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Robert Wood Johnson Medical School

BEST-CLI Is Practice Changing:

Use That Vein (in select patients)!

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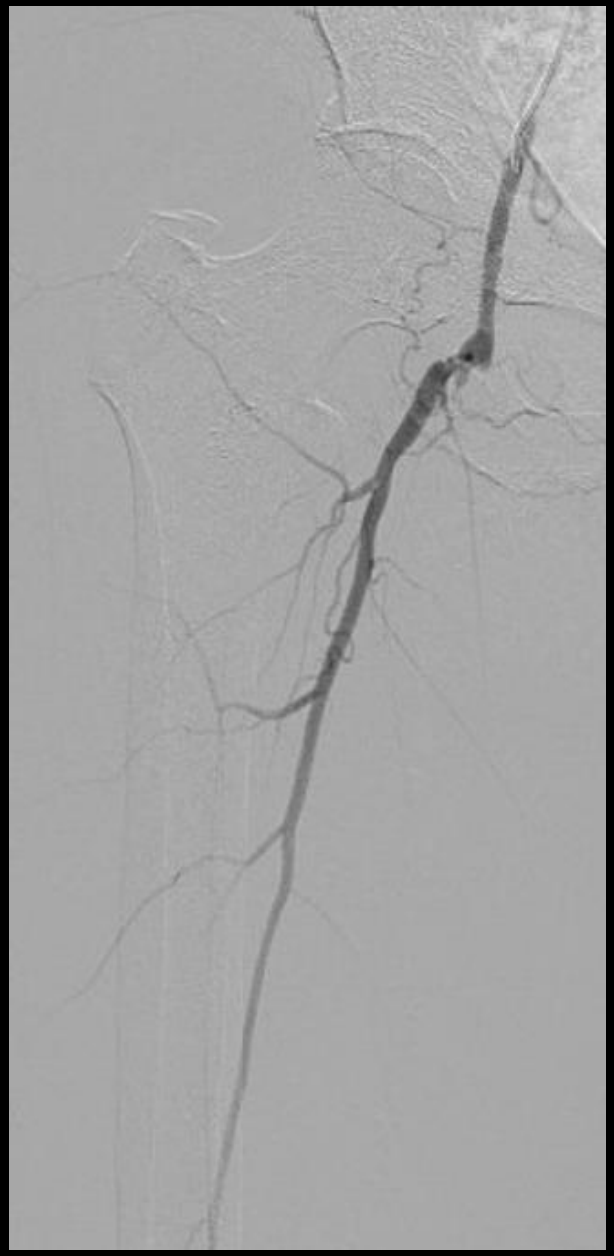
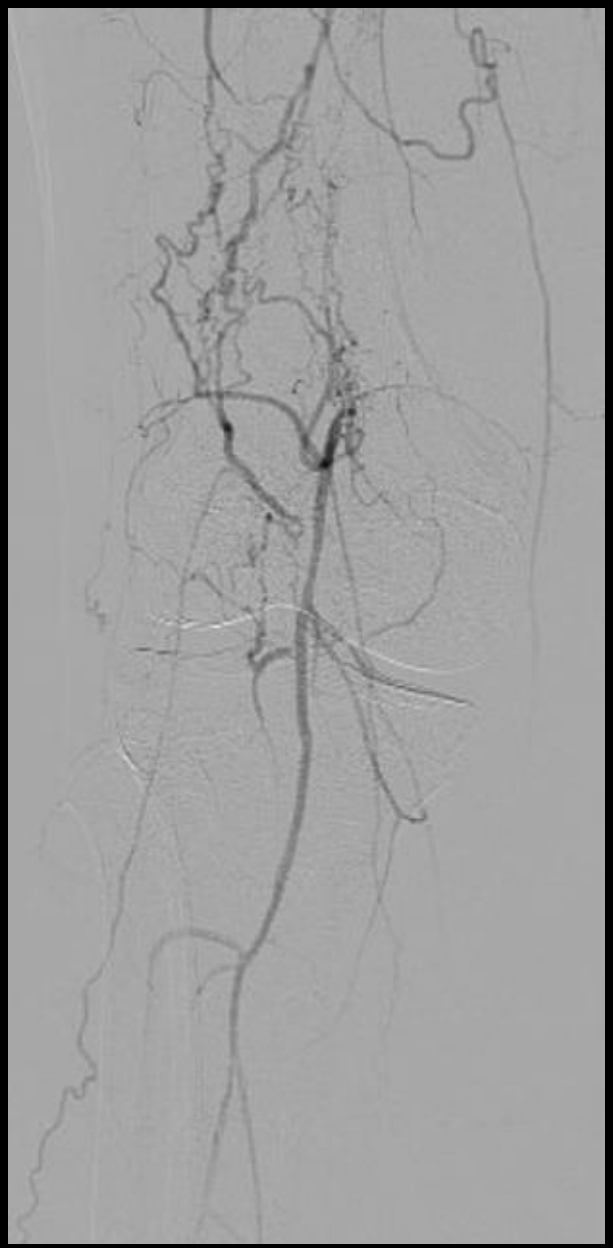
Disclosures:

Consultant for Terumo, Gore, Shockwave

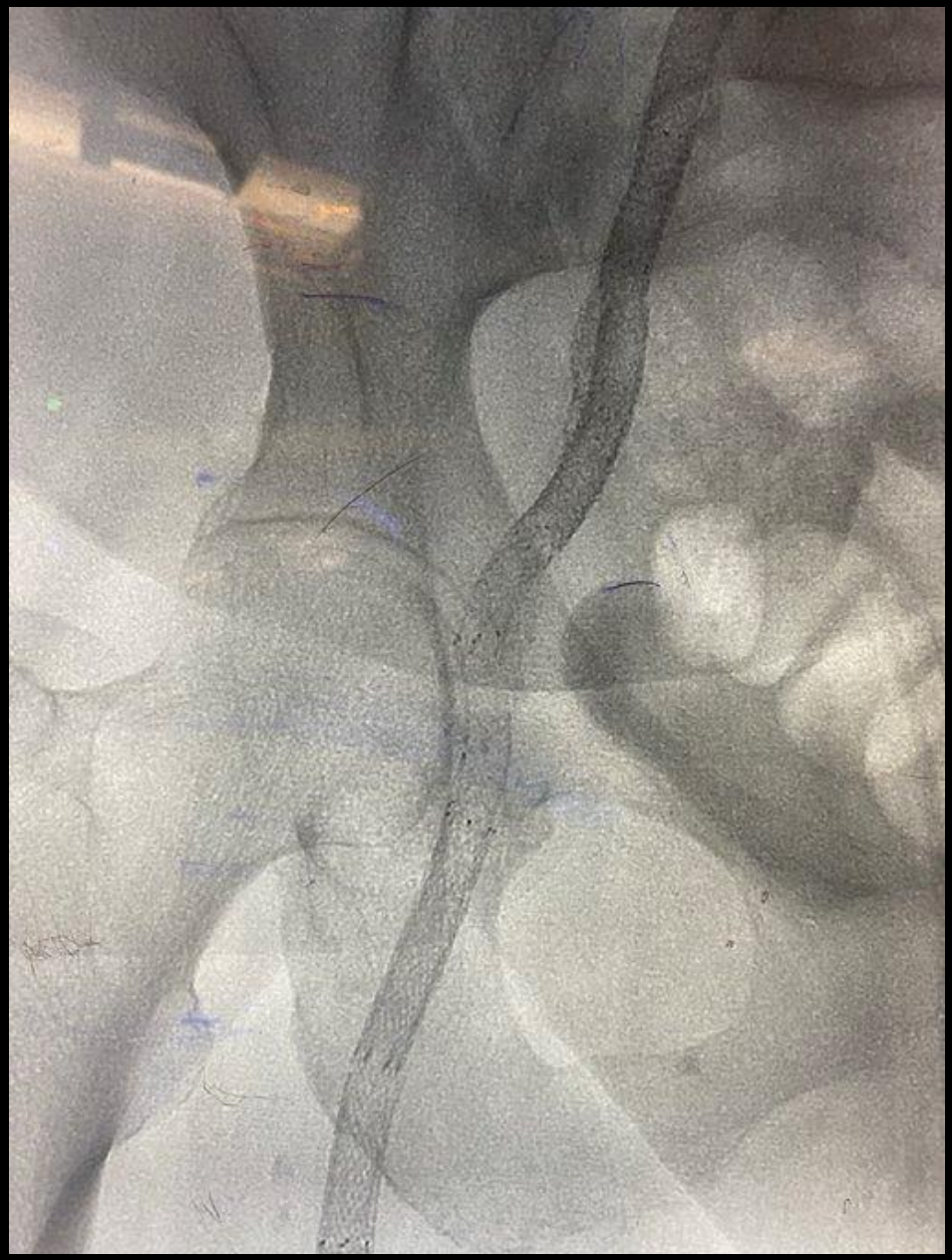
Marc (Anes) Bruce (Cards – retired) Bill (Vasc)






Spin that lesion!
DCB! Now Stent it!
STENT IT!


For shame! Lawrence, I'm surprised at you!




Endo?
Open?

RCTs for PAD (pre-2022)

BEST-CLI Trial: Overview

Prospective, randomized, multicenter, multispecialty, pragmatic clinical trial

Goal: to compare clinical effectiveness, functional outcomes and cost in patients with CLTI and infrainguinal PAD who are candidates for both open vascular surgery and endovascular therapy

BEST-CLI Study Design: Two Parallel Trials

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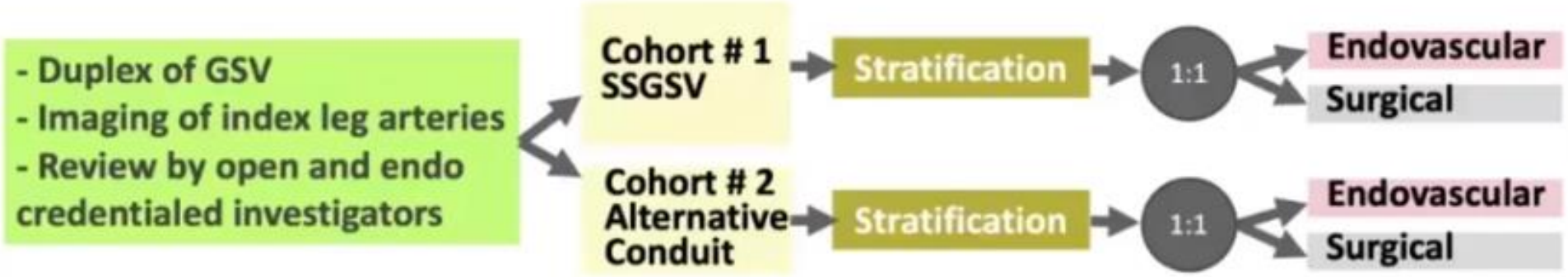
Patients with CLTI due to infrainguinal PAD
- not at excessive risk for surgery
- eligible for open and endo



Strata: Ischemic Rest Pain Alone vs. Tissue Loss
Significant Tibial Occlusive Disease vs. No Tibial Occlusive Disease

BEST-CLI Trial Design: Hypotheses

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- **Cohort #1 Patients with adequate single segment great saphenous vein (SSGSV)**

  Hypothesis: Bypass with SSGSV will outperform Endovascular Therapy

- **Cohort #2 Patients without adequate SSGSV**
  - *if randomized to Bypass Surgery, conduit may include arm vein, short saphenous vein, composite vein, cryopreserved vein, and prosthetic conduit*

  Hypothesis: Endovascular Therapy will outperform Bypass with Alternative Conduits

BEST-CLI Study Design: Endpoints

Primary Endpoint: Major Adverse Limb Event (MALE) or all-cause death

- All-cause death
- MALE
  - Above Ankle Amputation *or*
  - First Major Reintervention CLINICAL EVENTS COMMITTEE (CEC) ADJUDICATED
    - new bypass, surgical interposition graft, surgical thrombectomy, thrombolysis

Safety Endpoints: MACE (Major Adverse Cardiovascular Events)

- All cause Death
- MI CEC ADJUDICATED
- Stroke CEC ADJUDICATED

BEST-CLI Study Design: Endpoints

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Secondary Endpoints

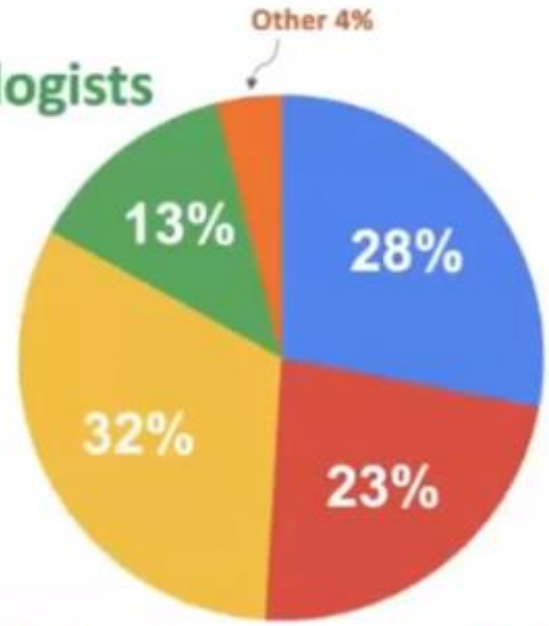
- Re-intervention and amputation free survival (RAFS)
- Amputation-free survival (AFS)
- Freedom from hemodynamic failure
- Freedom from clinical failure
- Freedom from MALE-POD (peri-operative death)
- Perioperative death (POD)
- Re-interventions (major and minor) in index leg
- Time to CLTI Resolution
- Presence of CLTI in Index Limb
- Number of re-interventions (major and minor) per limb salvaged

BEST-CLI International Participation

150 sites enrolled patients

BEST-CLI advocated for Multidisciplinary CLTI Teams

Vascular Surgeons, Interventional Cardiologists & Interventional Radiologists

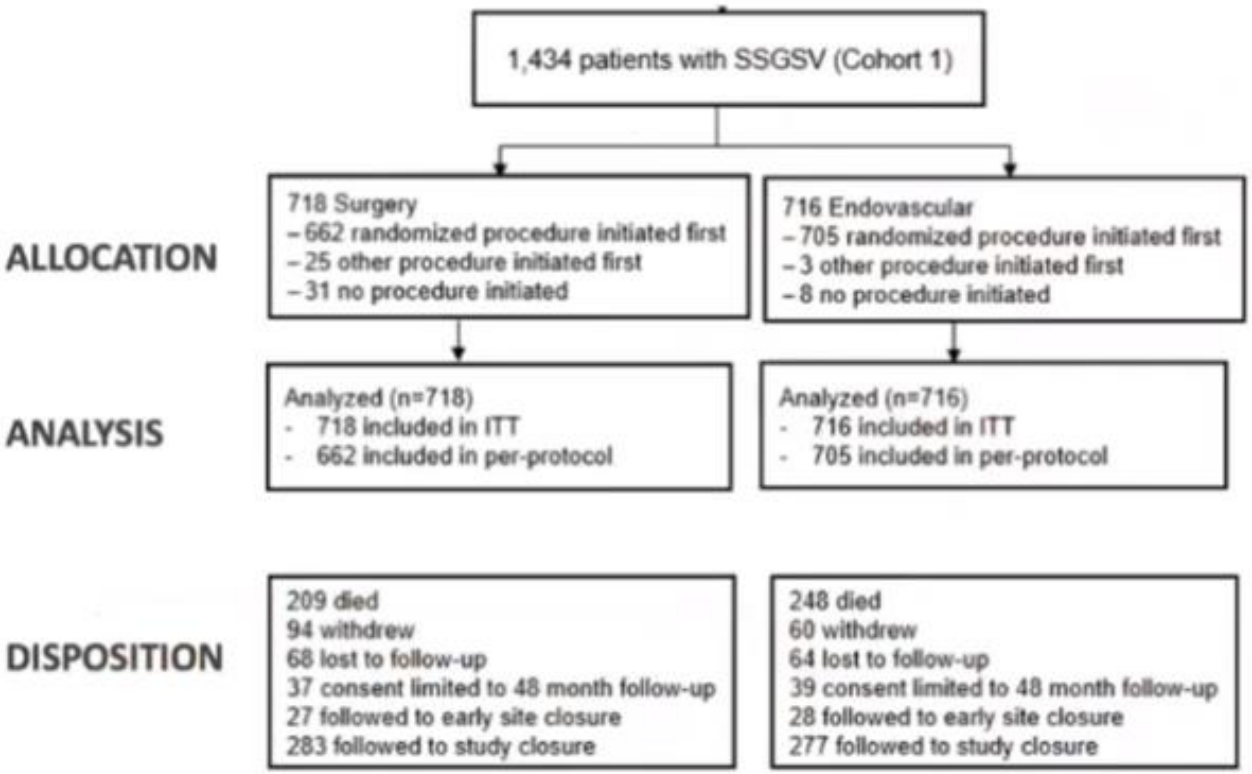


Vascular Surgeons only

Vascular Surgeons & Interventional Cardiologists

Vascular Surgeons & Interventional Radiologists

Cohort 1: Single Segment Great Saphenous Vein Available



Crossovers:

Surgery → Endo 3.5%

Endo → Surgery 0.4%

Follow up:

Median 2.7 years

Maximum 7.0 years

Lost to Follow up:

Surgery 9.5%

Endo 8.9%

Withdrawn:

Surgery 13.1%

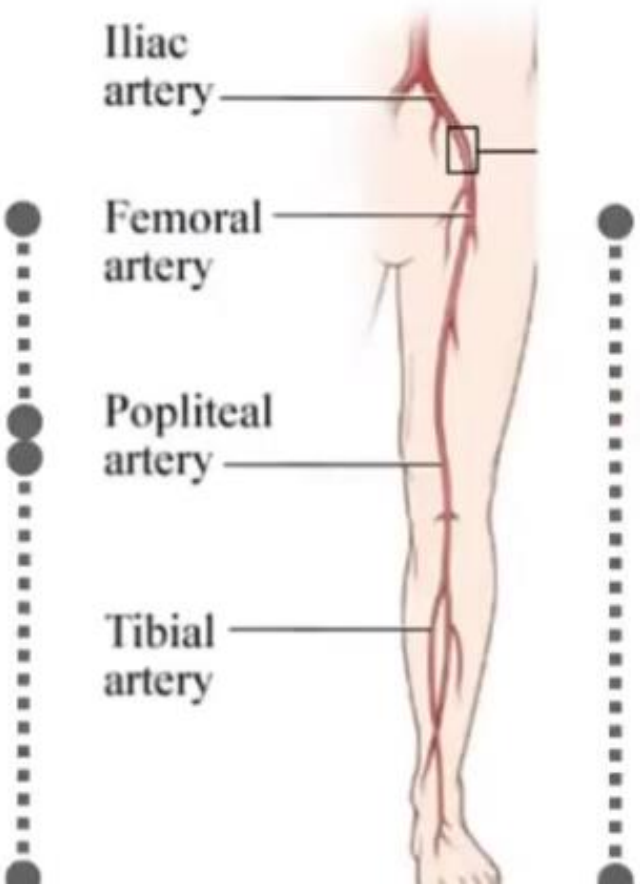
Endo 8.4%

Cohort 1: Revascularization Procedures - Bypass

698 procedures

307 Femoral-Popliteal

115 Popliteal-Tibial/Pedal



Femoral-Tibial/Pedal **276**

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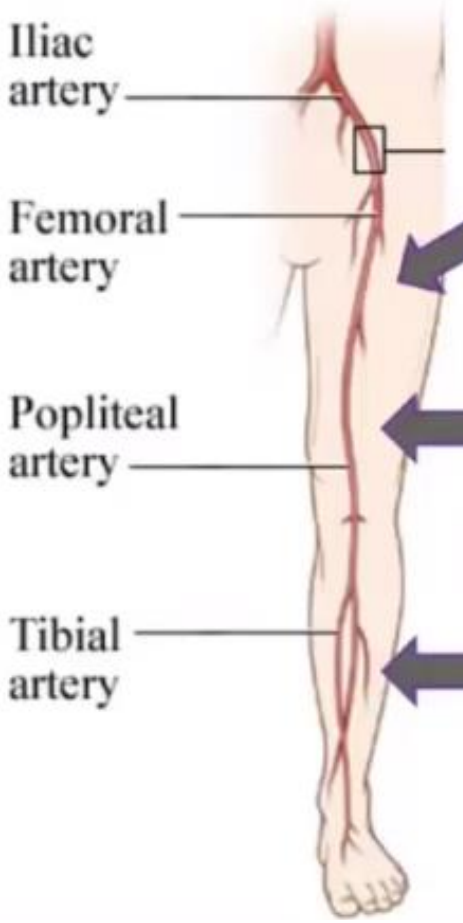
Cohort 1: Revascularization Procedures - Endovascular

1250 procedures



487 Superficial Femoral Artery Interventions

382 Popliteal Artery Interventions

381 Tibial/Pedal Artery interventions

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Endovascular Interventions

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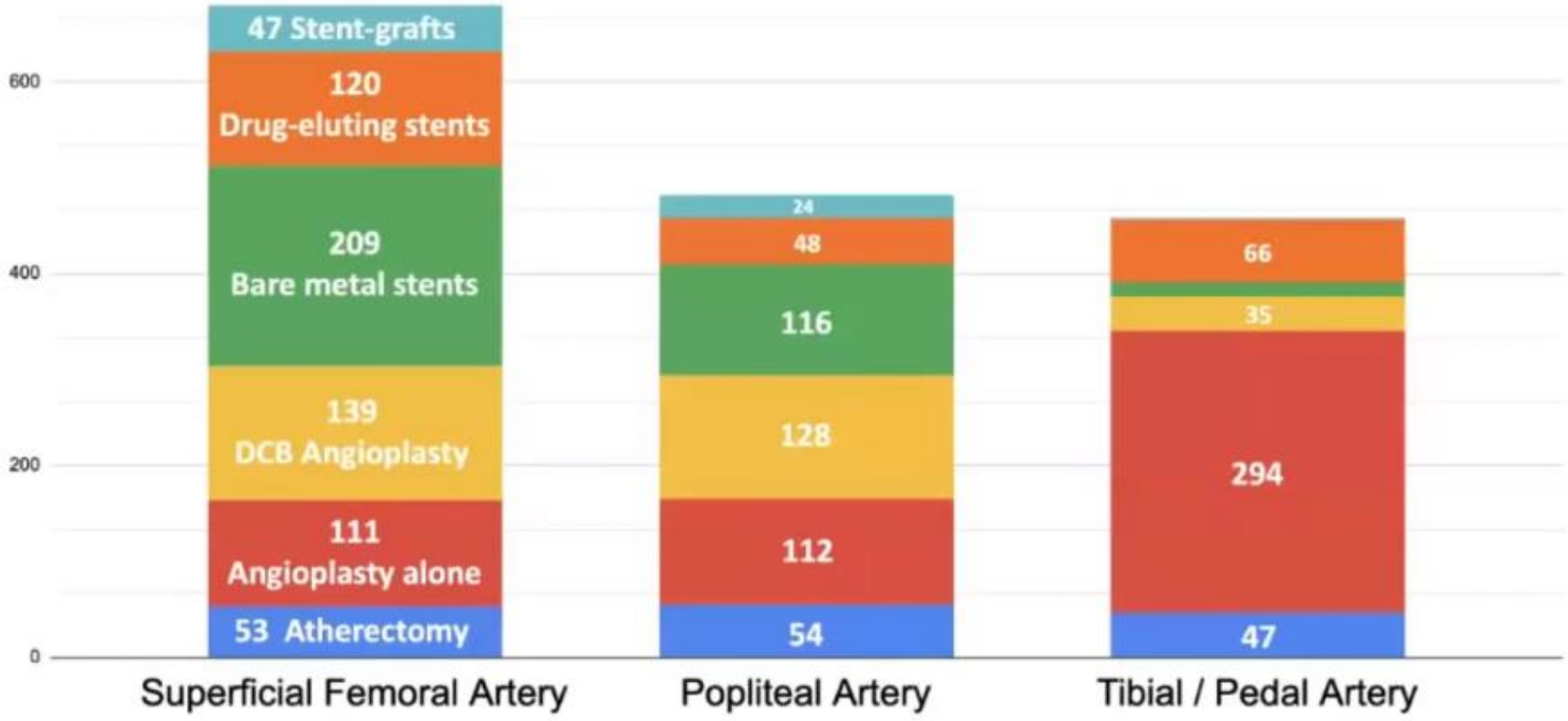

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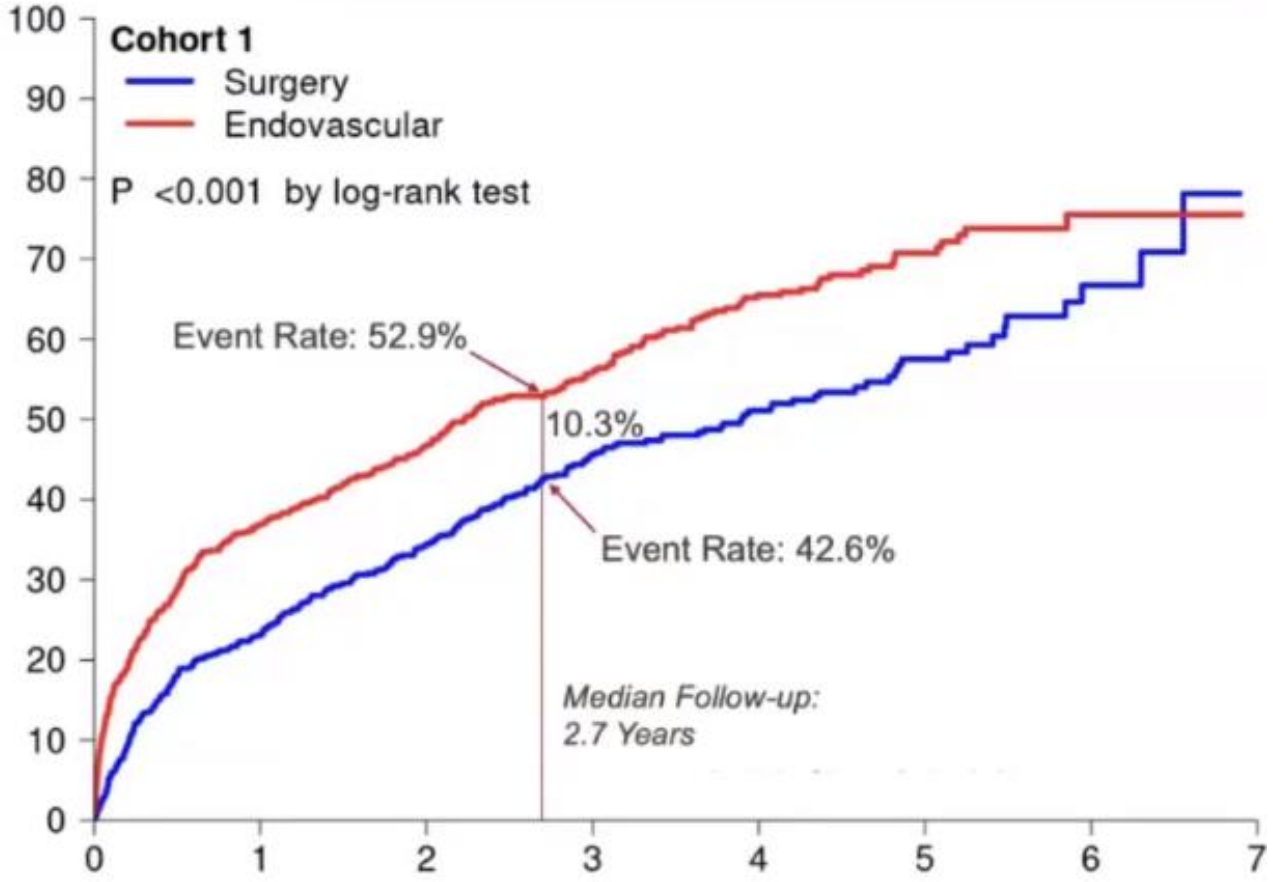
Primary Endpoint, and Components of the Primary Endpoint - Cohort 1

	Surgery (n=709)		Endovascular (n=711)		HR (95%CI)	P-value
Primary						
MALE or all cause death	302	42.6%	408	57.4%	**0.68 (0.59,0.79)**	<0.001
Secondary						
Major Reintervention on the Index Limb	65	9.2%	167	23.5%	**0.35 (0.27,0.47)**	<0.001
Above-ankle amputation of the index limb	74	10.4%	106	14.9%	**0.73 (0.54,0.98)**	0.04
All cause death	234	33.0%	267	37.6%	**0.98 (0.82,1.17)**	0.81

Primary Endpoint

MALE (Major Re-intervention, or Above-Ankle Amputation) or All-cause Death (%)



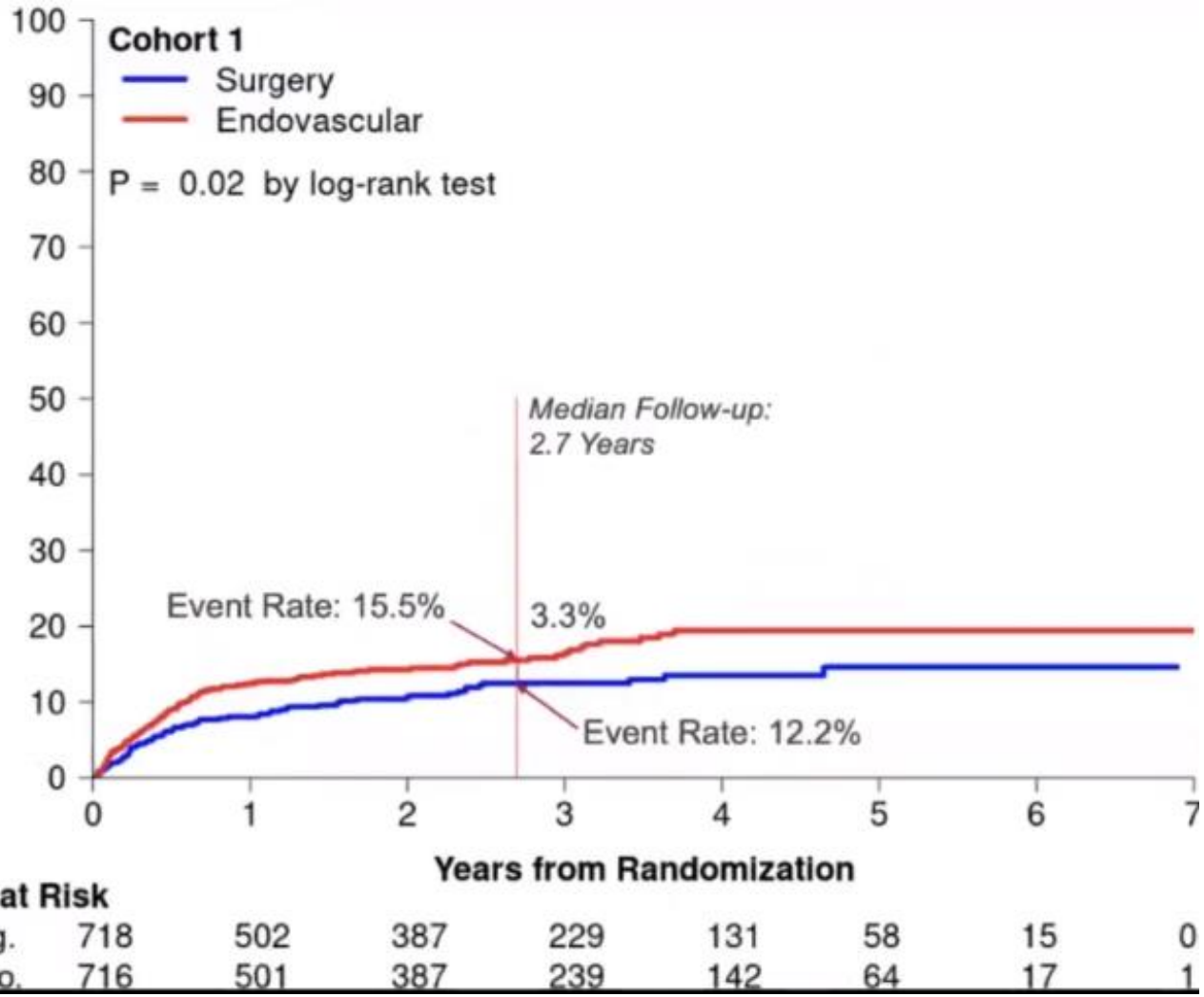
No. at Risk

Surg.	718	463	349	204	117	52	12	0
Endo.	716	404	304	175	102	46	14	0

BEST-CLI

Primary Endpoint Component

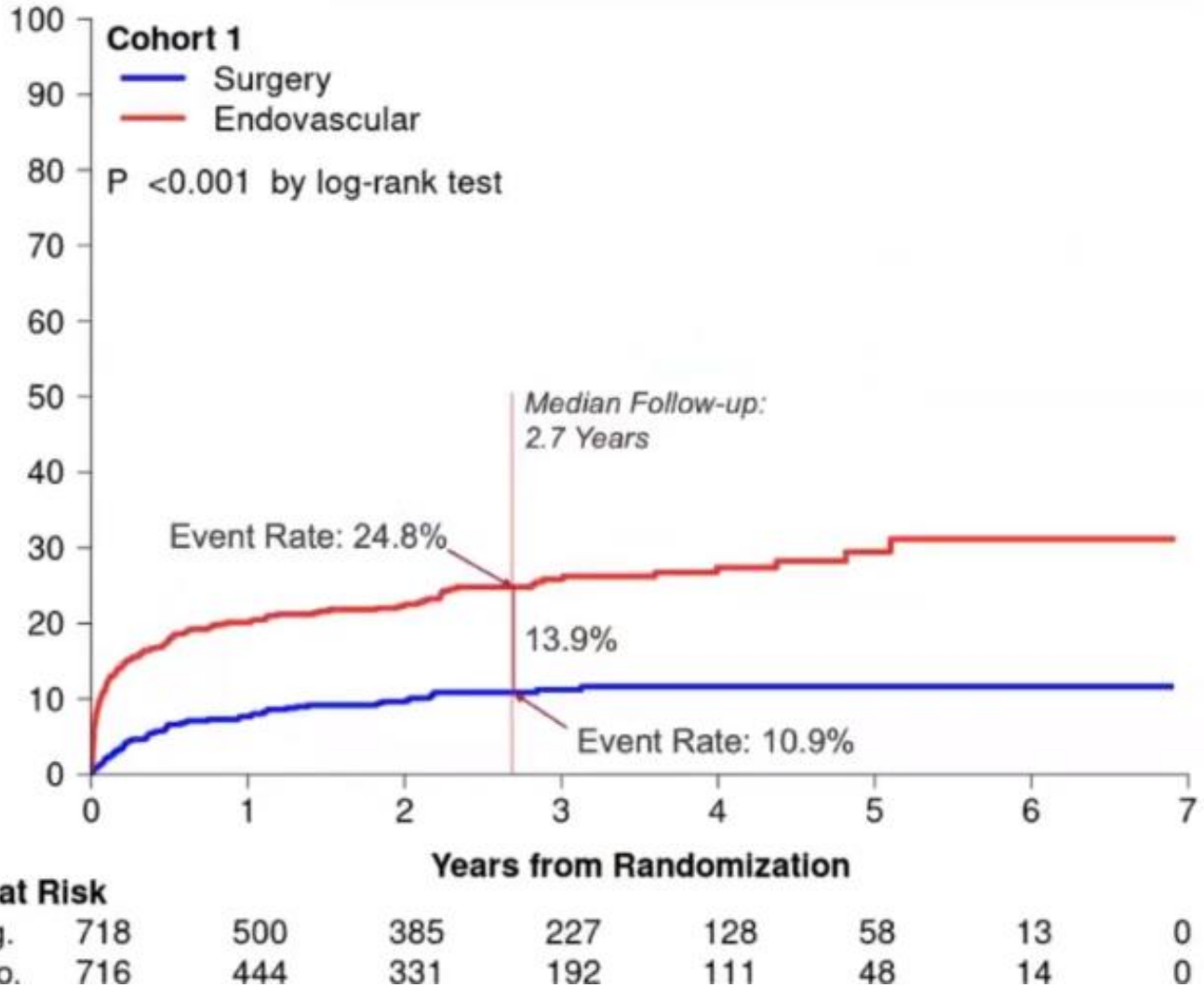
Above-Ankle Amputation (%)



BEST-CLI

Primary Endpoint Component

Major Re-intervention (%)

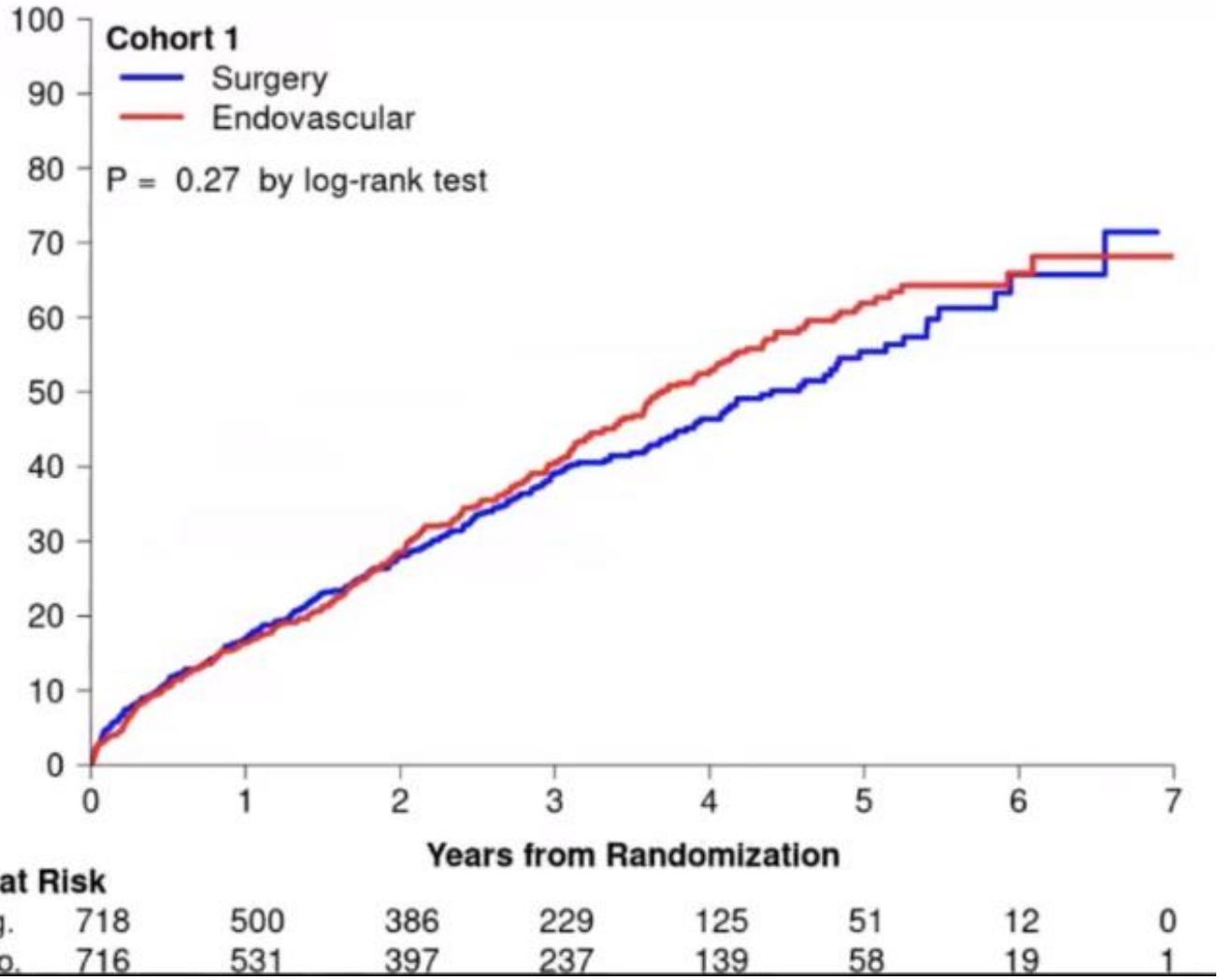


BEST-CLI

No. at Risk								
Surg.	718	500	385	227	128	58	13	0
Endo.	716	444	331	192	111	48	14	0

Primary Safety Endpoint

MACE (%)



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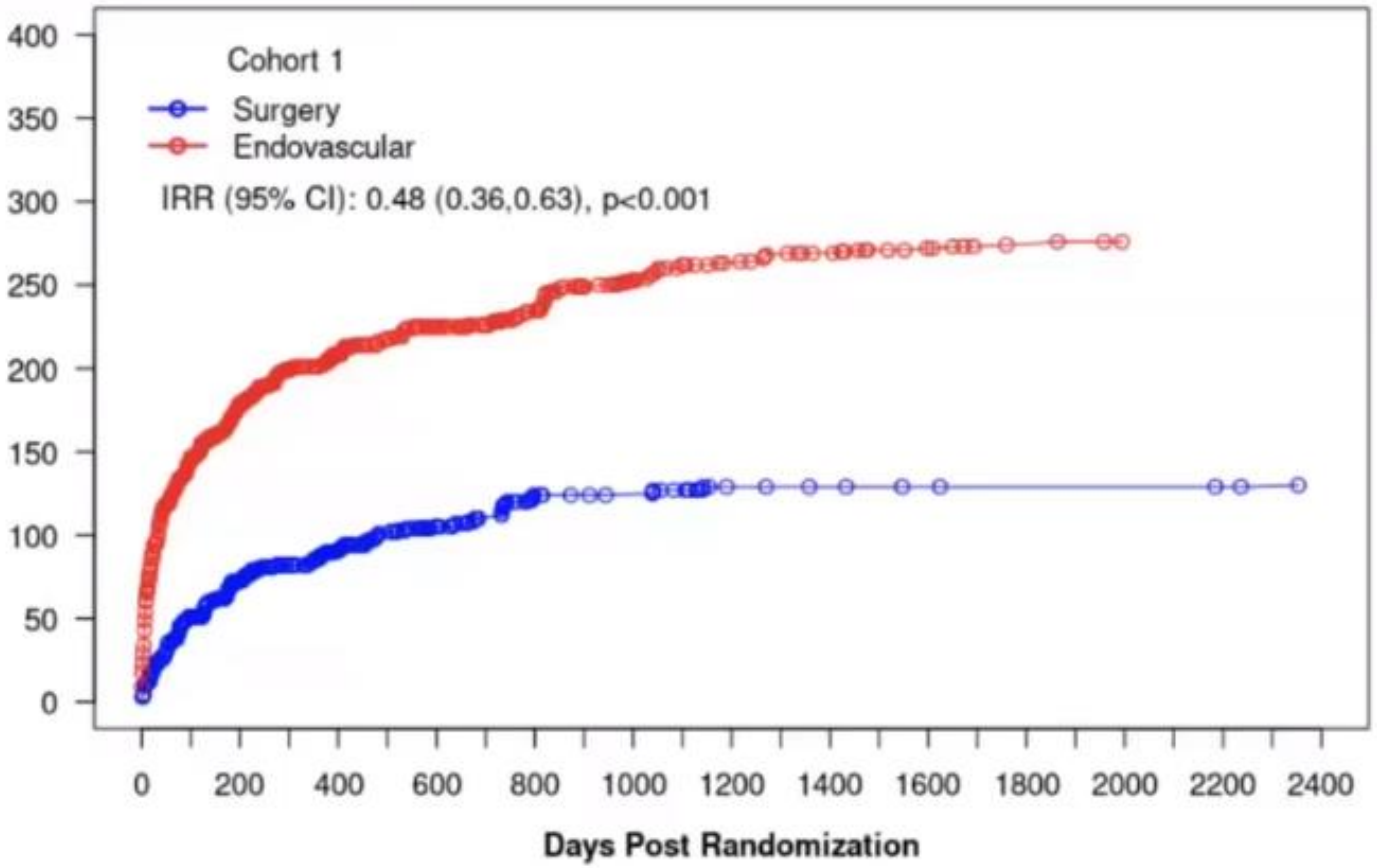
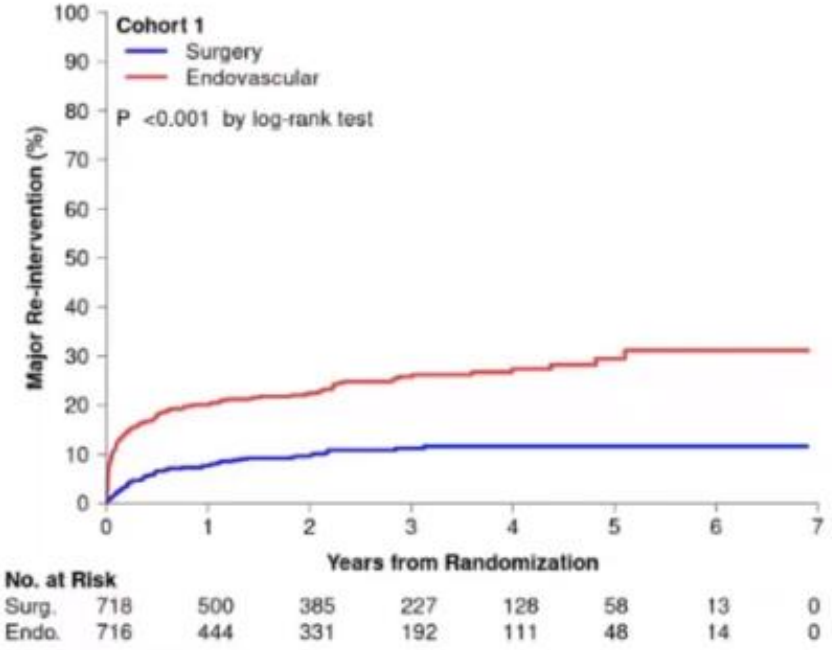
Secondary Endpoint

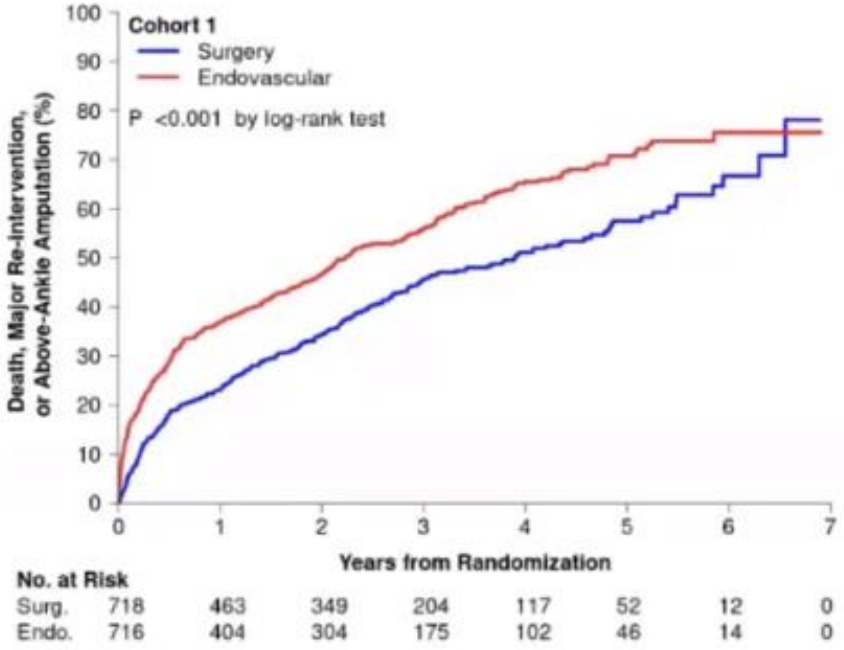
Total Number of Major Re-interventions



IRR: Incidence Rate Ratio

Is difference in curves driven by early failure in Endo Group?





99 of 233 (42.5%) first major re-interventions occurred within 30 days

-- 15 in Surgery Arm, 84 in Endo Arm

-- 80.8% reinterventions within Endo Arm was bypass alone

Technical Failure in the Endo Arm was 15%

--Of 108 cases of Technical Failure 66 patients (61%) were treated with bypass within 30 days

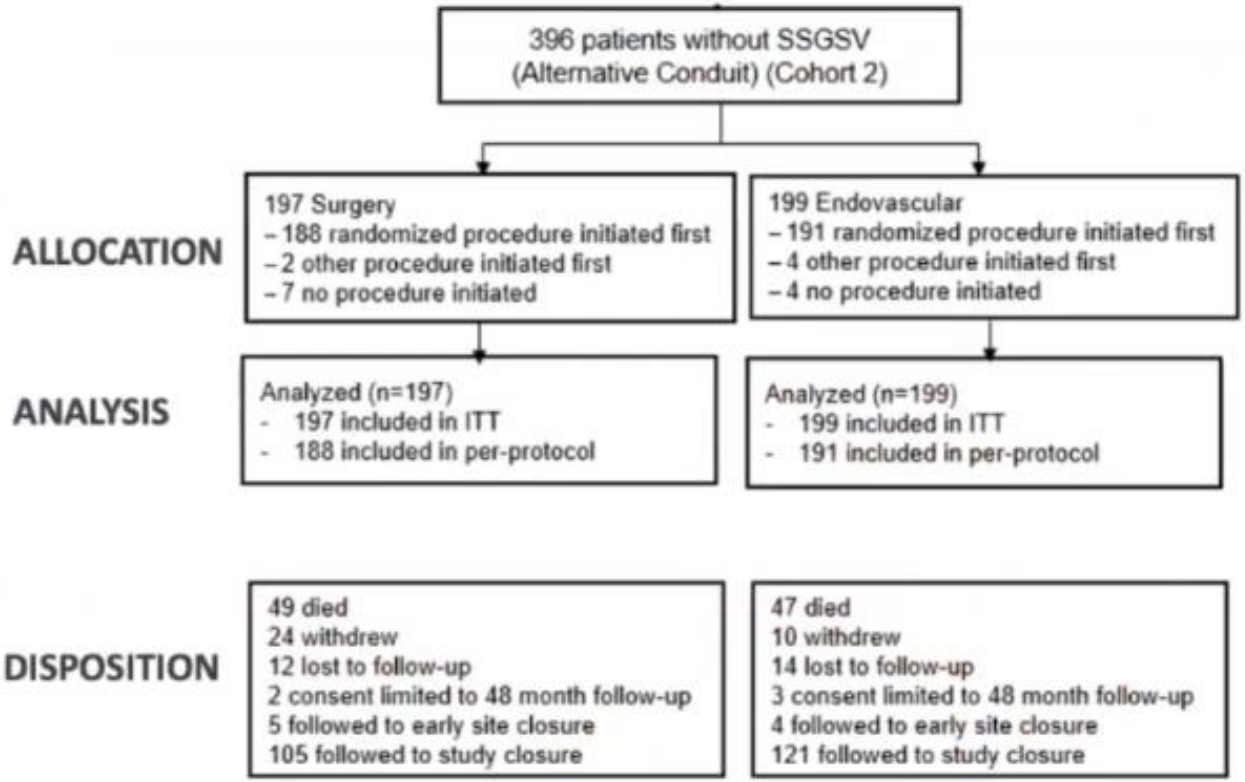
Sensitivity Analyses

- Excluding endo patients who had technical failure and a primary outcome event (MALE or death) or were censored within 30 days
- Excluding endo patients who had technical failure regardless of a primary event (MALE or death) or censoring within 30 days
- Excluding endo patients who either had a primary outcome event (MALE or death) or were censored within 30 days

	MALE or death Log-rank p value	Major Reintervention Log-rank p value
Time from randomization to the end of study, (excluded endo patients who had technical failure, and had event or censored within 30 days (i.e. excluded 69 patients from Endo group; 67 of them had major reintervention as their first event)	0.003	0.001
Time from randomization to the end of study, (excluded endo patients who had technical failure, regardless of they had the event or censored within 30 days. 108 endo patients excluded)	0.013	0.008
Time from 30 days to the end of study (excluded patients who had the primary outcome event or censored within 30 days). 195 patients (73 bypass (38 had event) and 122 endo (103 had event) patients excluded.	0.002	<0.001

Cohort 2: Patients without adequate SSGSV

BEST-CLI



Crossovers:

Surgery → Endo 1.0%

Endo → Surgery 2.0%

Follow up:

Median 1.6 years

Maximum 5.1 years

Lost to Follow up:

Surgery 6.1%

Endo 7.0%

Withdrawn:

Surgery 12.2%

Endo 5.0%

BEST-CLI

Primary Endpoint, and Components of the Primary Endpoint - Cohort 2

	Surgery (n=194)		Endovascular (n=199)		HR (95%CI)	P-value
Primary						
MALE or all cause death	83	42.8%	95	47.7%	**0.79 (0.58,1.06)**	0.12
Secondary						
Major Reintervention on the Index Limb	28	14.4%	51	25.6%	**0.47 (0.29,0.76)**	0.002
Above-ankle amputation of the index limb	29	14.9%	28	14.1%	**1.10 (0.65,1.87)**	0.72
All cause death	51	26.3%	48	24.1%	**1.15 (0.77,1.72)**	0.50

Study Limitations

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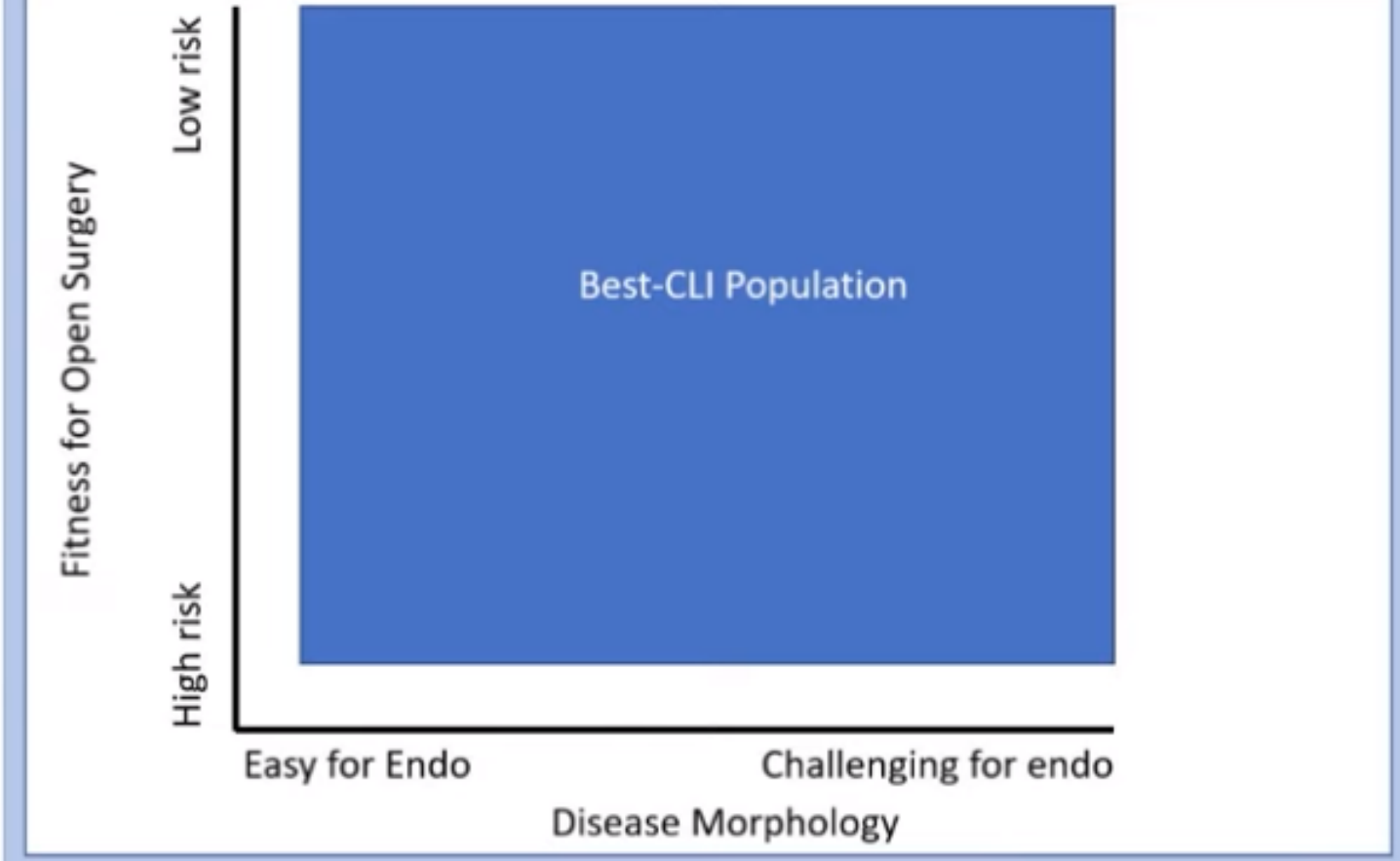
- Pragmatic Design
  - Possible selection and operator bias in enrollment and intervention
  - Equipoise and eligibility were determined locally and likely to be variable
  - Procedural heterogeneity
- Cohort 2 was likely underpowered
- Anatomic complexity yet to be evaluated
- Percentage of female patients lower than targeted
- Use of paclitaxel-coated balloons and stents during enrollment affected by Katsanos meta-analysis

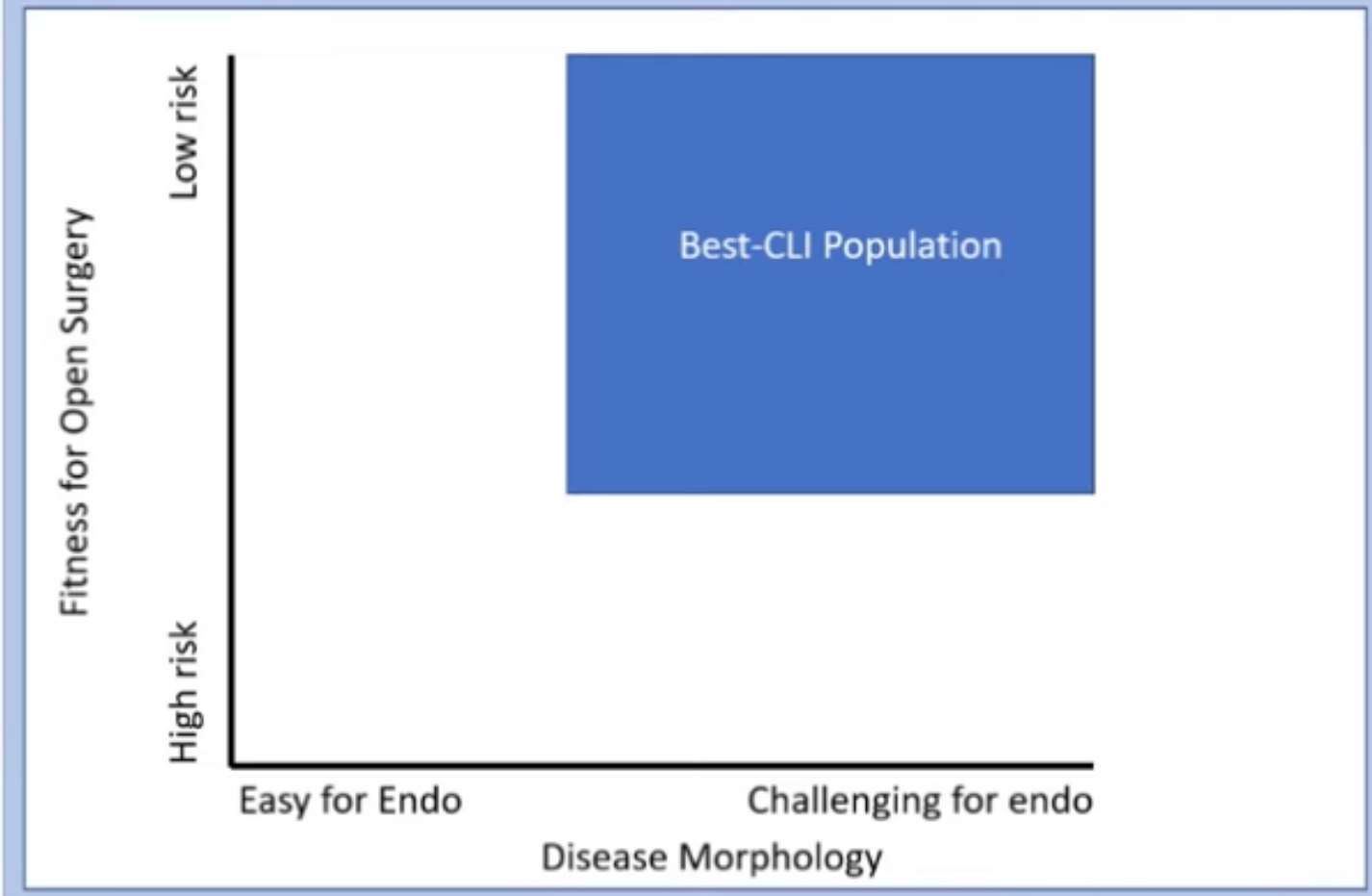
BEST-CLI Generalizability

The Challenge of Clinical Equipoise



BEST-CLI Generalizability

Challenge of Clinical Equipoise

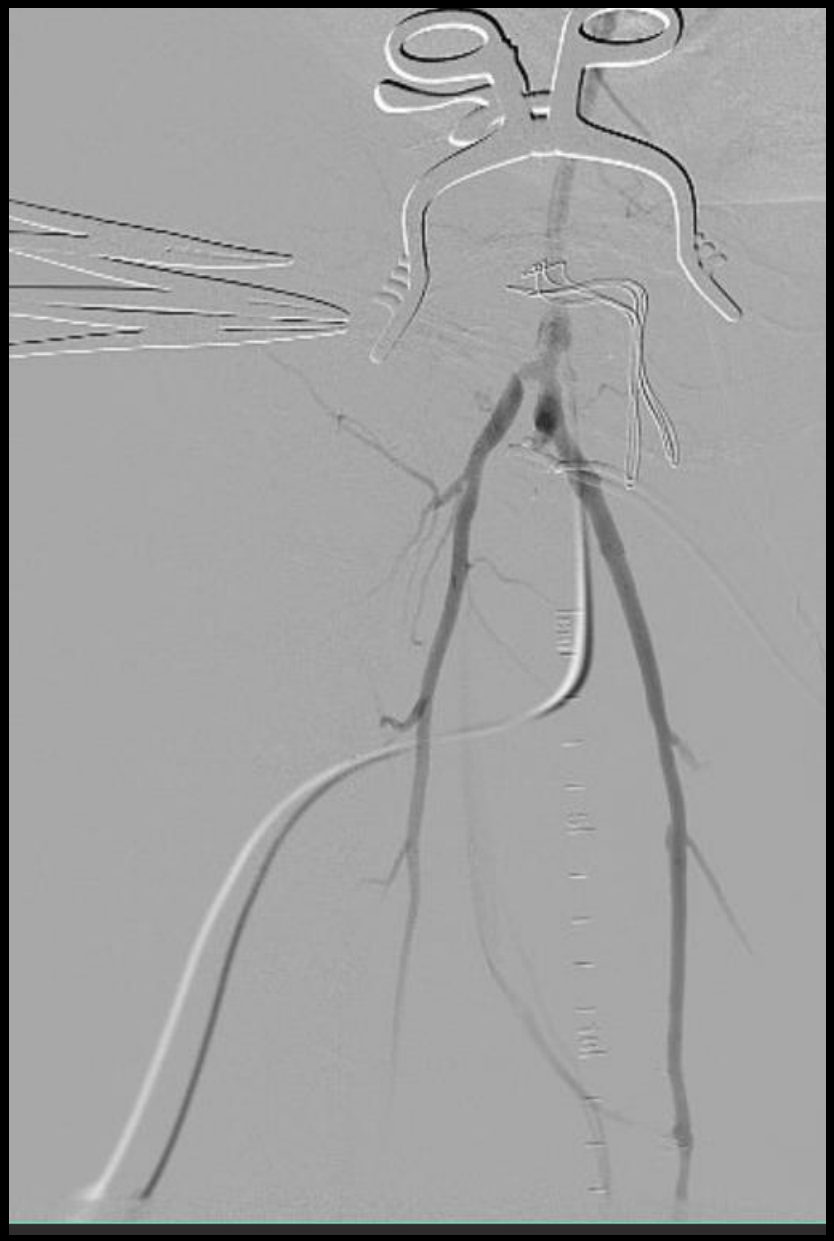


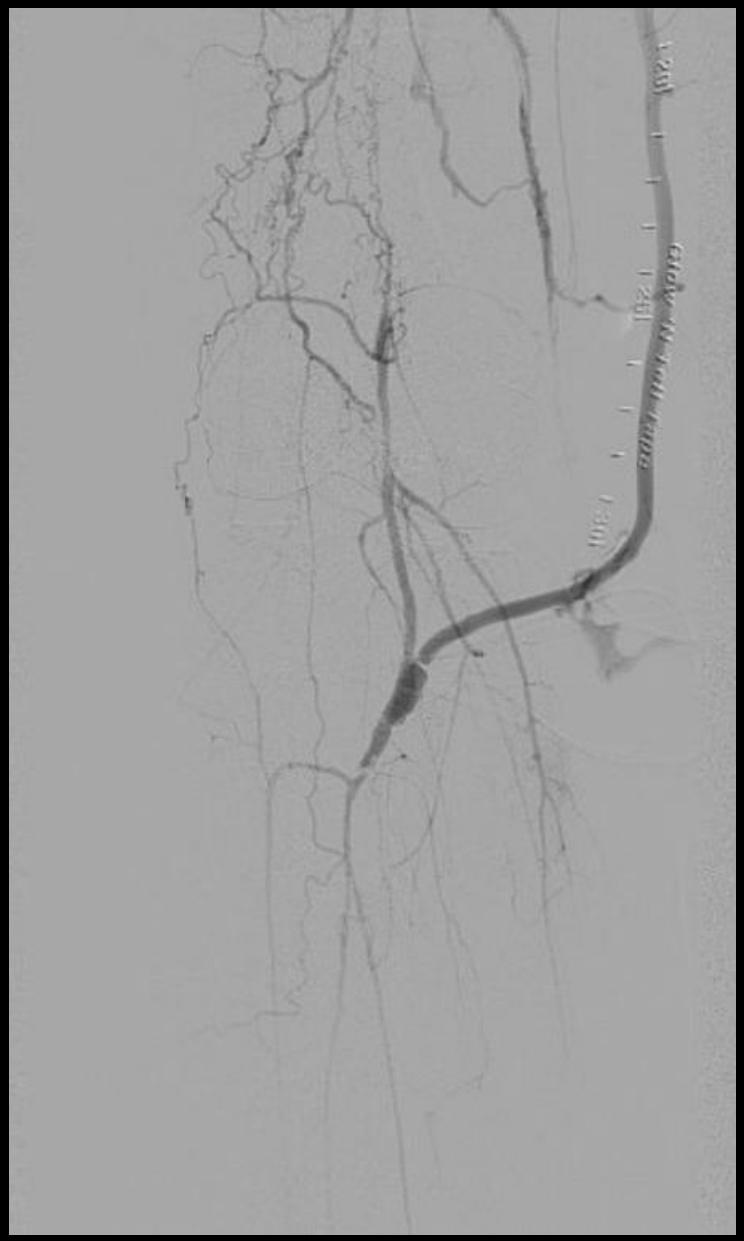
Summary

- Surgery was more effective than endovascular therapy among CLTI patients with adequate saphenous vein who were eligible for either strategy
  - Reduced MALE or all cause death: RRR = 32%; ARR = 10.3% @ 2.7 yrs; NNT = 10
  - Fewer major amputations : RRR = 27%; ARR = 3.3% @ 2.7 yrs; NNT = 30
  - Fewer major reinterventions: RRR = 65%; ARR = 13.9% @ 2.7 yrs; NNT = 7
- In patients who *did not* have adequate saphenous vein, there were no significant differences in the primary efficacy endpoint
- There were no differences in perioperative mortality or MACE
- Mortality and MACE were similar over the course of follow-up

Conclusions

- In CLTI, both surgical and endovascular revascularization are effective and safe
- Bypass with **adequate saphenous vein** is a more effective strategy for patients deemed suitable for both open and endovascular approaches
- Patients who are candidates for limb salvage should undergo an evaluation of surgical risk and conduit availability
- Bypass with adequate saphenous vein should be offered as a first line treatment option for suitable candidates with CLTI, as part of fully informed, shared decision-making
- Level 1 evidence from BEST-CLI does not support an "endovascular-first" approach to all patients with CLTI
- BEST-CLI supports a complementary role for open and endovascular revascularization strategies and highlights need for expertise in both for optimal care of these patients





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