Expanding Catheter Therapeutics

Below Knee Intervention

Seung-Whan Lee, MD, PhD

Asan Medical Center,
University of Ulsan College of Medicine, Seoul, Korea

BTK intervention

PCI-LIKE

PCI Like, but Not a Coronary Artery

- Technique of infrapopliteal artery angioplasty is quite different from iliac or SFA intervention.
- The vessel size of BTK is < 4 mm.
- Wires for angioplasty are 0.018 or 0.014 inch.
- Balloons sizes are between 3.5 mm and 2.0 mm.
- All equipments are quite similar to coronary devices.
- Technical demand for PTA is also percutaneous coronary intervention (PCI) like procedures.

Anatomic Challenges
Infrapopliteal disease

- Excellent collaterals normally
- One tibial artery is enough
- If Sx (+), it means severe and extensive diseases

Anatomic Challenges
Infrapopliteal disease

- High surgical risk patients: old age and other several comorbidities, such as DM and IHD

- Bypass surgery is technically demanding and has 1.8–6% perioperative mortality

Classification of disease

*T*ransatl*A*ntic inter*S*ociety *C*onsensus document

Preferred Treatment

- Group A consists of single stenoses shorter than 1 cm. **PTA**
- Group B consists of multiple focal (<1 cm) stenoses of tibial trifurcation.
- Group D consists of occlusions longer than 2 cm and diffusely diseased tibial vessels **Surgery**

However, due to the improvements in equipment and technique, endovascular therapy is now considered a feasible option in groups C–D. In addition the presence of co-morbid conditions and operator skills should be considered when making the final decision.

Why?

PTA for intrapopliteal lesions

- High risk population of Surgery
- Low-risk and minimally invasive procedure.
- Shorter intervention time (< 2 h); surgery (4h)
- Avoids general anesthesia
- Shorter the hospital stay.
- Possible repeat PTA.

How do you treat ?

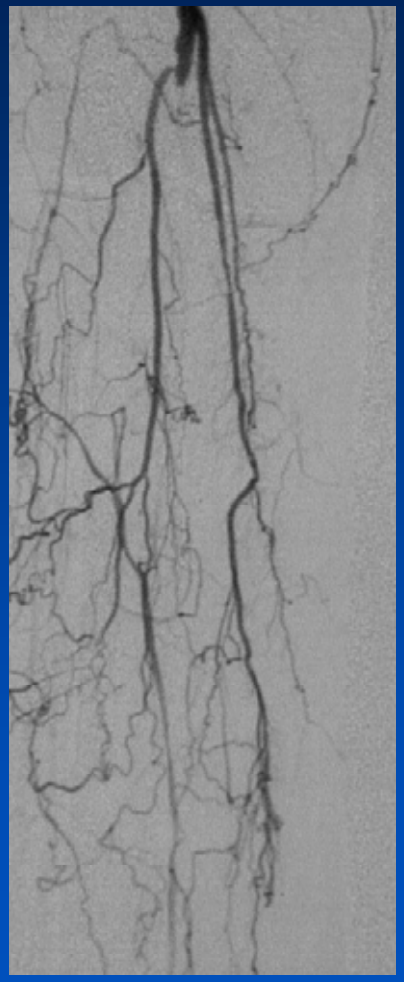
intrapopliteal lesions

- Significant co-morbidities
- Absence of suitable veins for bypass
- Inadequate sites for distal anastamosis

  -No angiographically visible tibial vessels,

  -Vessels ≤ 1 mm in diameter,

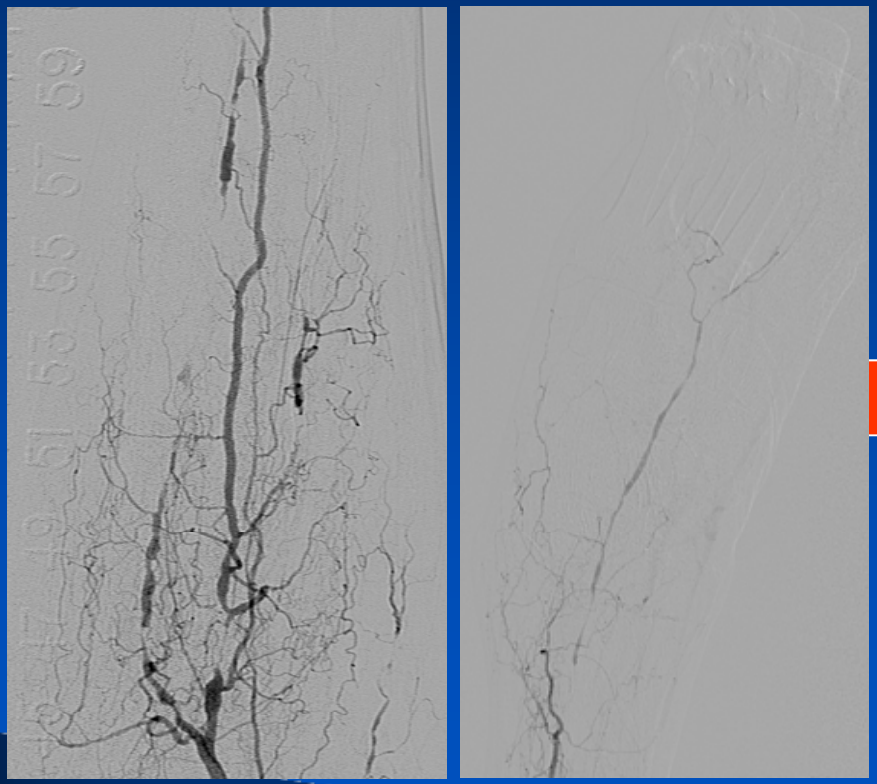
  -Diffusely diseased vessels



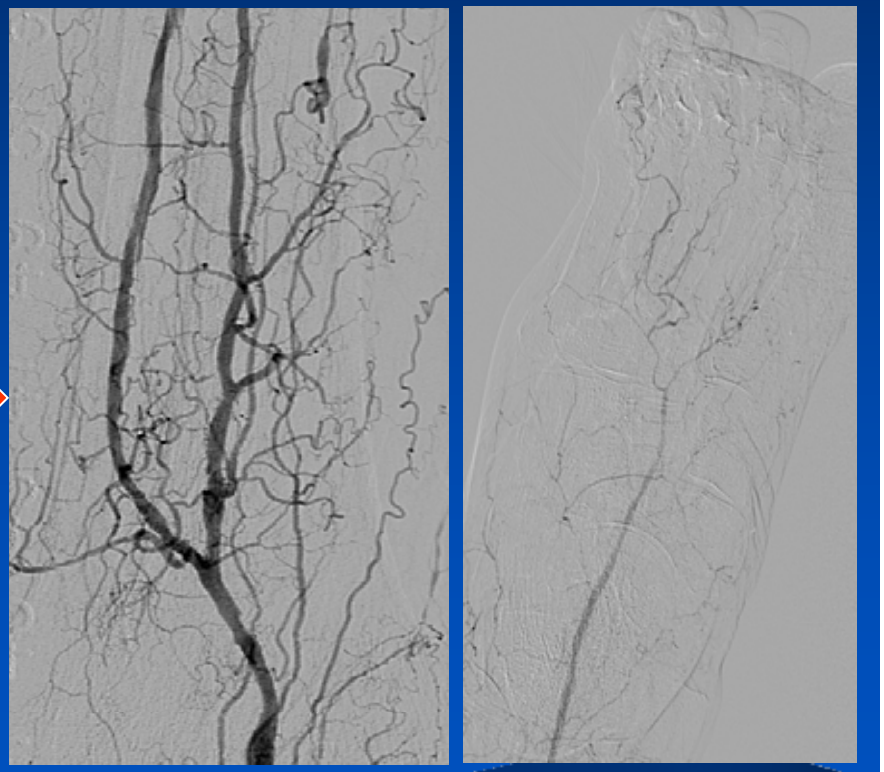
72yo Female

- DM foot ulcer, DM ESRD on HD

Before



After



Indication

PTA for intrapopliteal lesions

- Critical limb ischemia
- Moderate to severe claudication (debate)
- Prevention of proximal PTA or bypass failure

Critical limb ischemia

Clinical description	Fontaine class	Rutherford category	ABI	Symptom
Asymptomatic	I	0	0.85-1	none
Mild claudication	IIa	1	0.5-0.8	Walking distance>200m
Moderate claudication	IIb	2	0.5-0.8	Walking distance=100-200m
Severe claudication	IIb	3	0.5-0.8	Walking distance<100m
Ischemic rest pain	III	4	<0.5	Resting pain
Minor tissue loss	IV	5	<0.5	Minor tissue loss (ulceration)
Major tissue loss	IV	6	<0.5	Major tissue loss (gangrene)

Critical limb ischemia

- High mortality rate (46% at 5 years)
- 25% amputation despite attempts at revascularization.
- Successfully treated patients survive longer and have an better quality of life compared with amputated patients.
- Even in unavoidable amputation, infrapopliteal PTA may allow a lesser amputation in patients who would otherwise have needed a major amputation

Moderate to severe claudication

Clinical description	Fontaine class	Rutherford category	ABI	Symptom
Asyı		0	0.85-1	none
Mild	a	1	0.5-0.8	Walking distance>200m
Mod	b	2	0.5-0.8	Walking distance=100-200m
Seve	b	3	0.5-0.8	Walking distance<100m
Ische	I	4	<0.5	Resting pain
Minc	/	5	<0.5	Minor tissue loss (ulceration)
Majc	/	6	<0.5	Major tissue loss (gangrene)

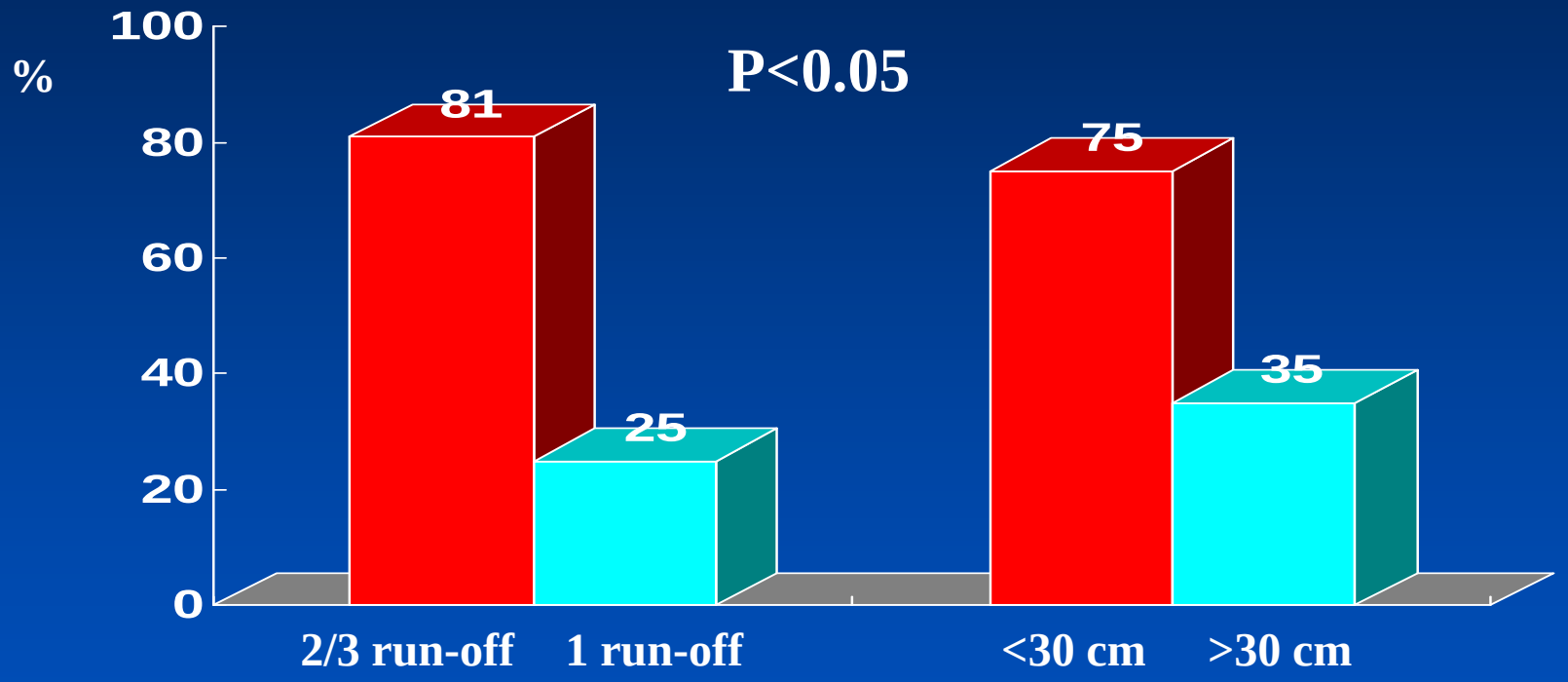
- PTA is recommended in simple lesion with moderate to severe claudication

Prevention of proximal PTA or bypass failure

- PTA is effective in treating graft stenosis
- Distal run-off influences long-term patency rates after femoropopliteal PTA or bypass surgery

Subintimal Angioplasty: factor affecting primary patency sfter SFA intervention

N=51, primary patency at 12 Mo:50%



Run-off vessels	0.30 (0.11-0.87)
Length of occlusion (cm)	1.02 (1.00-1.04)

Lazaris AM et al. Eur J Vasc Endovasc Surg 2006; 32: 668-674

Which vessels ?

Clinical goals

- **Limb salvage**
- **Symptom improvement**

Which vessels ?

- One tibial artery is enough
- The more is the better
- Tibial artery is better than peroneal artery

Angiosome Concept

Angiosome – 3D anatomic unit fed by a source artery (skin, subcutaneous tissue, fascia, muscle and bone)

Taylor, et al. Br J Plastic Surgery 1987;40:113

Angiosome concept

Six c

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- A
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- P
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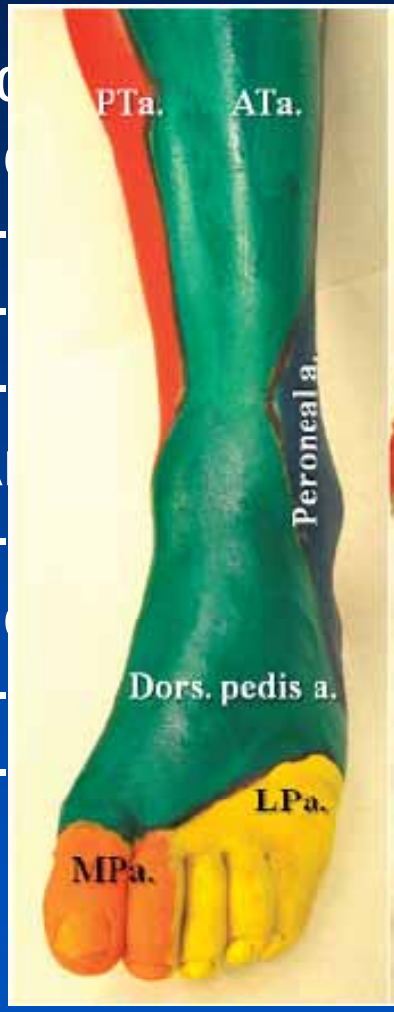
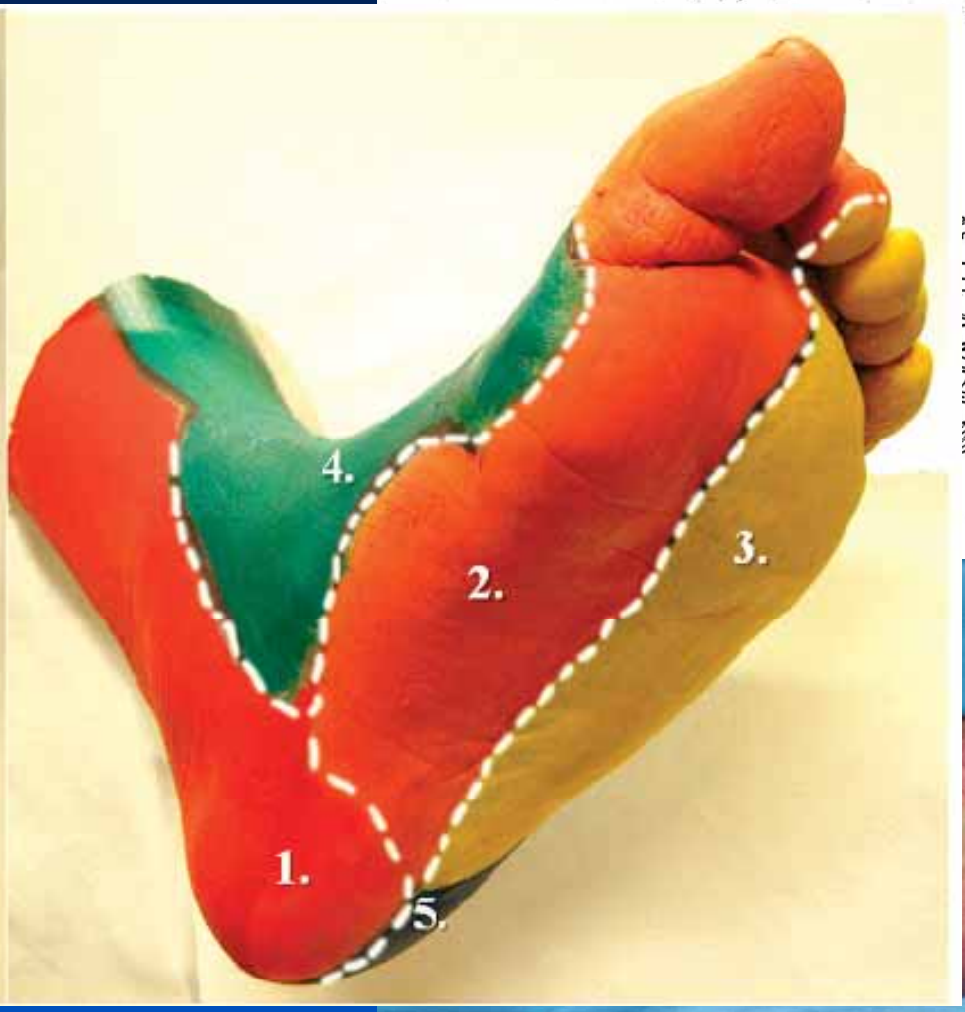
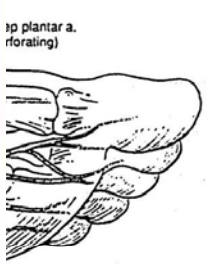
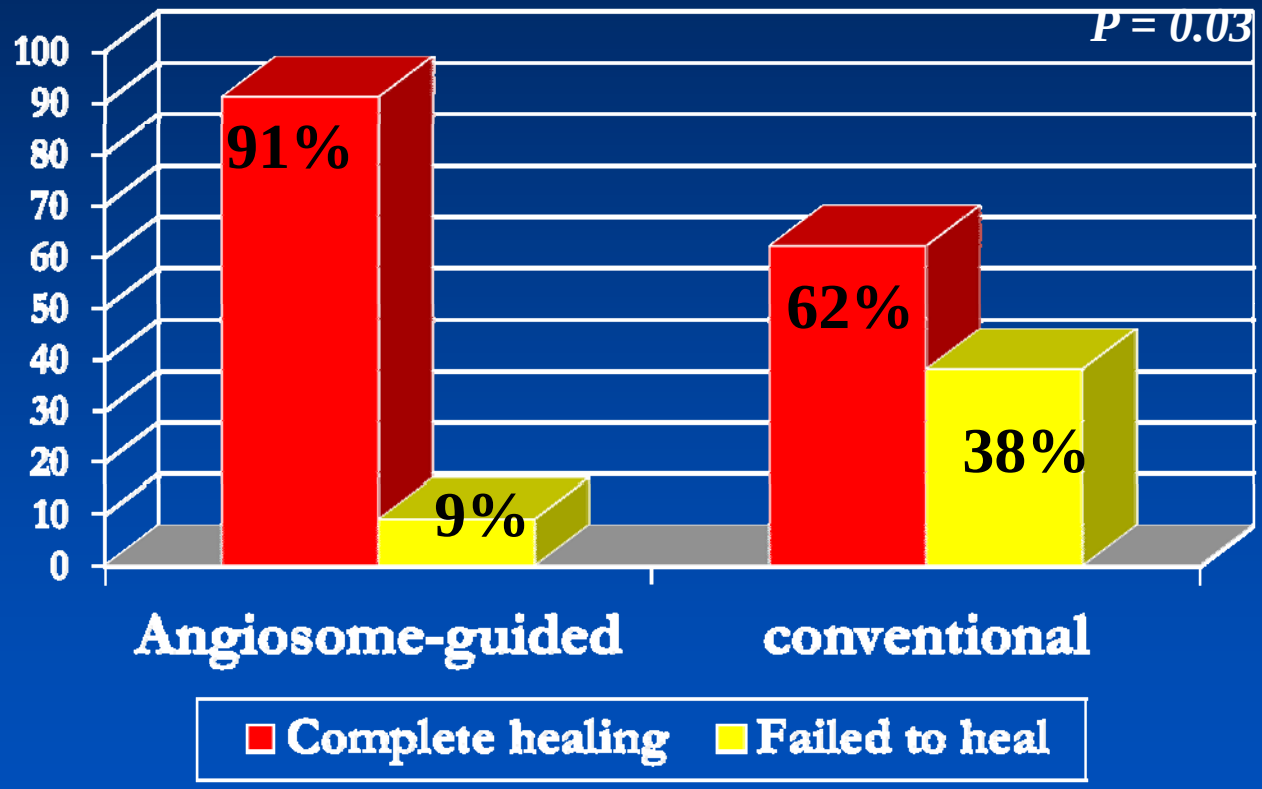






Angiosome-targeted Intervention



Neville RF, et al. Ann Vasc Surg 2009; 23(3):367-373

RESULTS of PTA

Technical success

- The technical success rates : 78% to 100%.
- Occlusion length >10 cm is an adverse factor both for technical success and patency.

Complications of PTA

- Complication rate : 2-6%
- **Puncture site hematoma**
- Acute arterial occlusions by spasm or dissection: (stent or liberal use of antispasmodics)
- Embolic occlusion: thrombolysis or thrombectomy
- Arterial perforations (3.7%): rarely require intervention
- 30-day mortality : 1.7% vs. bypass surgery :1.8-6%

Results of infrapopliteal disease

- 144 patients/155 PTA
  - 86% with critical limb ischemia
  - 66% with DM, 45% with renal failure
  - TASC A (7%), B (18%), C (39%), D (35%)
- Successful Revascularization in 95% of lesions
- 40-month Follow-Up
  - Primary patency--62%
  - Ulcer healing --64%
  - Limb salvage—86.2%
  - **Survival---54%**

Conrad MF., et al. J Vasc Surg 2009;50:799-805

Meta-analysis of BTK PTA series:

Table II. Meta-analysis results of crural percutaneous transluminal angioplasty and popliteal-to-distal bypass[a]

Result	*1 month*	*6 months*	*1 year*	*2 years*	*3 years*
Primary patency					
PTA	77.4 ± 4.1	65.0 ± 7.0	58.1 ± 4.6	51.3 ± 6.6	48.6 ± 8.0
Bypass	93.3 ± 1.1	85.8 ± 2.1	81.5 ± 2.0	76.8 ± 2.3	72.3 ± 2.7
P	<.05	<.05	<.05	<.05	<.05
Secondary patency					
PTA	83.3 ± 1.4	73.8 ± 7.1	68.2 ± 5.9	63.5 ± 8.1	62.9 ± 11.0
Bypass	94.9 ± 1.0	89.3 ± 1.6	85.9 ± 1.9	81.6 ± 2.3	76.7 ± 2.9
P	<.05	<.05	<.05		
Limb salvage					
PTA	93.4 ± 2.3	88.2 ± 4.4	86.0 ± 2.7	83.8 ± 3.3	82.4 ± 3.4
Bypass	95.1 ± 1.2	90.9 ± 1.9	88.5 ± 2.2	85.2 ± 2.5	82.3 ± 3.0
Patient survival					
PTA	98.3 ± 0.7	92.3 ± 5.5	87.0 ± 2.1	74.3 ± 3.7	68.4 ± 5.5
Bypass	NA	NA	NA	NA	NA

NA, Estimates not available; *PTA*, percutaneous transluminal angioplasty.
[a]Values are pooled estimate and standard error.

30 papers published between 1990-2006

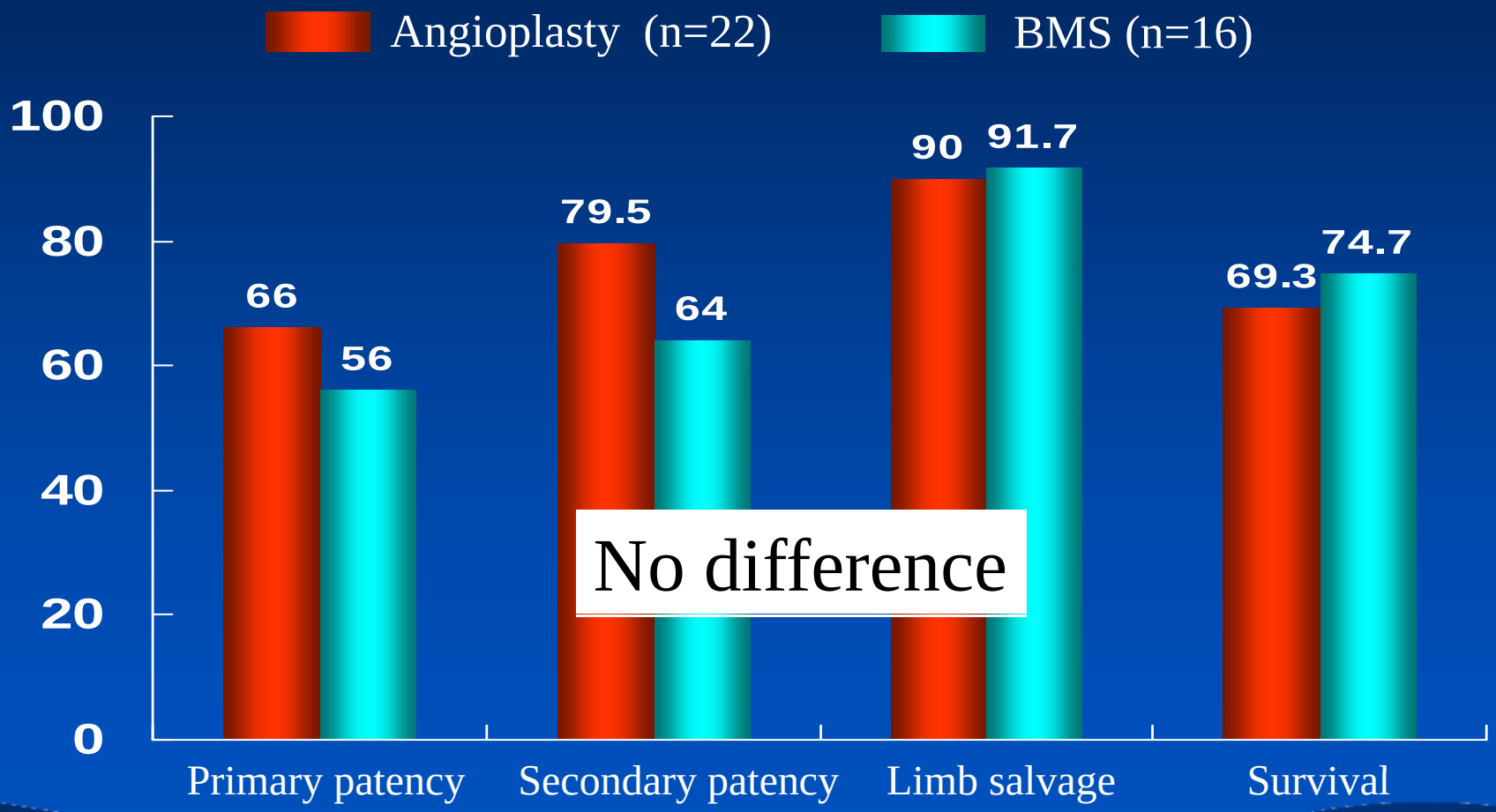
2557 patients

Romiti M et al. JVS 2008;47:975-981

PTA vs. BMS

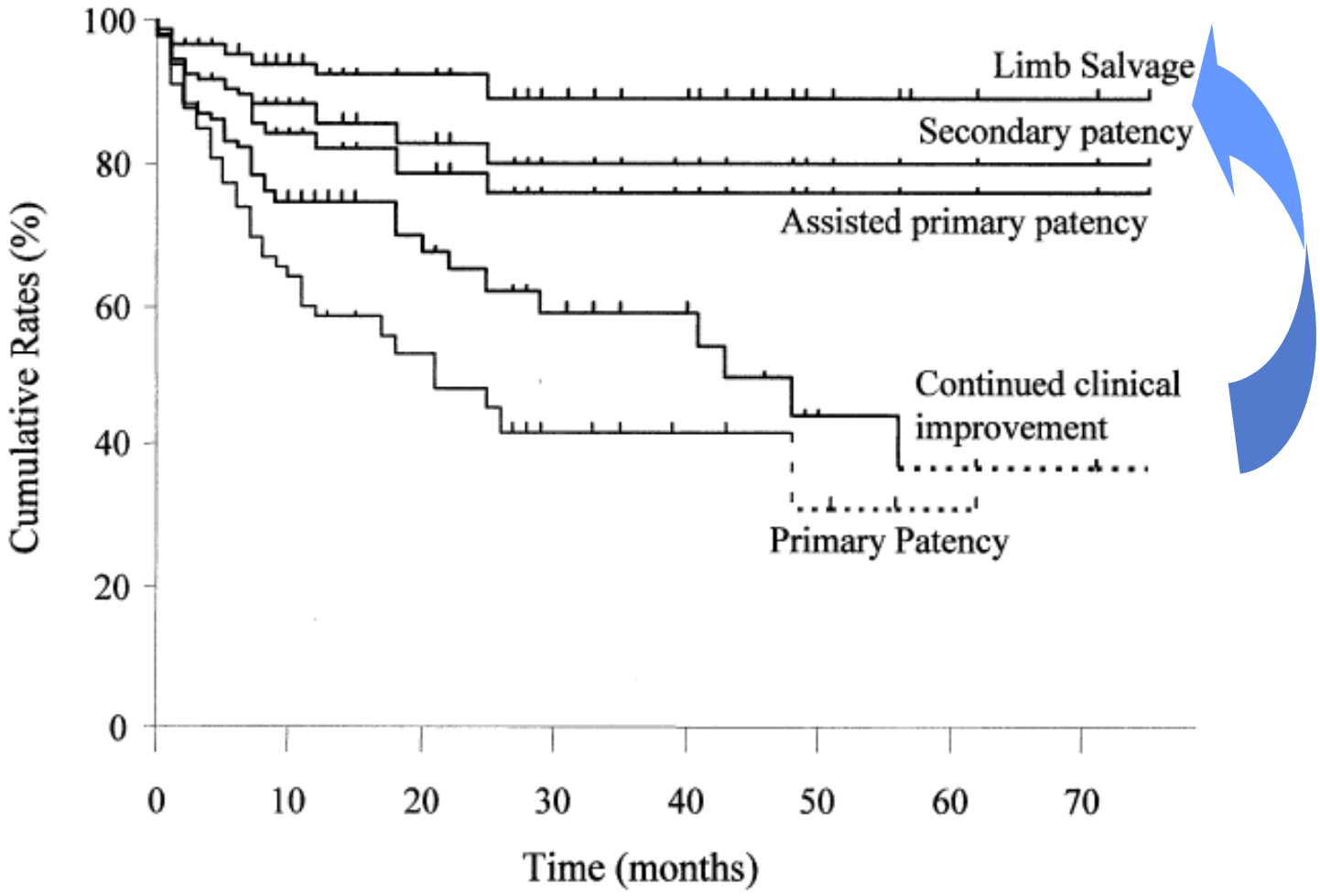
Randomized trial (length: 2-15 cm)

Clinical outcomes @ 12 months



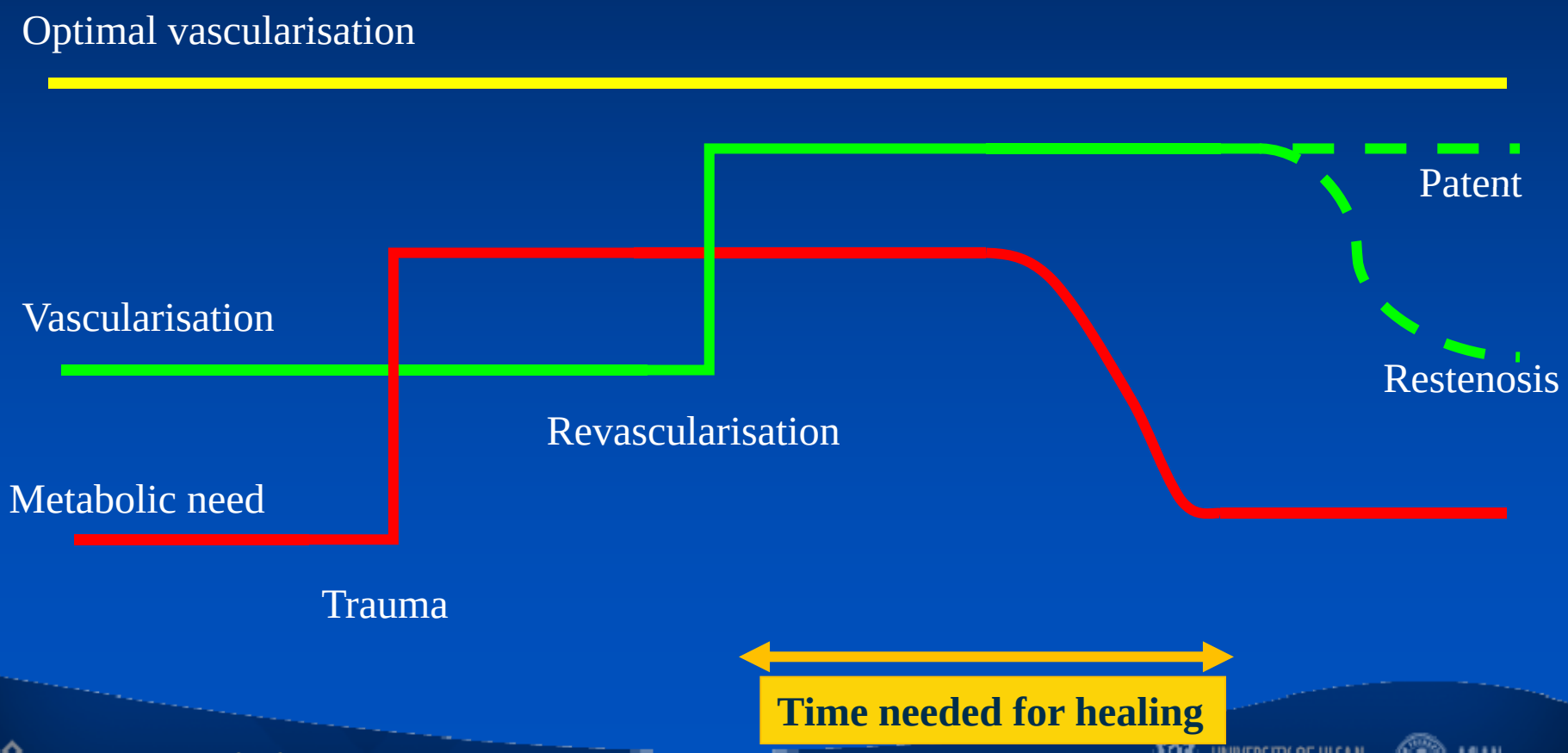
Radon C, et al. Cardiovasc Intervent Radiol 2010; 33:260–269

Discrepancy between primary patency and limb salvage



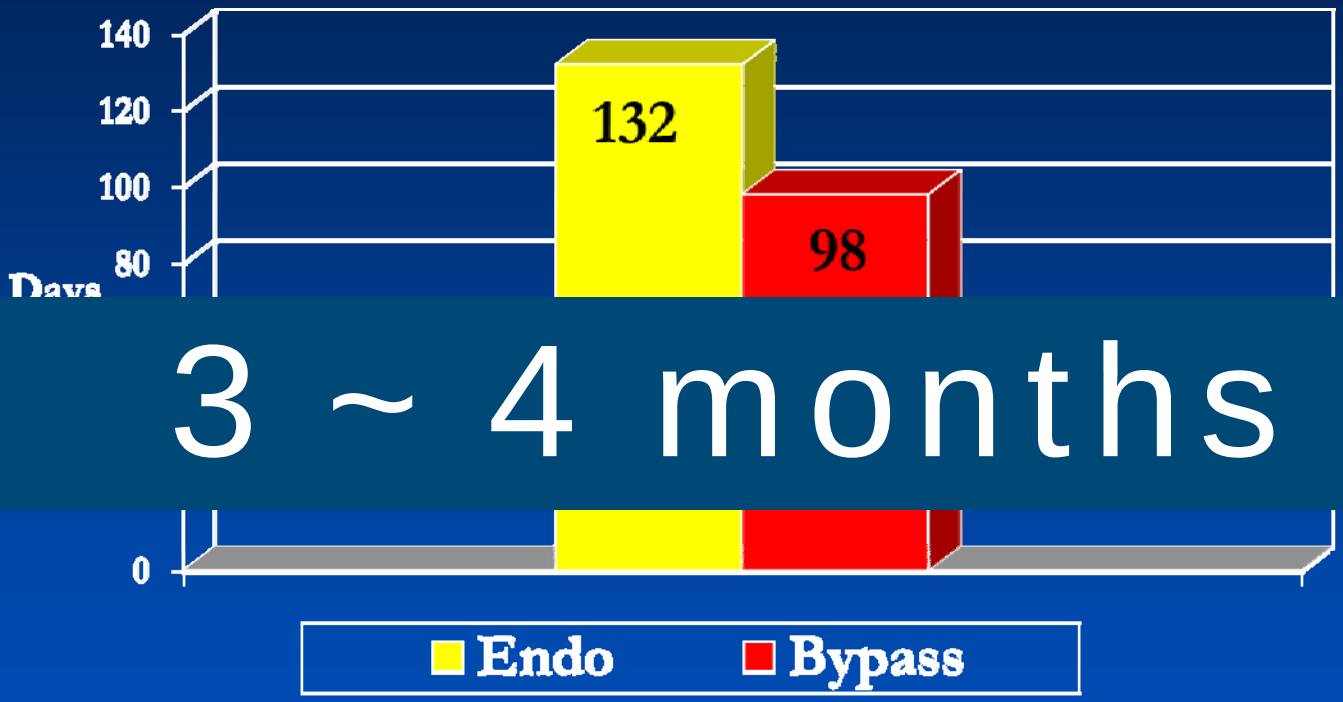
Kudo T et al. JVS 2005;41:423-435

Is long term patency needed for ulcer healing ?



Vermassen F 2010

Time to complete healing



3 ~ 4 months

Group	Bypass	Endovascular	P value
Wound size	142	148	
A (0 – 5mm)	84 days	105 days	P = NS
B (5mm – 20mm)	102 days	128 days	P = NS
C (> 20mm)	115 days	164 days	P = 0.01

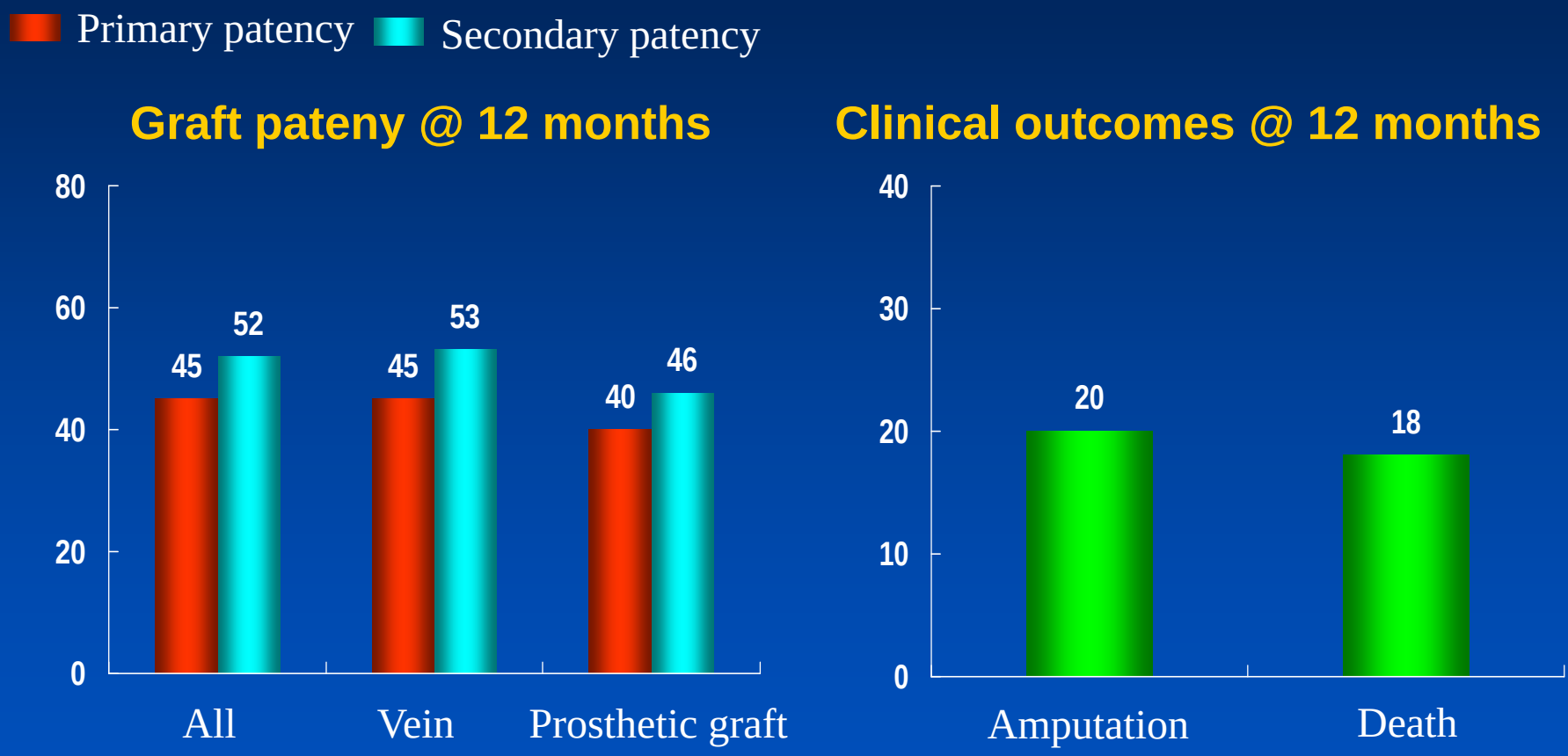
Discrepancy between primary patency and clinical success

- This feature is more prominent in patients with tissue loss, especially with ulcers, than in those with rest pain.
- Ulcer healing reduces the oxygen demand and as a consequence less blood flow is generally required to maintain tissue integrity compared with the amount required for initial ulcer healing.
- Collaterals may therefore be sufficient to preserve tissue integrity if there is no further injury.

RESULTS of Surgery

Result of bypass surgery

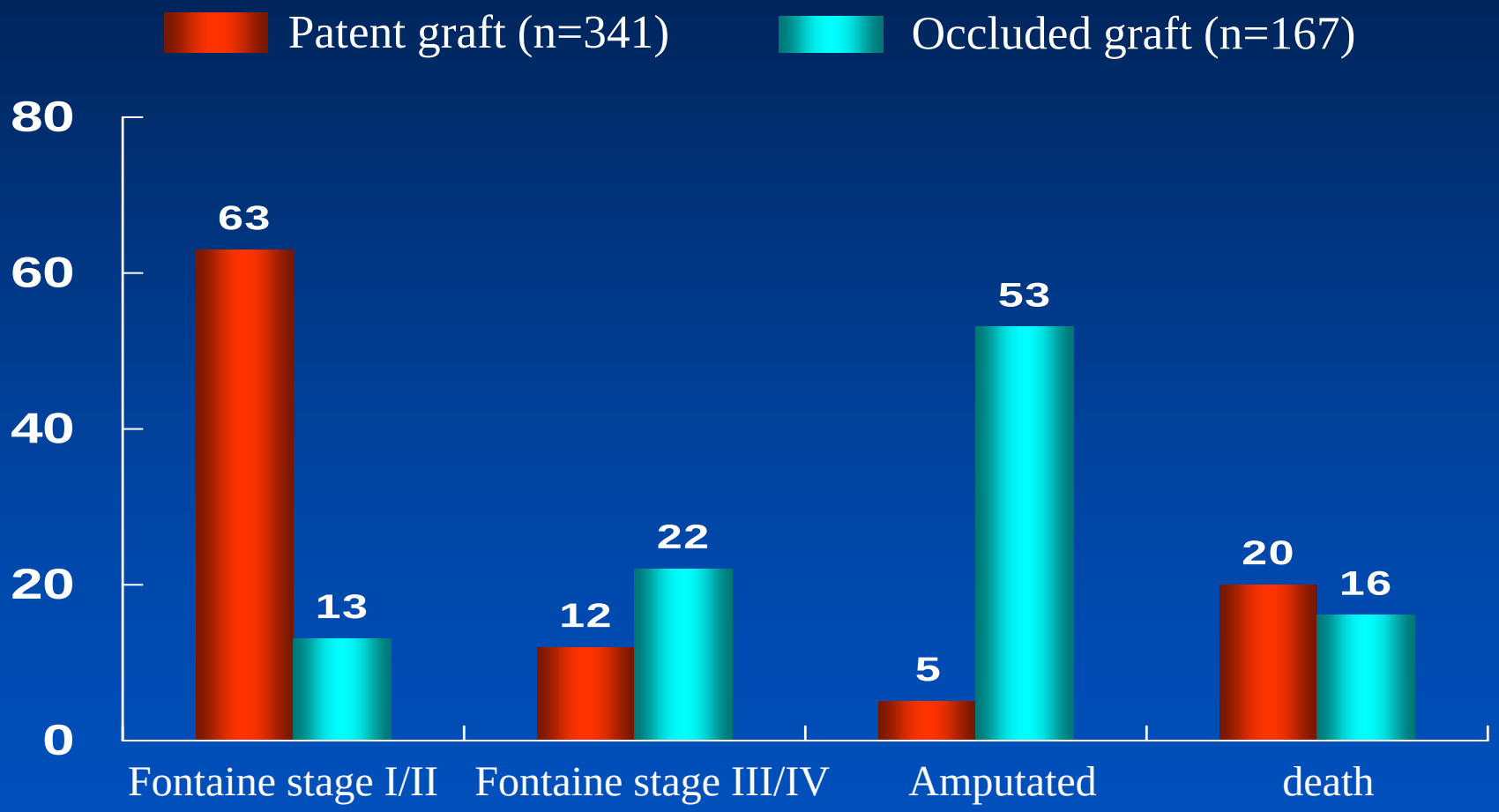
Total population: 517 patients



Eur J Vasc Endovasc Surg 1999;17:77–83

Patent vs. occluded graft

Clinical outcomes @ 12 months

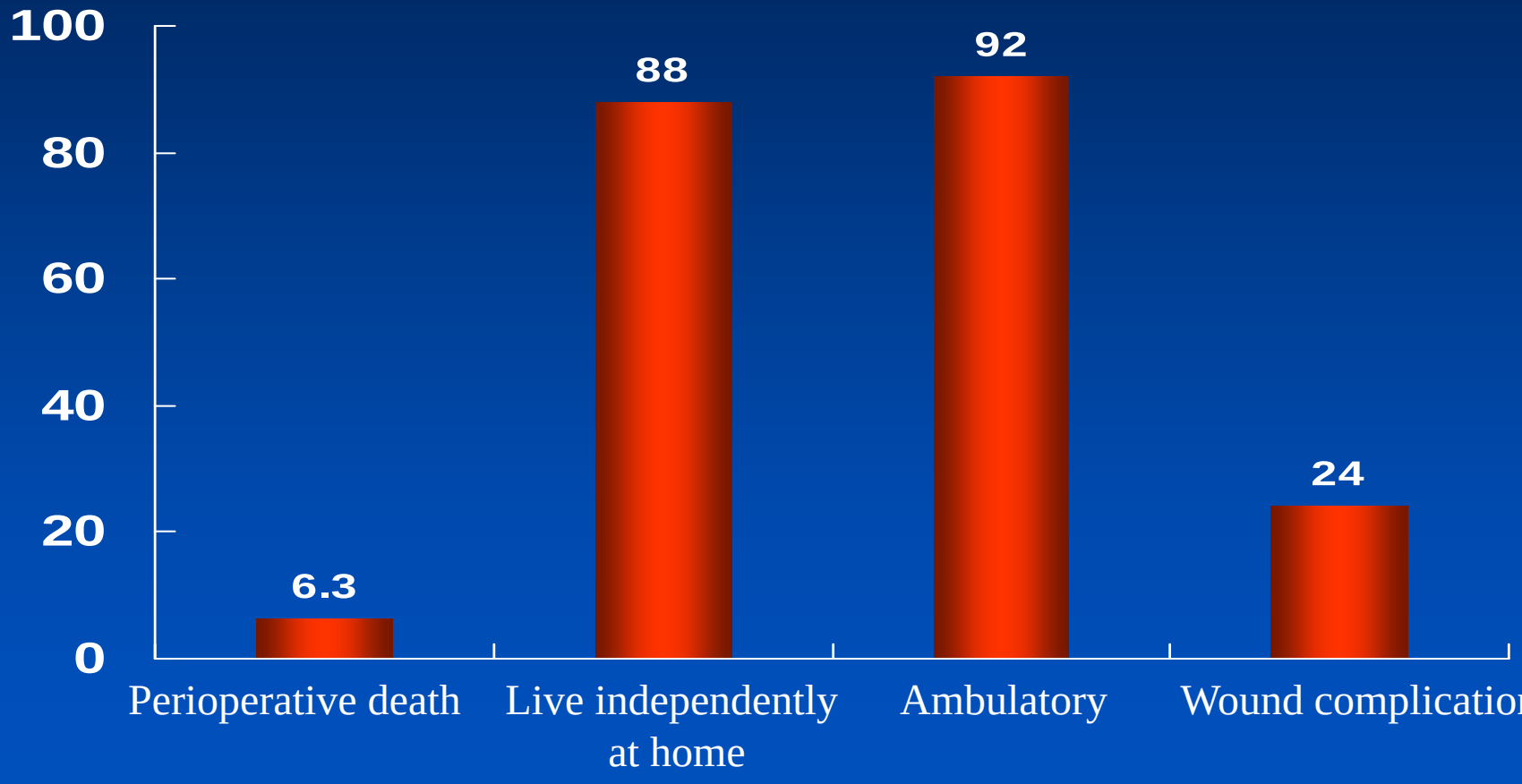


Eur J Vasc Endovasc Surg 1999;17:77–83

Early clinical outcomes after surgery

Total population: 112 patients

Wound (operative and ischemic) healing : a mean of 4.2 months, and
22% had not achieved complete wound healing at the time of last FU or death.

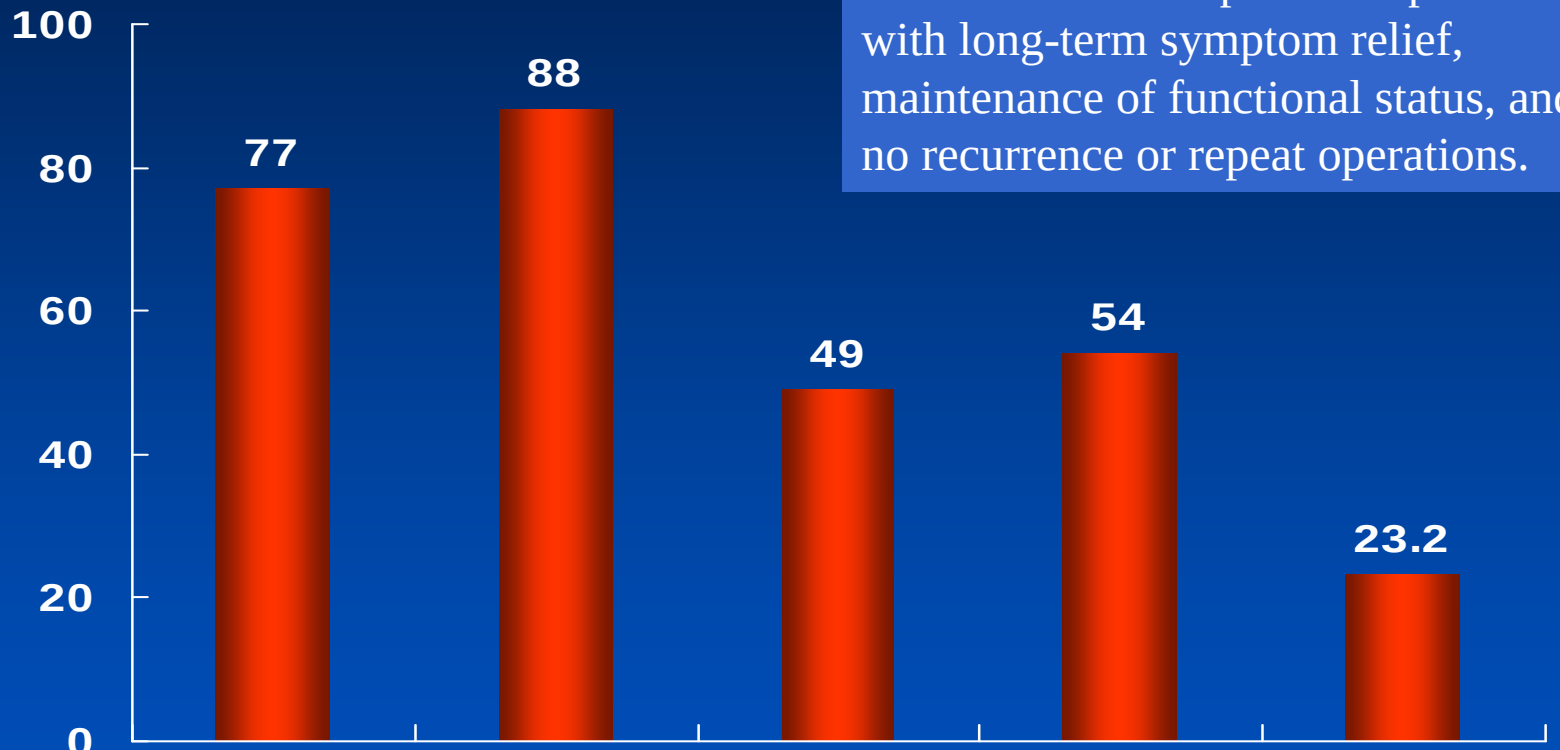


J Vasc Surg. 1998;27:256-63

Long-term outcomes

Clinical outcomes @ 5 years

Only 14.3% achieved the ideal surgical result of an uncomplicated operation with long-term symptom relief, maintenance of functional status, and no recurrence or repeat operations.



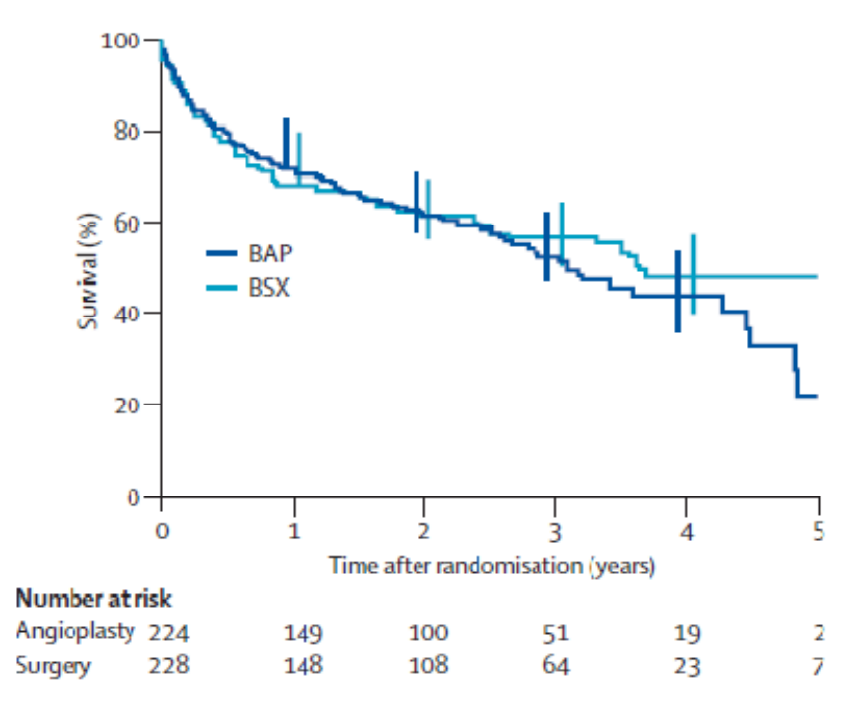
J Vasc Surg. 1998;27:256-63

BASIL trial

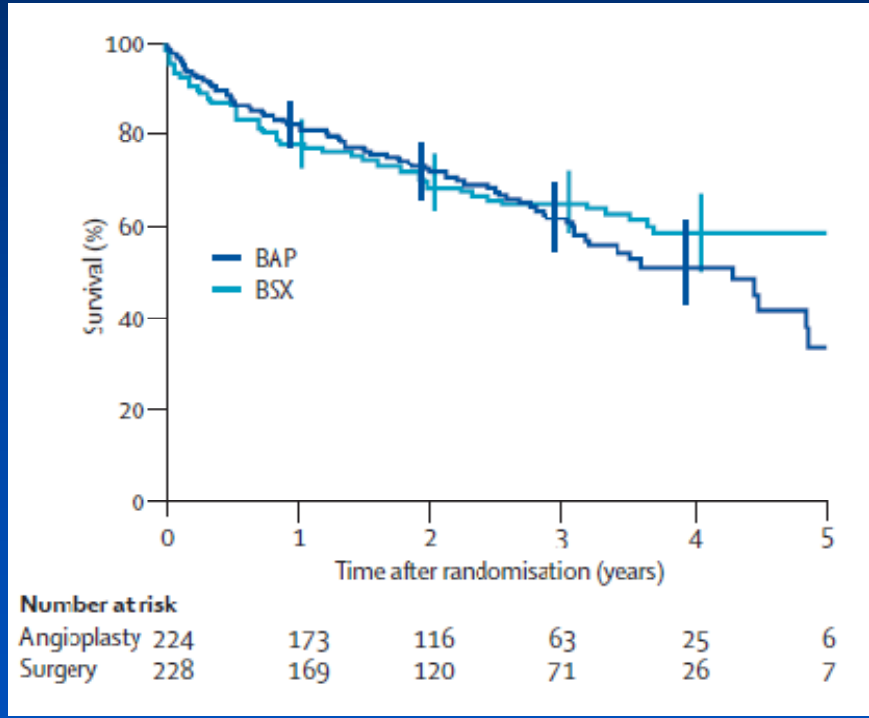
(Multicenter randomized trial for infrainguinal severe ischemia)

Surgery vs. Balloon angioplsty

Amputation-free survival



Mortality-free survival



Lancet. 2005;366:1925-34

New approach

68yo Male with Diabetic Foot

- Hypertension, Long standing diabetes
- DM ESRD on HD

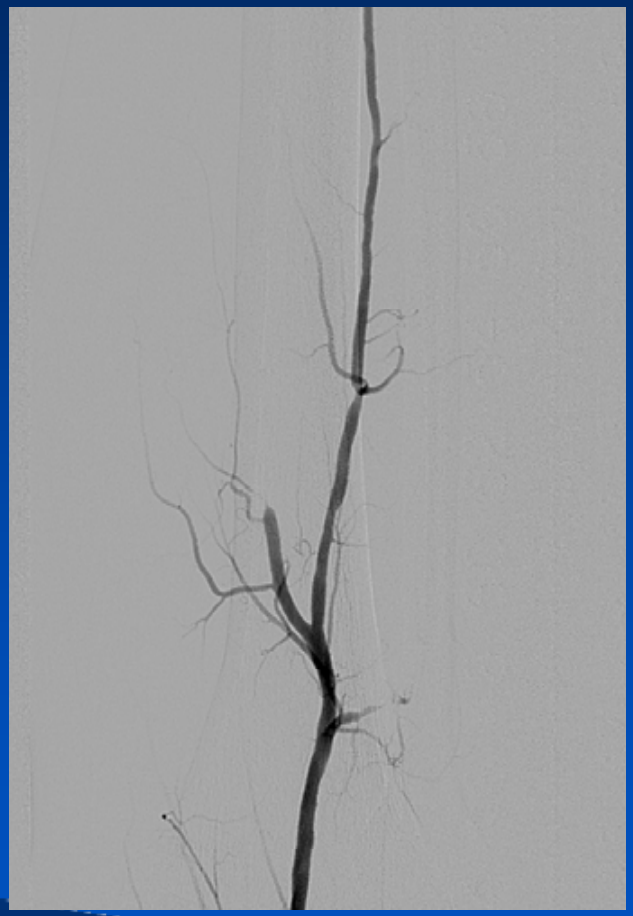
First Treatment

Before

After

However, Incomplete wound healing and Restenosis Occurred and We need more than balloon…

Three months later



2nd Treatment

New approach

- Laser angioplasty
- Cutting balloon.
- Coated stent
- Drug-eluting stents
- Absorbable metal stent

New approach

- Laser angioplasty
- Cutting balloon.
- Coated stent
- Drug-eluting stent
- Absorbable metal stent

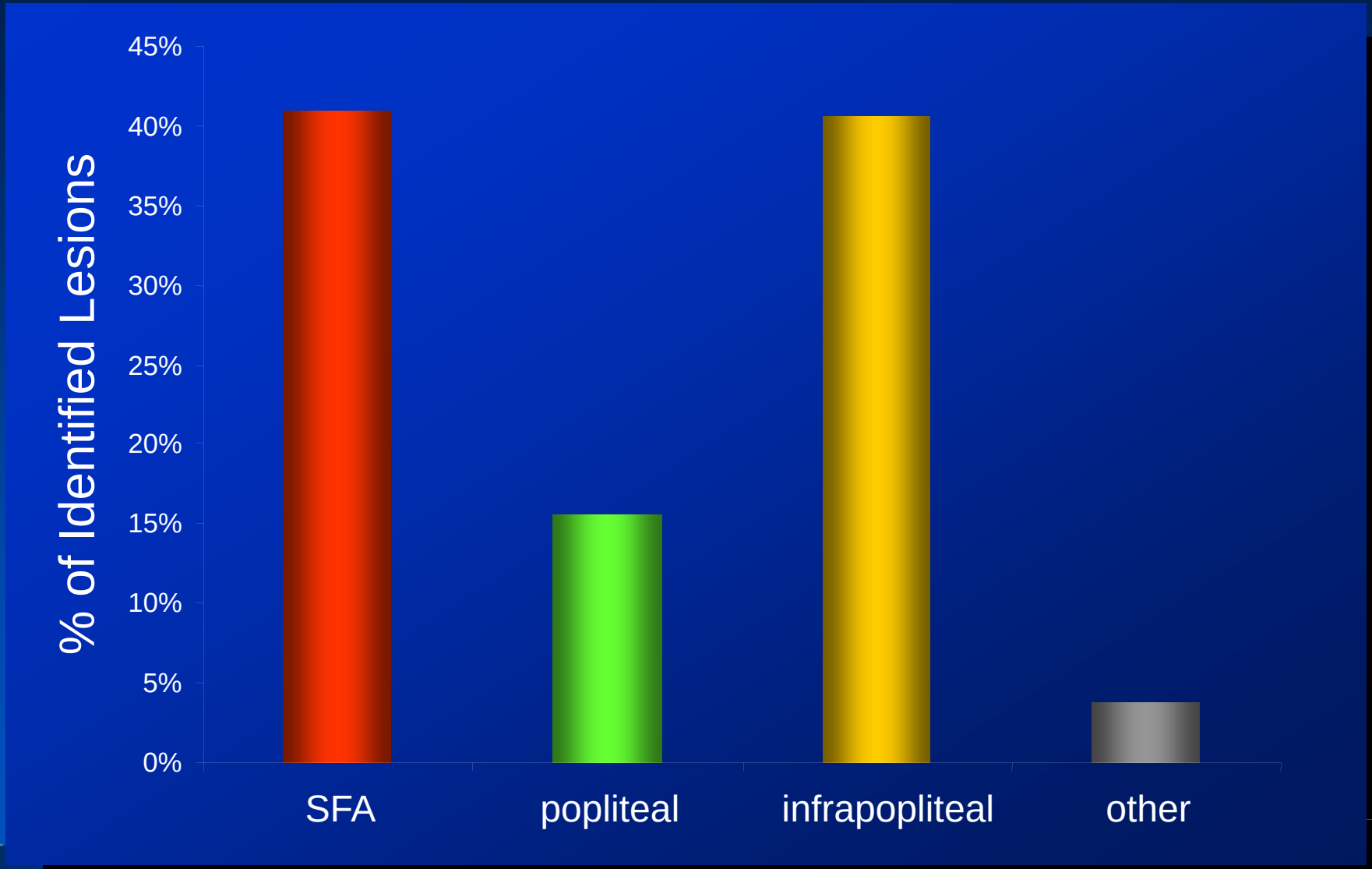
Laser Angioplasty for Critical Limb Ischemia

Results of the LACI Phase 2 Clinical Trial

LACI Phase 2 Registry

- **Prospective, multi-center study**
- **Patients with CLI**
  - Rutherford Category 4-6
  - poor surgical candidates
- **Treatment:** ELA of SFA, popliteal and/or infrapopliteal arteries, with adjunctive PTA and optional stenting
- **Primary Endpoint**: limb salvage at 6 months
  - freedom from amputation at or above the ankle

Vascular Lesion Locations (N=406)



Main Endpoints

per-patient basis

	LACI	Control	p
Surgical intervention*	2%	34%	<.001
At 6 months:			
Died	10%	13%	ns
Survived with:			
Limb salvage	93%	87%	ns
Persistent CLI	34%	31%	ns

* bypass or endarterectomy

New approach

- Laser angioplasty
- Cutting balloon.
- Coated stent
- Drug-eluting stents or balloon
- Absorbable metal stent

Cutting balloons

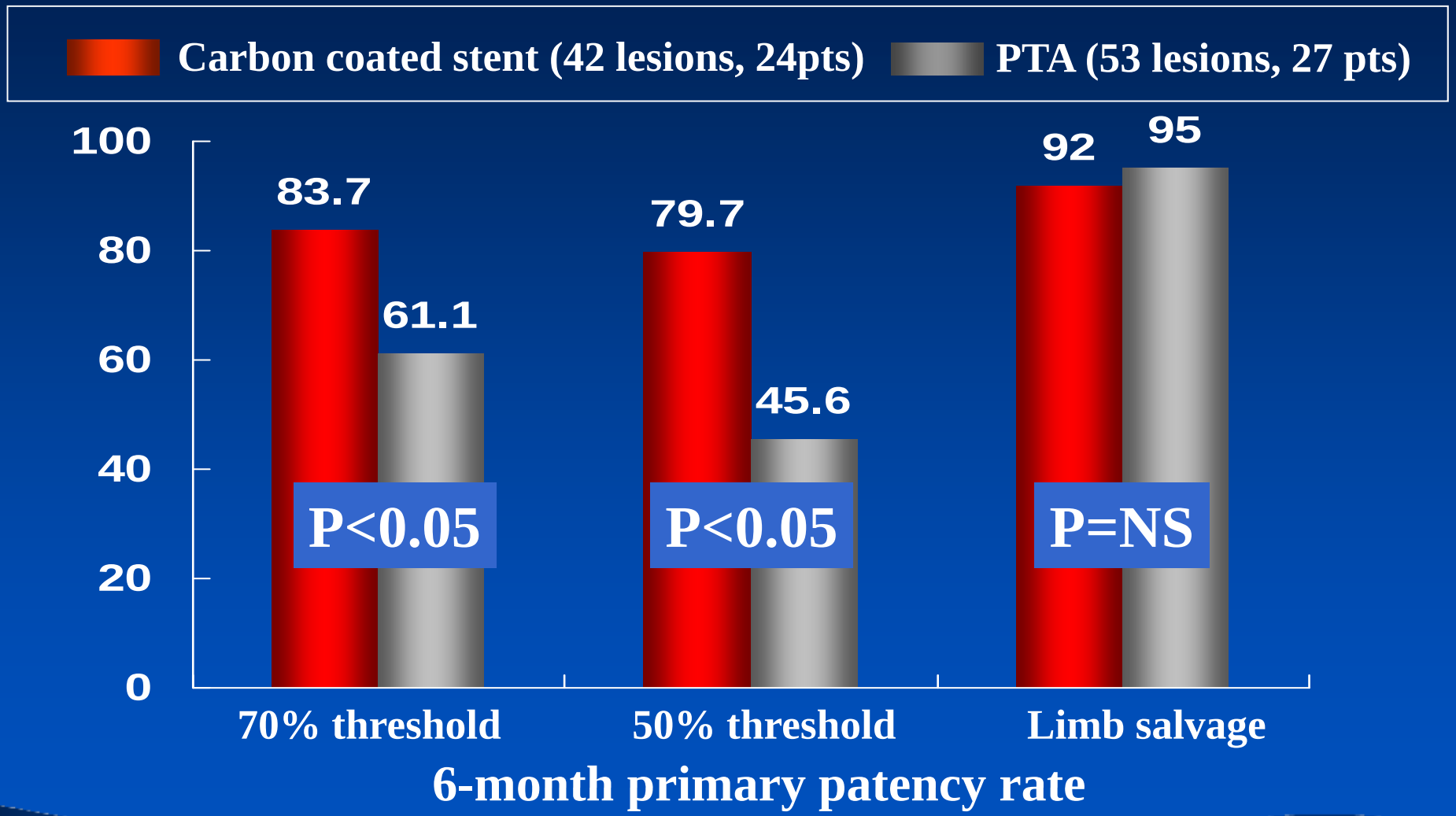
- Although application of this technique in peripheral arteries is still limited, it appears that it is effective in the treatment of resistant femorodistal bypass stenoses and complex infrapopliteal obstructions such as ostial and bifurcational lesions

New approach

- Laser angioplasty
- Cutting balloon.
- Coated stent
- Drug-eluting stents or balloon
- Absorbable metal stent

Carbofilm coated stents vs. PTA

Prospective randomized trial



Cardiovasc Intervent Radiol. 2006;29:29-38

New approach

- Laser angioplasty
- Cutting balloon.
- Coated stent
- Drug-eluting stents or balloon
- Absorbable metal stent

SiroBTK study with SES

30 patients, 62 arteries, 106 SES

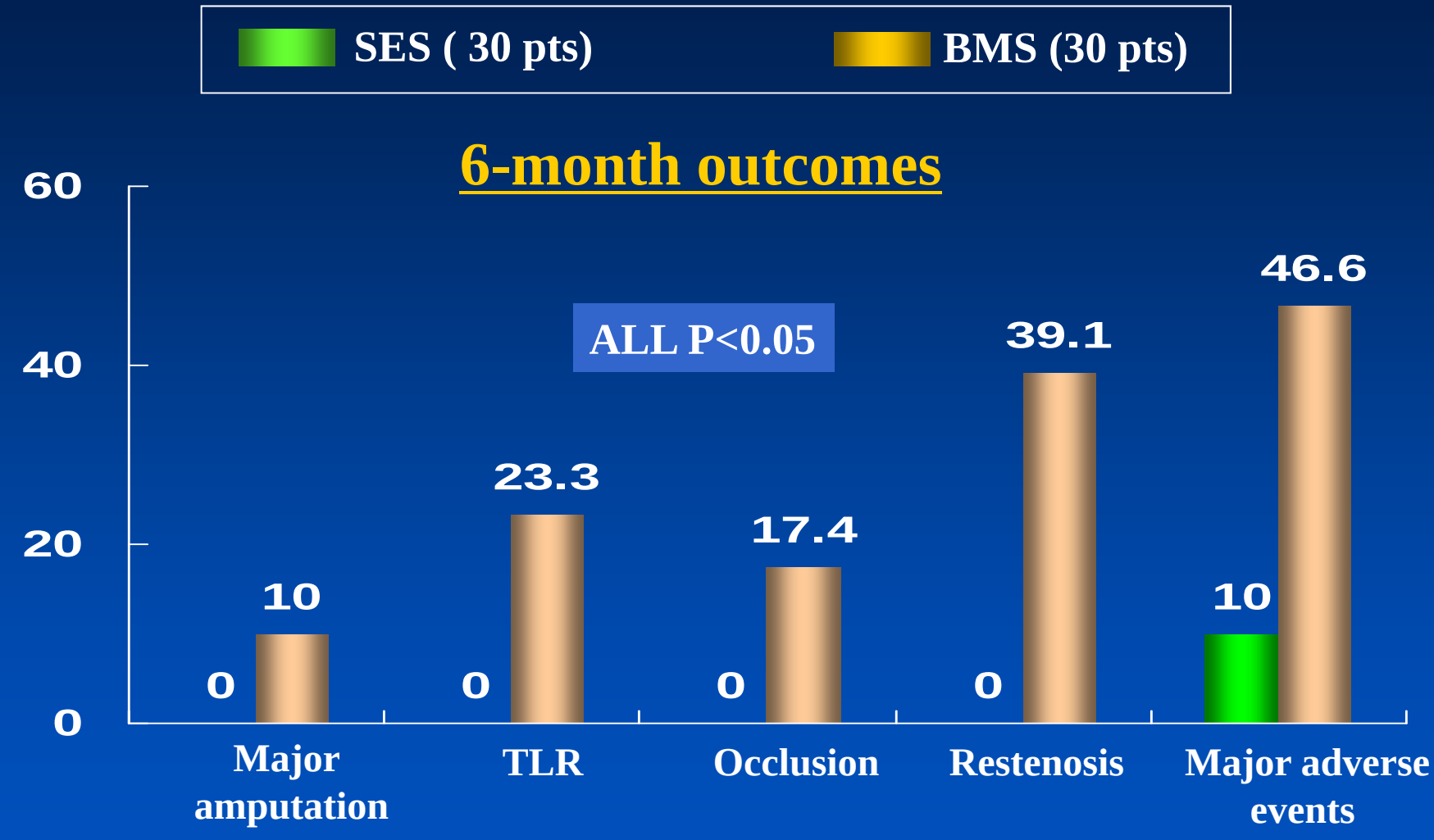
Primary endpoint: clinical improvement and healing of ulcer @ 1 & 7.7 months

- Angiographic and procedural success : 100%.
- 7 months outcomes

- Amputatiton 1 toe in one patient and 1 mid-foot in another.
- **Limb salvage : 100% of patients.**
- Death : two cardiac deaths unrelated to CLI
- Three recurrent homolateral claudication.
- **Mid-term clinical improvement : 100%**
- **Primary patency: 97% (56 patent arteries on 58 arteries).**

J Endovasc Ther. 2007;14:241-50.

SES vs. BMS

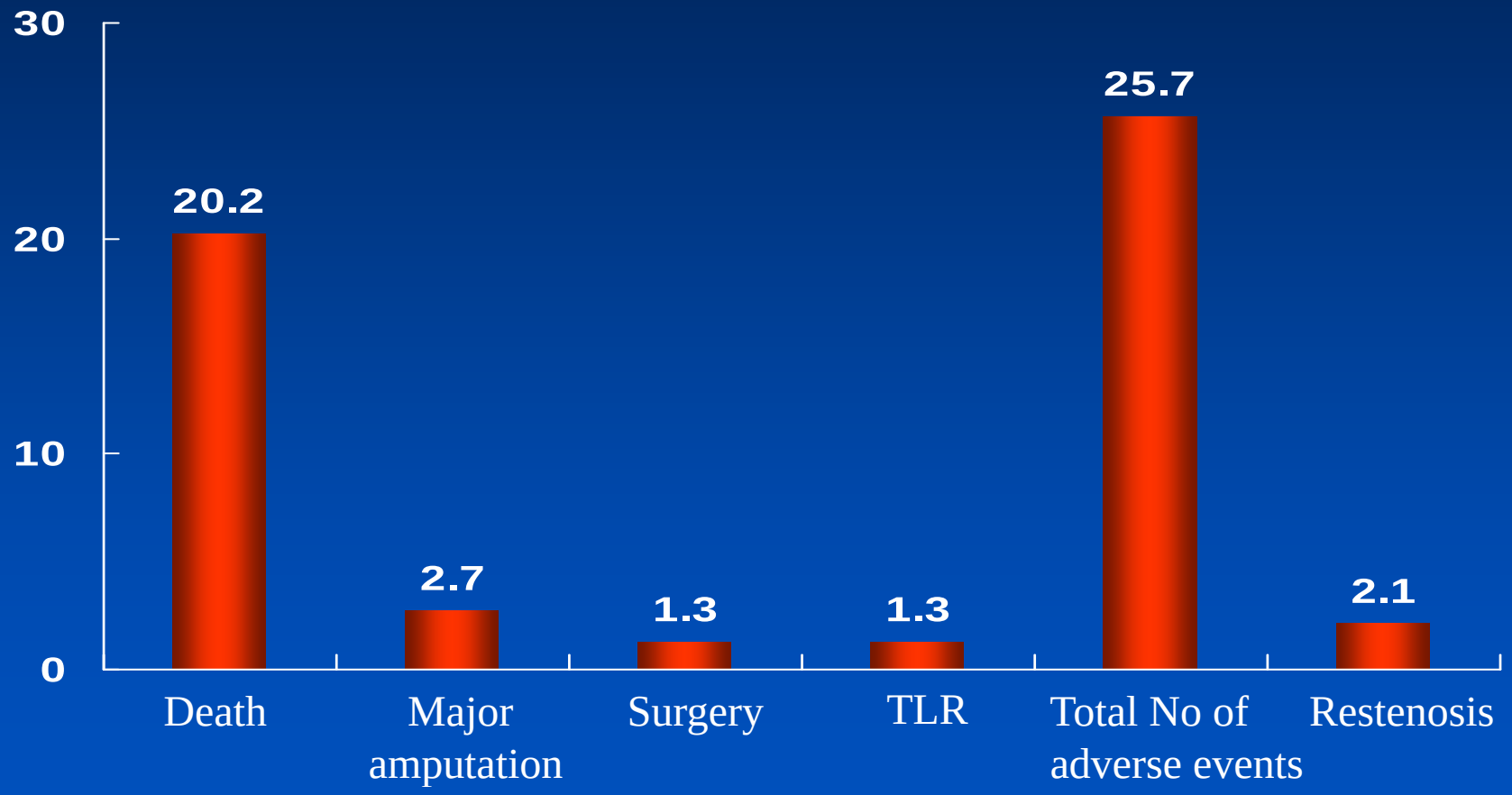


Eurointervention 2006;2:169–174.

BTK SES registry

Prospective nonrandomized single center registry

SES for Sxmatic focal infrapopliteal obstruction (n=74 pts)

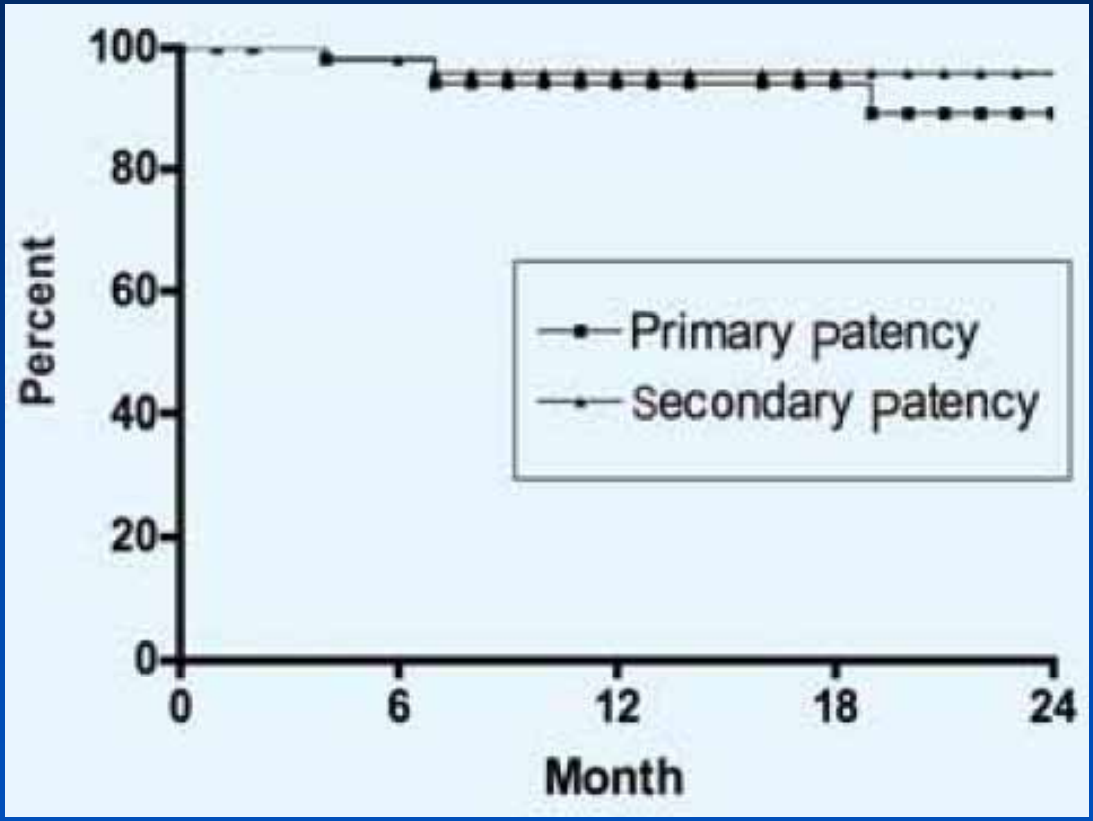


Endovascular today 2007;August.71-74

BTK SES registry

Prospective nonrandomized single center registry

SES for Sxmatic focal infrepopliteal obstruction (n=74 pts)



Patency at 24 months

Primary: 89.2%

Secondary: 95.9%

Endovascular today 2007;August.71-74

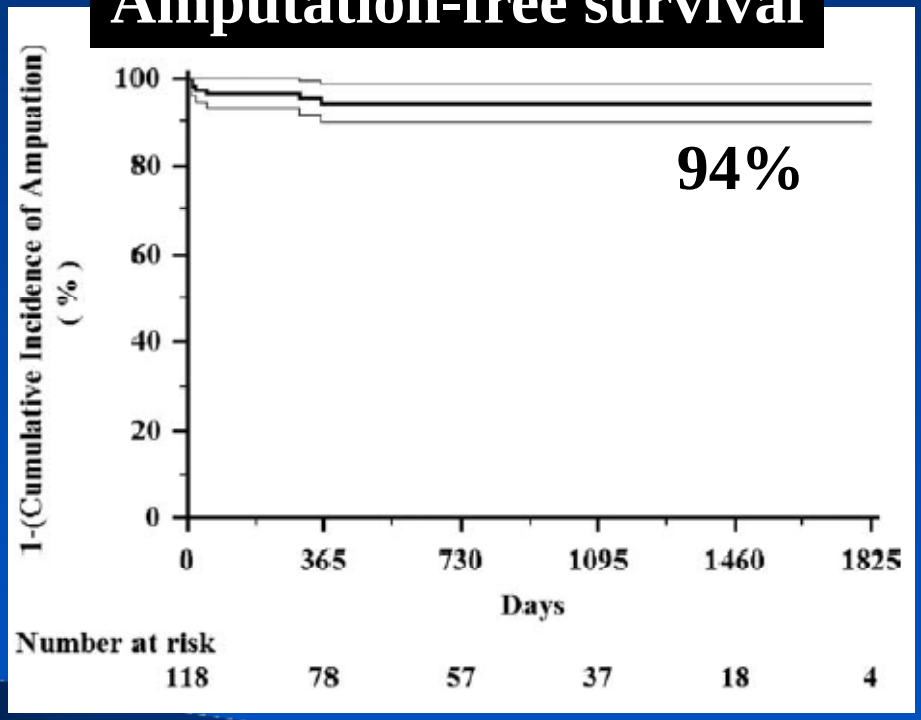
PaRADISE trial

(PReventing Amputation using Drug-elutIng StEnt)

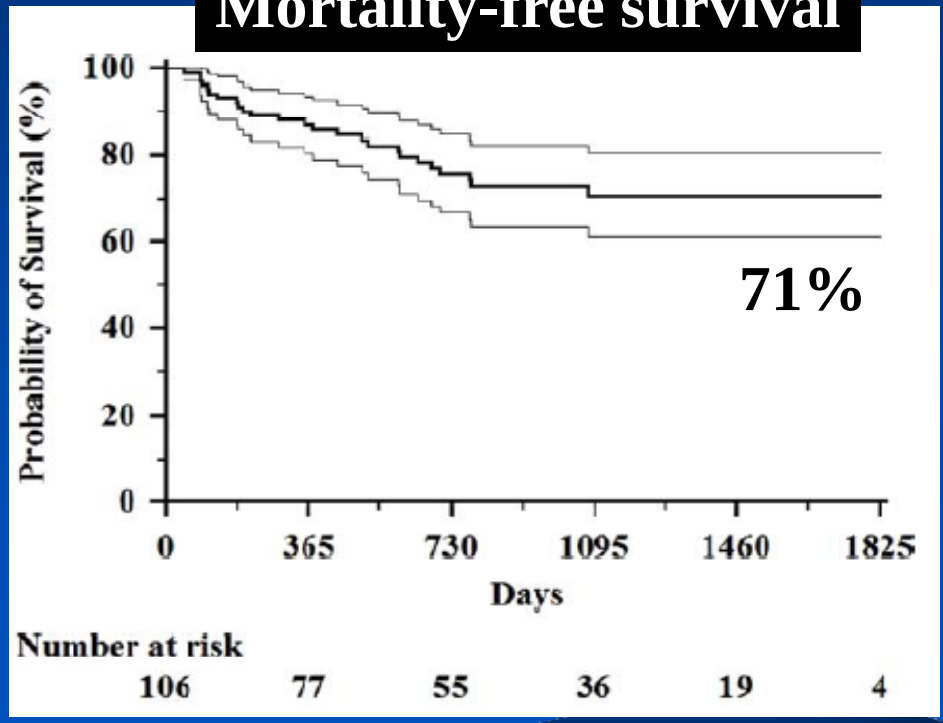
Critical limb ischemia (106 pts, 108 limbs, SES 83%, PES 17%)

- Stent number/limb: 1.9±0.9, Stent length : 60±13 mm
- Target limb revascularization: 15%
- Angiographic restenosis: 12% (follow-up rate 35%)

Amputation-free survival



Mortality-free survival

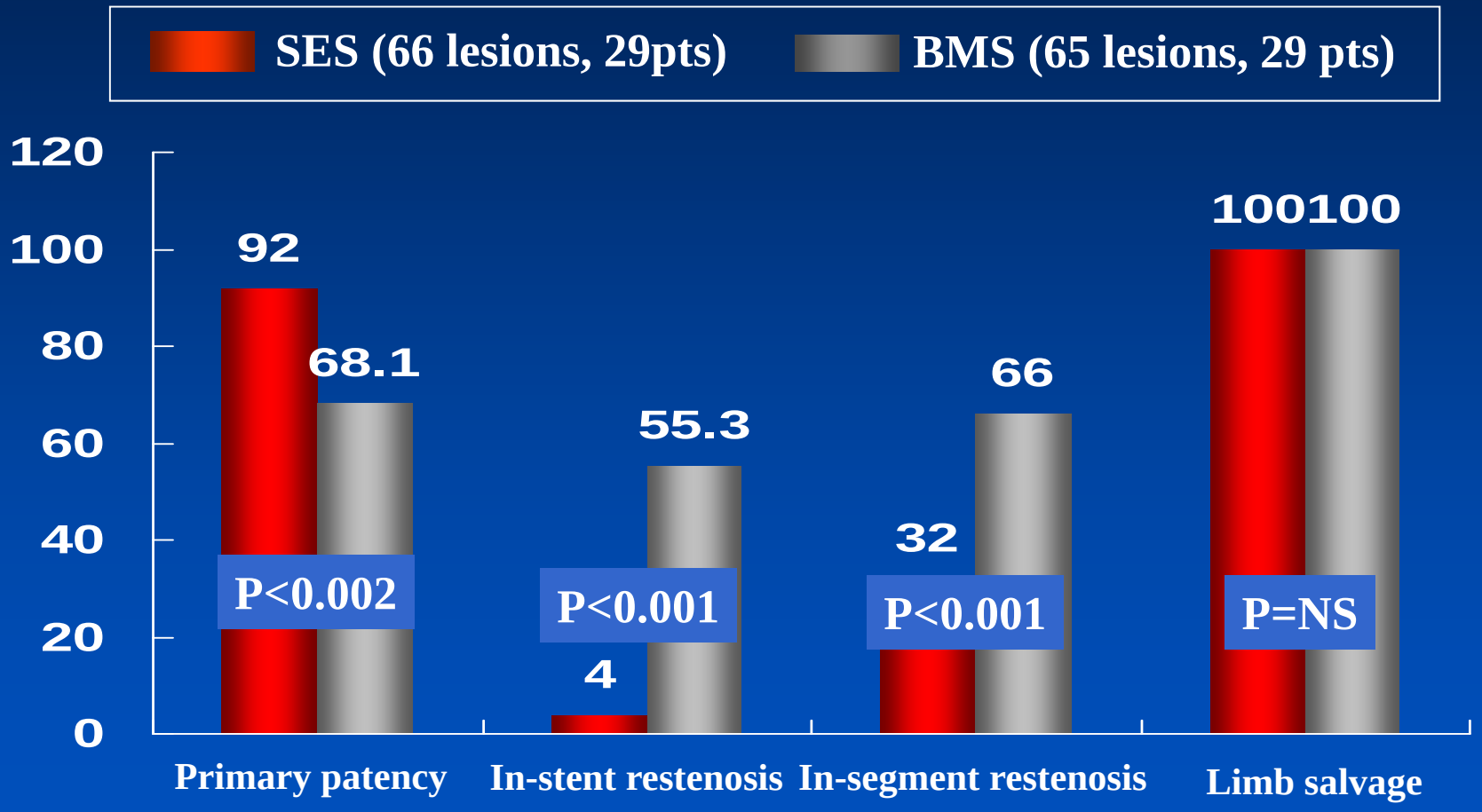


Feiring AJ et al. J Am Coll Cardiol. 2010;55:1580-9

SES vs. BMS for CLI

SES (29 pts) vs. BMS (29 pts) for bailout use

Endpoint: 1-year angiographic and clinical outcome

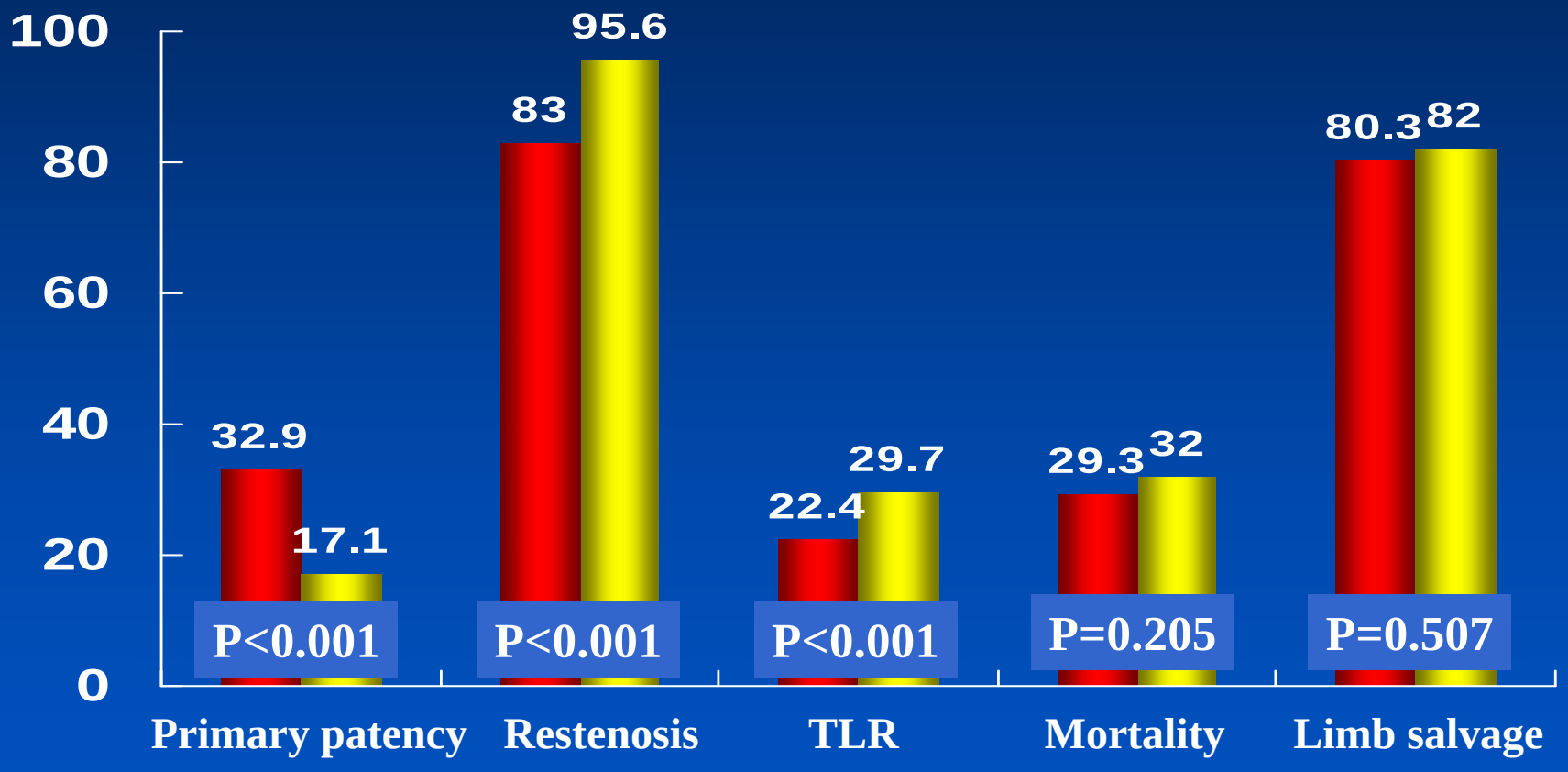


J Endovasc Ther 2005;12:685–95.

SES vs. BMS

SES (75 limb, 153 lesions) BMS (47 limb, 77 lesions)

3-year outcomes

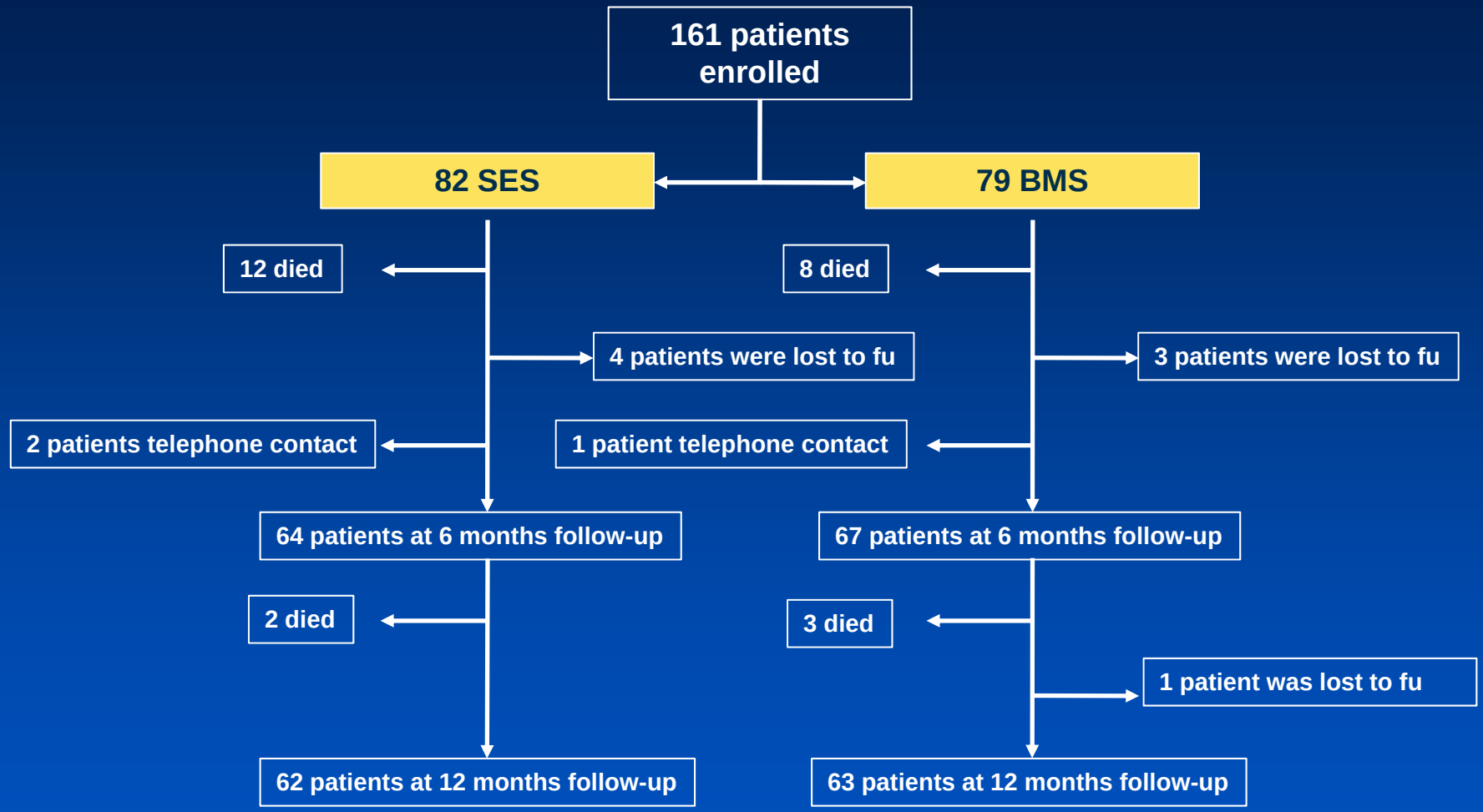


Siablis D et al. J Vasc Interv Radiol 2009; 20:1141–1150

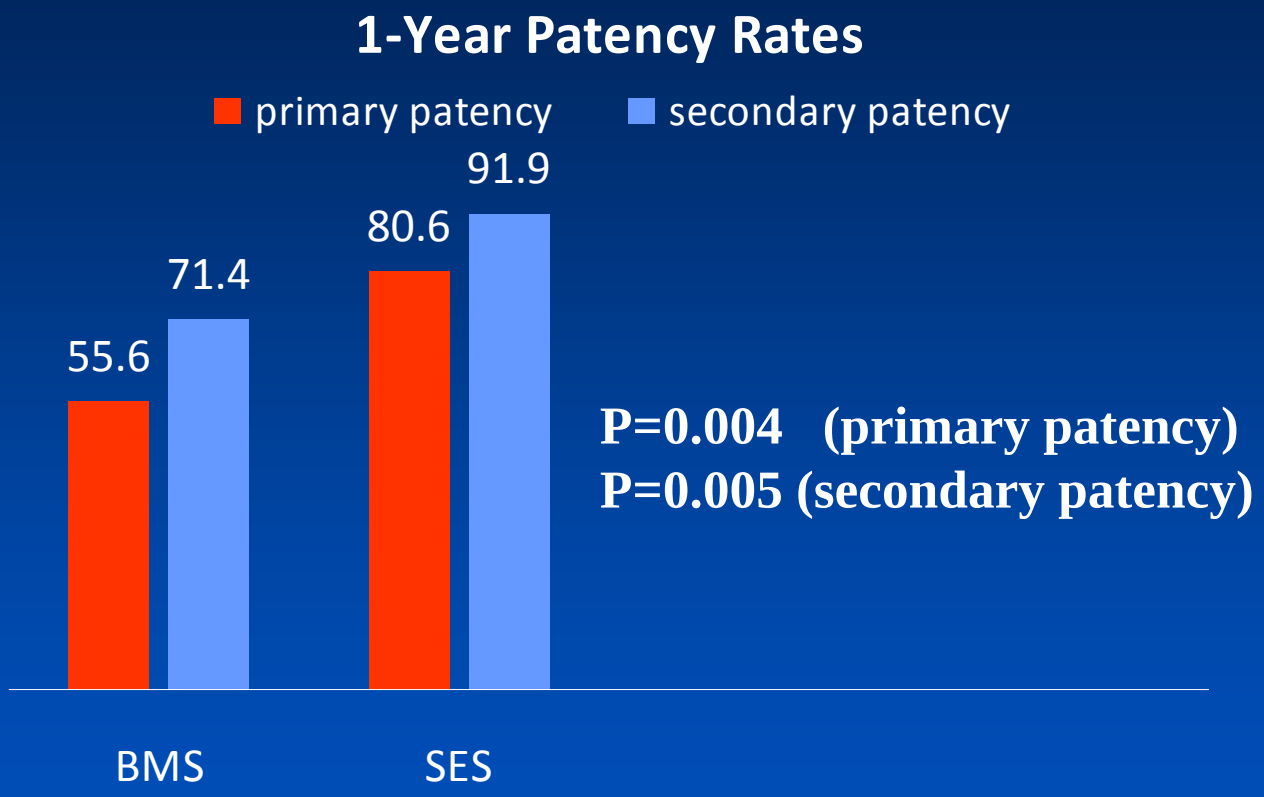
DES trials

Study	Test device	Control	Number
Drug-eluting balloon			
PICCOLO	PEB	Balloon	114
Drug-eluting stent			
ACHILESS	Cypher select	Balloon	200
DESTINY	Xience V	Vision (BMS)	140
YUKON	SES (Yukon)	Stent (Yukon)	130

YUKON-BTK Trial
Study Profile

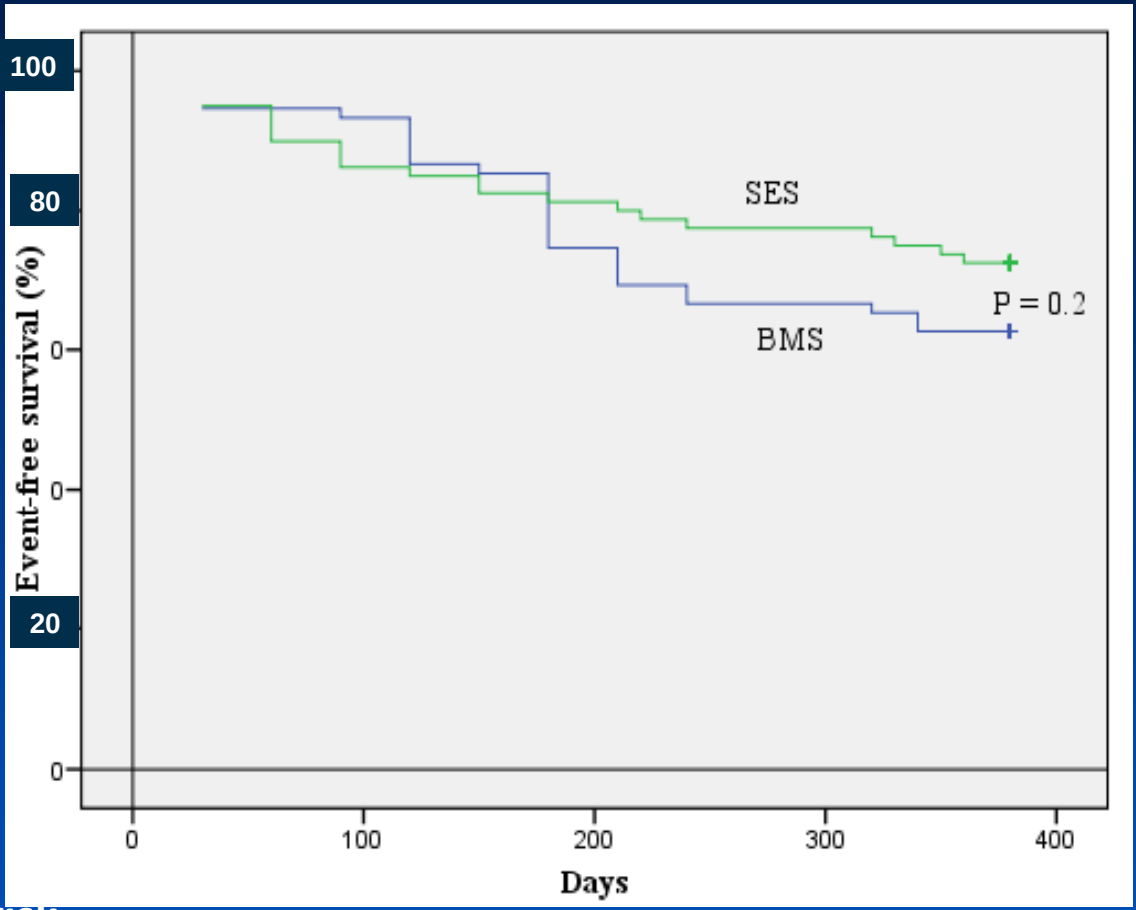


YUKON-BTK Trial
Primary & Secondary Patency



Event-free Survival at 12 months

Survival free from target lesion revascularisation, major and minor amputation, myocardial infarction and death was compared by Kaplan-Meier analysis with the use of the Mantel-Cox log-rank test.



No. at risk					
Sirolimus	82	71	64	63	62
Stent					

CardioVascular Research Foundation

Rastan et al. EHJ 2011 in revision

DESTINY study

Drug **E**luting **St**ents
In The Critically Ischemic Lower Leg

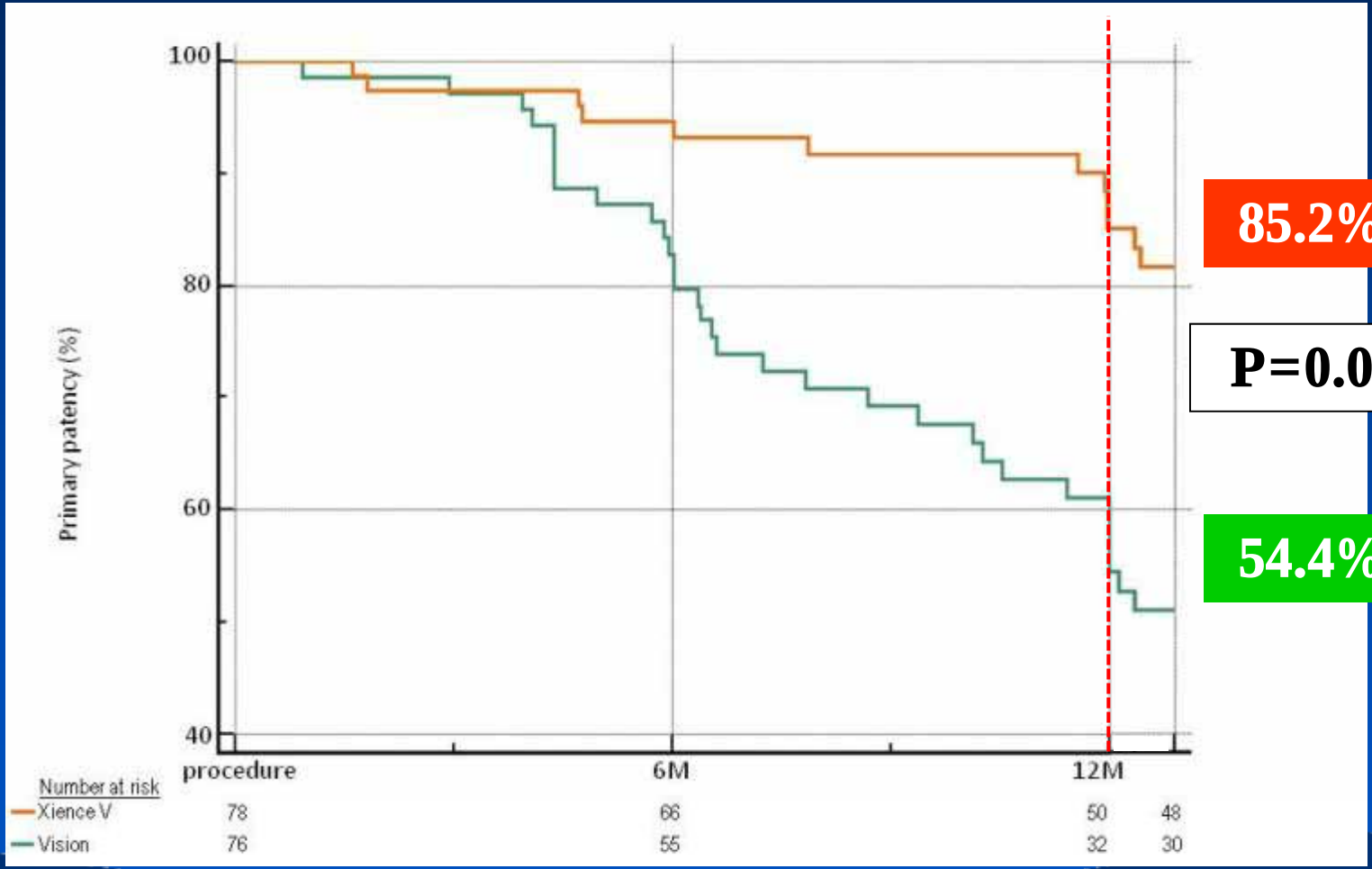
*a physician-initiated prospective randomized multicenter trial comparing the implant of a **d**rug **e**luting **st**ent (**XIENCE V**, Abbott Vascular) vs. a bare metal stent (**MULTILINK VISION**, Abbott Vascular) **in** the critically ischemic lower leg*

Multilink Vision – BMS

Xience V – DES

DESTINY - 12-month primary patency

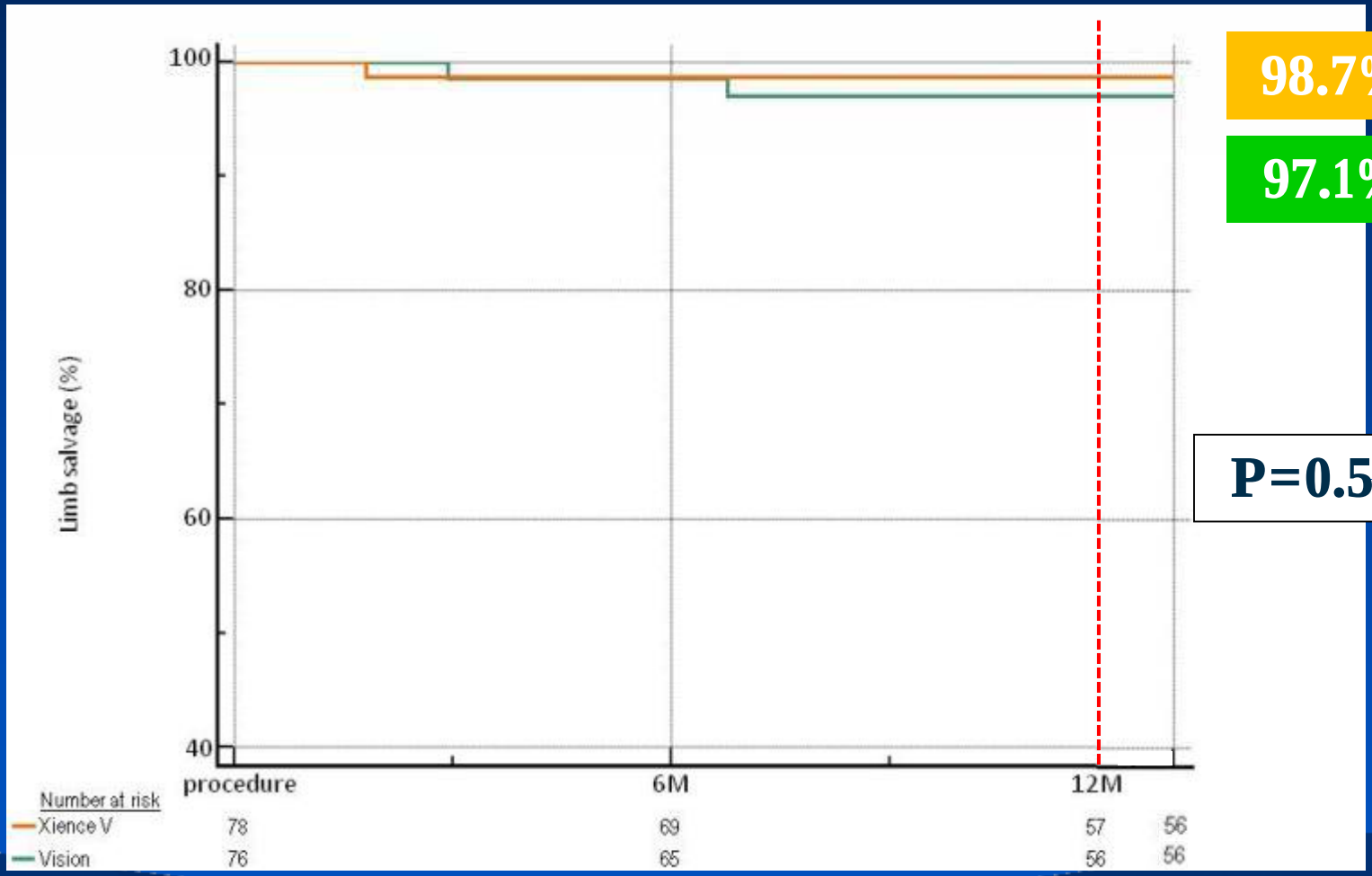
MultiLink Vision vs Xience V



Bosiers M. LINC 2011

12-month limb salvage

MultiLink Vision vs Xience V



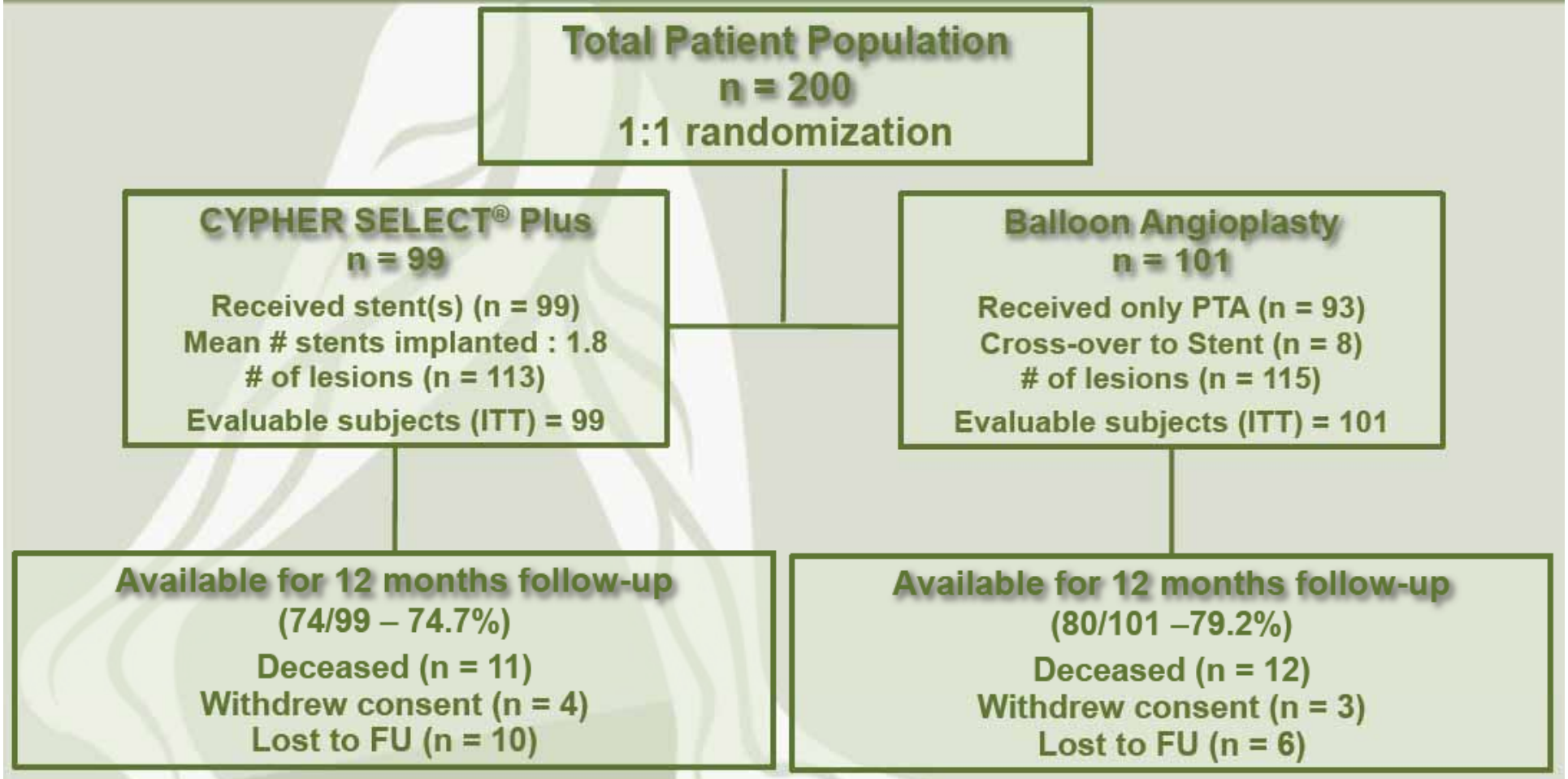
98.7%

97.1%

P=0.53

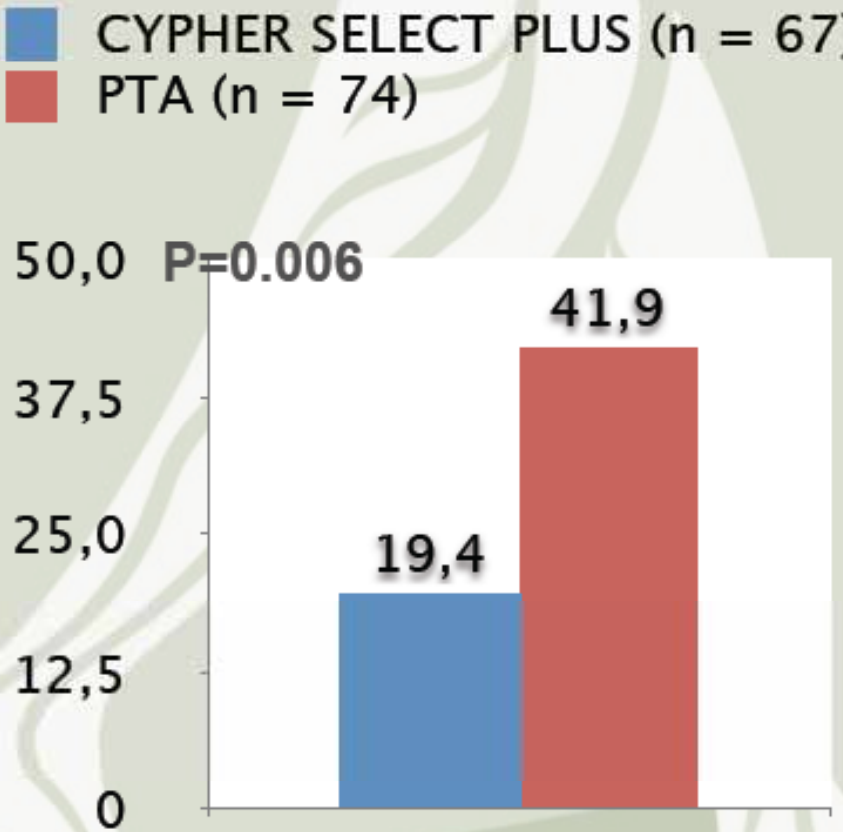
The ACHILLES Study

Patient Enrollment



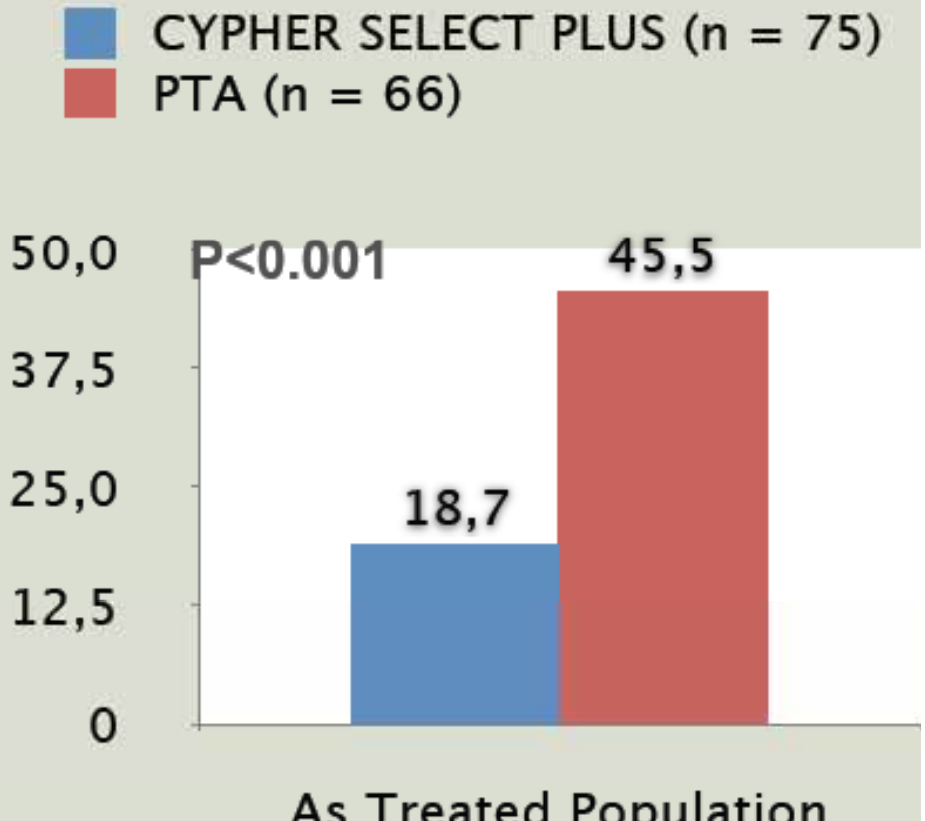
The ACHILLES Study

Primary Endpoint
12M In-Segment Binary Restenosis by QA



Preliminary Results at 12M FU

ITT Population

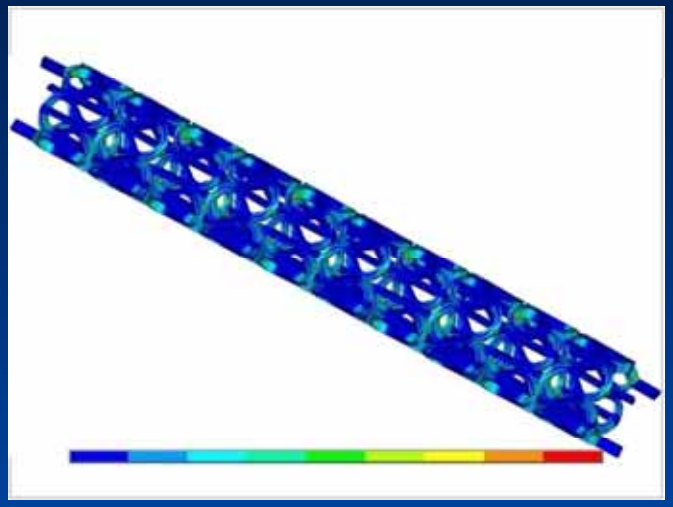


As Treated Population

New approach

- Laser angioplasty
- Cutting balloon.
- Coated stent
- Drug-eluting stents or balloon
- Absorbable metal stent

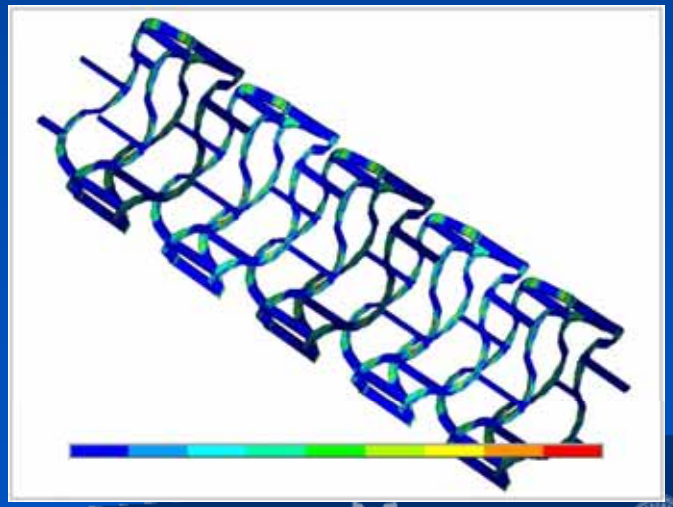
Absorbable Magnesium Stent



FEA: Crimped state

Recoil	~ 5%
Foreshortening	< 5%

* Investigational device only - not for sale -



FEA: Fully expanded state

Clinical Results

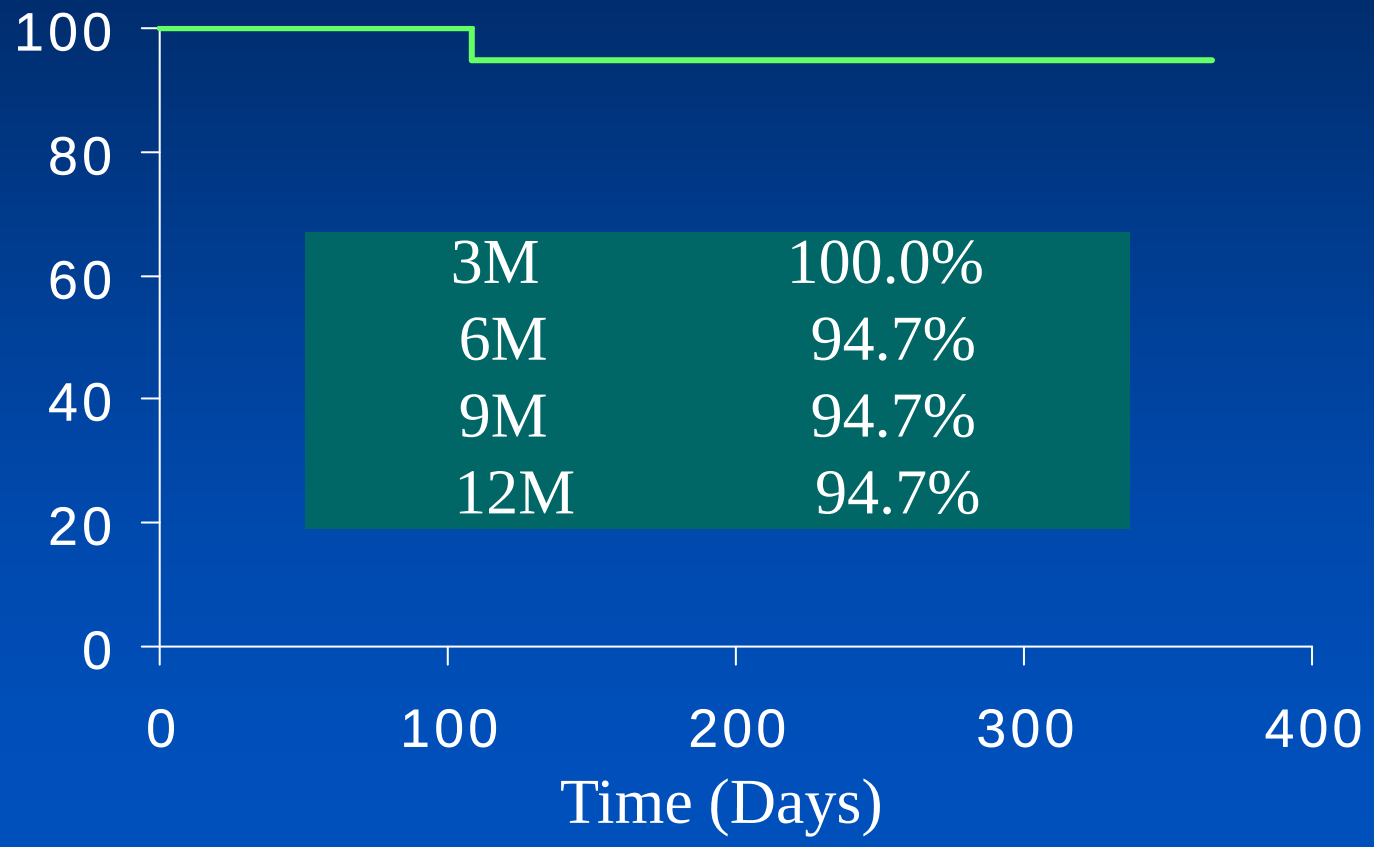
BEST-BTK

First in Man experience with the Biotronik absorbablE metal StenT Below The Knee

- 20 CLI patients (Rutherford 4-5) with BTK pathology
- Implants performed between December ‘03 – January ‘04

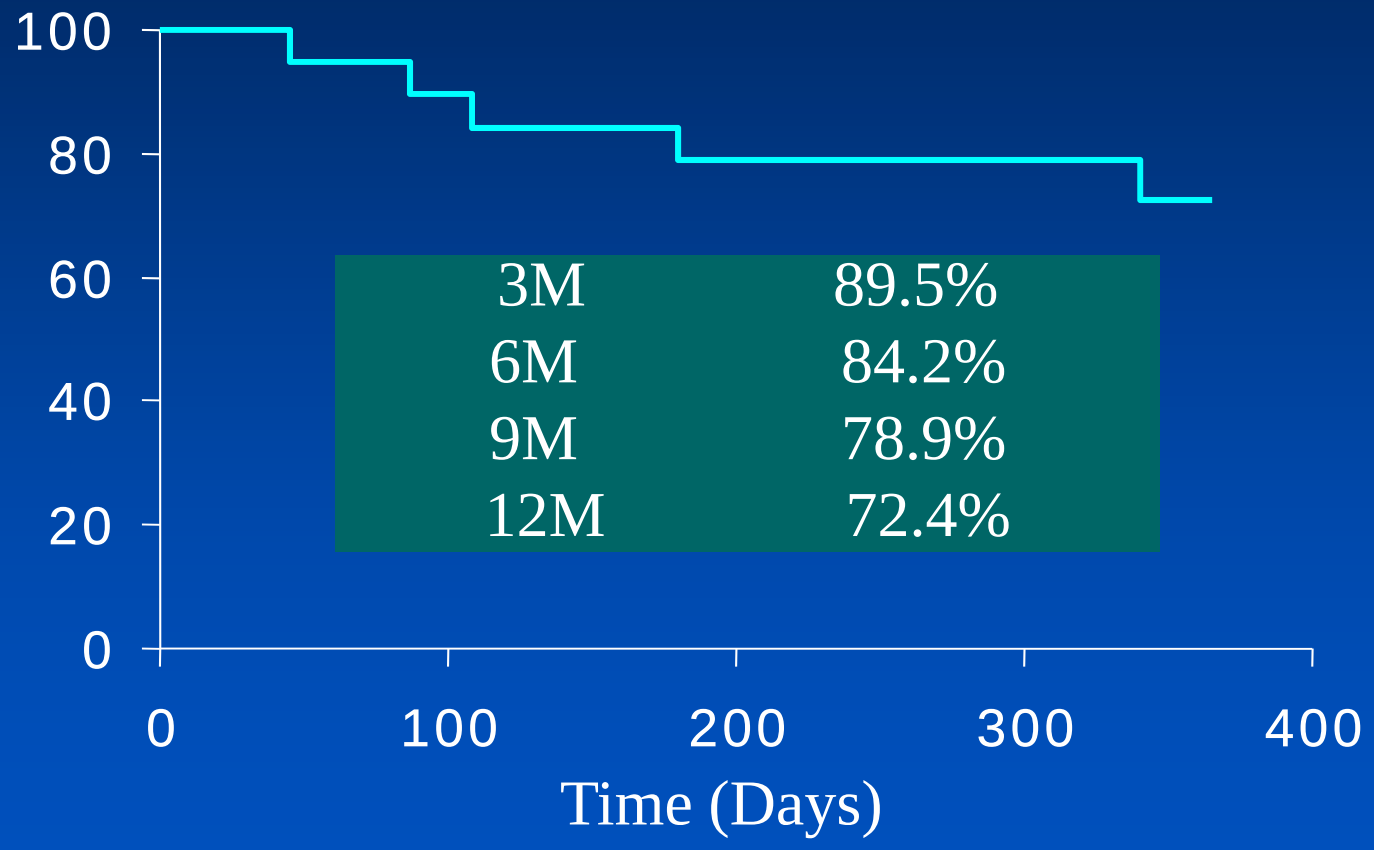
Limb Salvage After One Year

Limb Salvage Rate



High Patency Rate

Primary Clinical Patency



Conclusions I

- PTA is the preferred treatment strategy
- With tremendous improvements in interventional devices and techniques, long and multiple stenotic and occlusive lesions can be treated successfully with PTA.
- PTA carries a lower morbidity and mortality compared with surgery and would be considered as the first treatment option in all patients.

Conclusions II

- Clinical success is superior to angiographic patency
- DESs have a consistent and profound effect on the mid-term reduction of restenosis. However, long-term results remain doubt.
- While there is growing familiarity and acceptance of DESs in endovascular procedures to treat BTK lesions, we should be considered against the fact that there was no large randomized clinical trial with long-term data comparing DESs with the current BTK interventional standard of PTA.

Anatomic Challenges Infrapopliteal disease

- Atherosclerotic disease confined to the infrapopliteal arteries may be asymptomatic due to the excellent collateral network between tibial arteries
- One patent tibial artery is often sufficient to keep a patient free from ischaemic symptoms
- When these patients present with CLI, they often have severe, extensive three-vessel disease and only 20–30% have a simple, focal lesion with good distal run-off

Anatomic Challenges Infrapopliteal disease

- Patients are usually elderly with several comorbidities, such as diabetes and coronary artery disease, which increases the surgical risk
- Femorodistal and pedal bypass surgery is technically demanding and associated with a 1.8–6% perioperative mortality

Why?
PTA for intrapopliteal lesions

- The highest likelihood of coronary heart disease in patients with infrapopliteal disease.
- PTA is a low-risk and minimally invasive procedure, which rarely compromises a later surgical procedure, and at the same time preserves the saphenous vein for future coronary or lower extremity distal bypass surgery.
- The total intervention time of infrapopliteal PTA (less than 2 h), is shorter than time of surgery (4h)
- Avoids general anaesthesia and shorteer the hospital stay, compared with surgical treatment.
- Repeat PTA, unlike repeat surgical bypass operations, can be easily performed in case of restenosis.