and then undergone the opposite treatment. BSX distal anastomoses were divided approximately equally between the above and below knee popliteal and crural arteries; most originated from the common femoral artery. About 25% of the grafts were prosthetic. At 5 years, 1 in 3 patients had died and 1 in 4 had undergone a major amputation. Most amputations (70%) were of the BTA alone (36%) or combined with the popliteal artery (42%) and crural arteries (28%). Outcome of vein BSX was better for AFS ($P = 0.003$) but not OS ($P = 0.38$, log-rank tests) than prosthetic BSX. There were no differences in outcome between approximately equal numbers of transluminal and subintimal BAP. AFS ($P = 0.006$) but not OS ($P = 0.06$, log-rank test) survival was significantly worse after BSX after failed BAP than after BSX as a first revascularization attempt (median, 2.1 vs 4.2 years). Of patients undergoing BSX, 30% died within 30 days of surgery. Of those surviving surgery, BSX outcomes after failed BAP are significantly worse than for BSX performed as a first revascularization attempt. BSX with vein offers the best long-term AFS and OS and, overall, BAP appears superior to prosthetic BSX. (J Vasc Surg 2010;51:1505-1516.)

Questions from BEST-CLI Trial

- How does an infrainguinal bypass after failed endovascular treatment (secondary bypass) perform in comparison with bypass performed as first-line therapy (primary bypass) in patients with CLTI?
- Does Endo-first treatment "burn bridges" for a secondary bypass?



esvs KRAKÓW 2024

BEST-CLI

Bypass After Failed Endovascular Intervention is Associated with an Increased Risk for Major Limb Amputation Among Patients with CLTI

Alik Farber, Matthew Menard, Michael S. Conte, Kenneth Rosenfield, Caitlin Hicks, Gheorghe Doros, Michael B. Strong, Kim Houlind, Philippe Kolh, Jeffrey J. Siracuse

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Objectives of BEST-CLI

Compare Primary Bypass and Primary 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

Objective of *secondary* analysis:

Compare Primary Bypass (pts initially randomized to bypass) *versus* Secondary Bypass (pts undergoing bypass on index limb after initially randomized to/treated successfully with endo)

Methods

- Outcomes
  - Primary: ipsilateral above ankle amputation, analyzed with death as a competing risk
  - Secondary: Above ankle amputation or all-cause death
- Unadjusted, Adjusted, Matched Analyses
  - age, gender, race, WIfI Stage, randomization strata, diabetes, ESRD, previous index infrainguinal reconstruction and smoking history

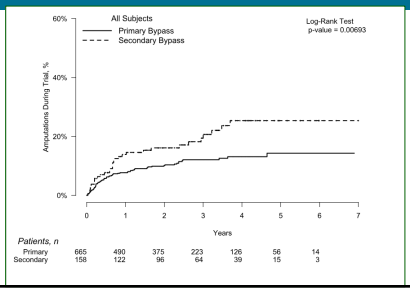
Results

- 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

Unadjusted Outcomes at 1 Year

Outcomes	Primary Bypass	Secondary Bypass	P-Value
All Cohorts			
Major Amputation	***8.55%***	***14.4%***	***.006***
Amputation/Death as Competing Risk	***8.11%***	***14%***	***.002***
Amputation/Death	19.1%	17.5%	.587
Cohort 1			
Major Amputation	***7.7%***	***13.9%***	***.008***
Amputation/Death as Competing Risk	***7.35%***	***13.5%***	***.003***
Amputation/Death	16.8%	17.3%	.884
Cohort 2			
Major Amputation	11.8%	16.2%	.483
Amputation/Death as Competing Risk	10.9%	15.9%	.277
Amputation/Death	27.9%	18.3%	.311

Kaplan-Meier Analysis – Amputations in Cohort 1 Following *Primary versus Secondary Bypass*



Secondary Bypass: *Early (<30d) vs Late (>30d)*

- Amputation at 1-year
  - early SB - **17.7%**
  - late SB - **10.1%**

  (NB Primary BP - **8.1%**)
- Early SB was associated with amputation (HR 2.07, 95% CI 1.27 – 3.37, P=.003)
- Late SB was not, but trended (HR 1.31, 95% CI 0.76 – 2.23, P=.33)

Summary

- Secondary bypass was associated with a higher major amputation risk
  - When SSGSV available (Cohort 1)
  - Findings hold true when restricted to patients with initial Endo technical success (removing those with early Endo failures)
  - Secondary Bypass early (≤30d) after Endo had worse outcomes
- Unknowns:
  - Were these poor Endo candidates in first place
  - How good were Endo results in these patients
  - Did early Endo failure select out poor protoplasm patients who are more likely to fail all therapies?

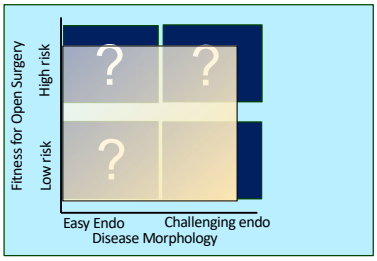
Limitations

- BEST-CLI 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 since SB, by definition, meets the criterion

Balanced View

- BEST-CLI may not reflect real world
  - Equipoise required…pts were deemed to be "candidate" for both Open and Endo, but…
    - Pts with simple endo may not have been enrolled
    - Was the same scrutiny utilized for to exclude patients for both therapies? What percentage of patients were enrolled who were…
      - Poor candidate for Open?
      - Poor candidate for Endo?
    - Were more patients randomized who were not likely to do well with Endo?

BEST-CLI Enrollment: Challenge of Equipoise



Did investigators have equipoise when disease morphology was straightforward for endo or patient unfit for open surgery?
What percentage enrolled were:
- "Easy for Endo"?
- "High Risk for Surgery"?

Other Considerations

- What about failed surgery? Can this also lead to less favorable subsequent endo (or repeat surgical) outcomes?
- Failed of *ANY* revascularization may compromise the next "rescue" procedure…
- This could simply be a marker of poor patient/vessel/limb substrate, rather than a bridge burned.

Conclusions

- PB for CLTI performs better than SB overall, even after technically successful Endo
- Initial Endo in CLTI patients with adequate SSGSV is not a "free shot"
- Careful selection of initial therapy is always appropriate. More data needed to predict successful outcome of endo
- Patients who are candidates for limb salvage should undergo an evaluation of surgical risk and conduit availability, and careful assessment of likelihood of successful endo.
- Bypass with adequate SSGSV should be offered as a first line treatment option for suitable candidates with CLTI, as part of fully informed, shared decision-making