How to Maintain Long-Term Patency of SFA CTO: Pharmacologic or Technical Address

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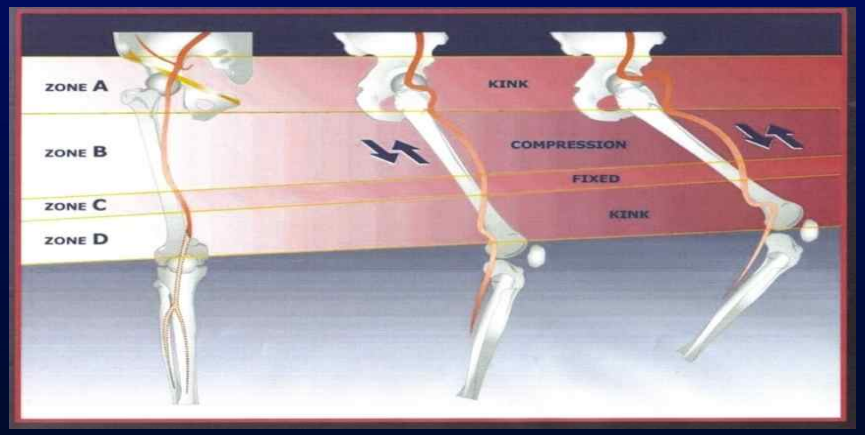
Femoro-popliteal Lesions
-Specific Problems-

- Long occlussion > short stenosis(TASC: C/D)
- Diffuse and multifocal obstruction
- A long and calcified lesion

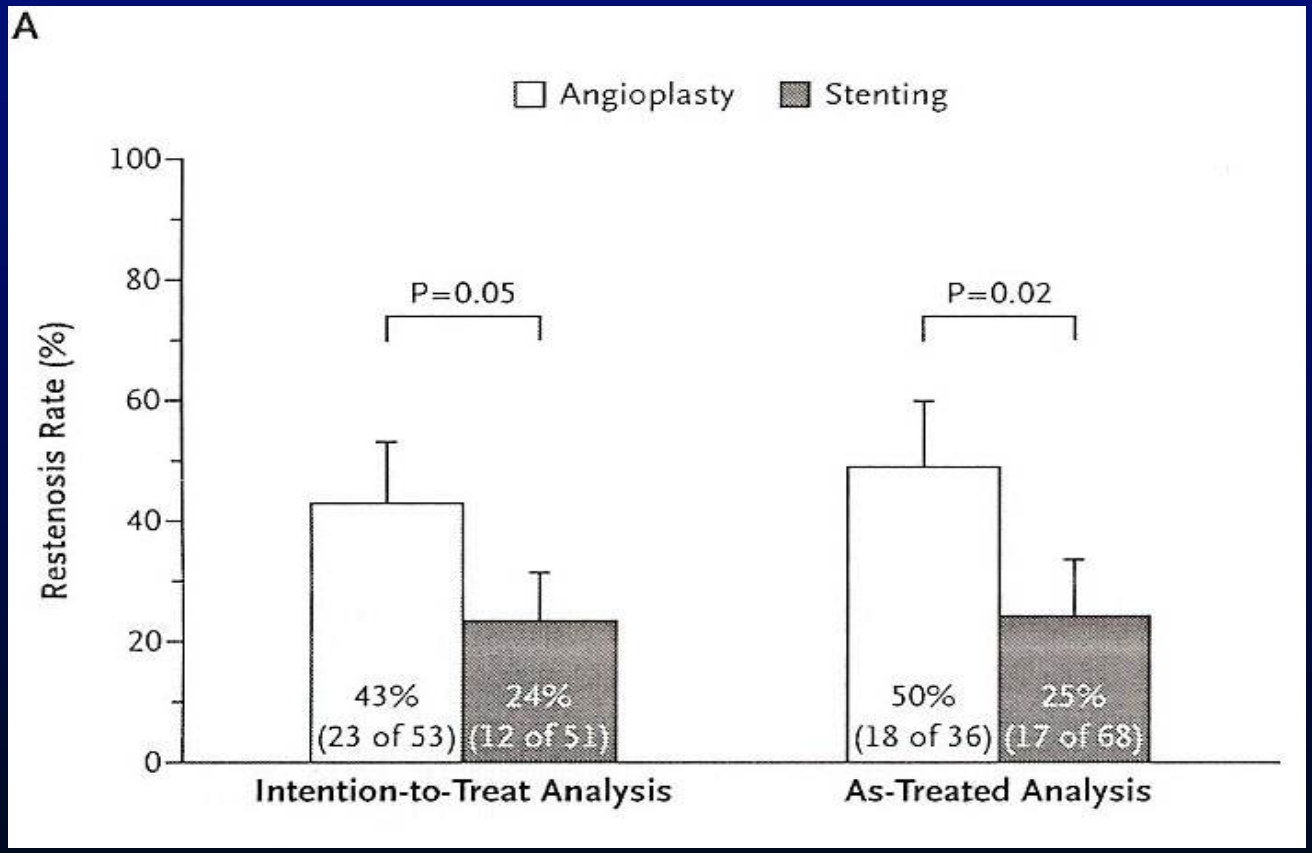
- Run-off Problem (0 - 3 Vessels)
- Mechanical Stress
  - Extension
  - Torsion
  - Compression
  - Flexsion



SFA is the last bastion in trying to achieve favorable endovascular results!!

ABSOLUTE trial (Absolute/Dynalink stent, Abbott)

-Primary endpoint-



Absolute stent (Abbott)

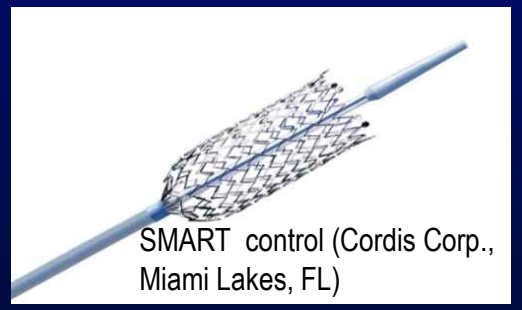
Schillinger M et al. N Engl J Med 2006; 354:1879-88

Nitinol Stent vs. Angioplasty alone -

Multicenter, Prospective, Randomized trial (Evidence level A)

- FAST trial (Luminexx, BARD)
- RESILIENT trial (Life stent, BARD)
- ABSOLUTE trial (Absolute stent, Abott)
- DURABILITY 1 trial (Protégé EverFlex stent, ev3)
- STROLL (Smart stent, JJ, Cordis)

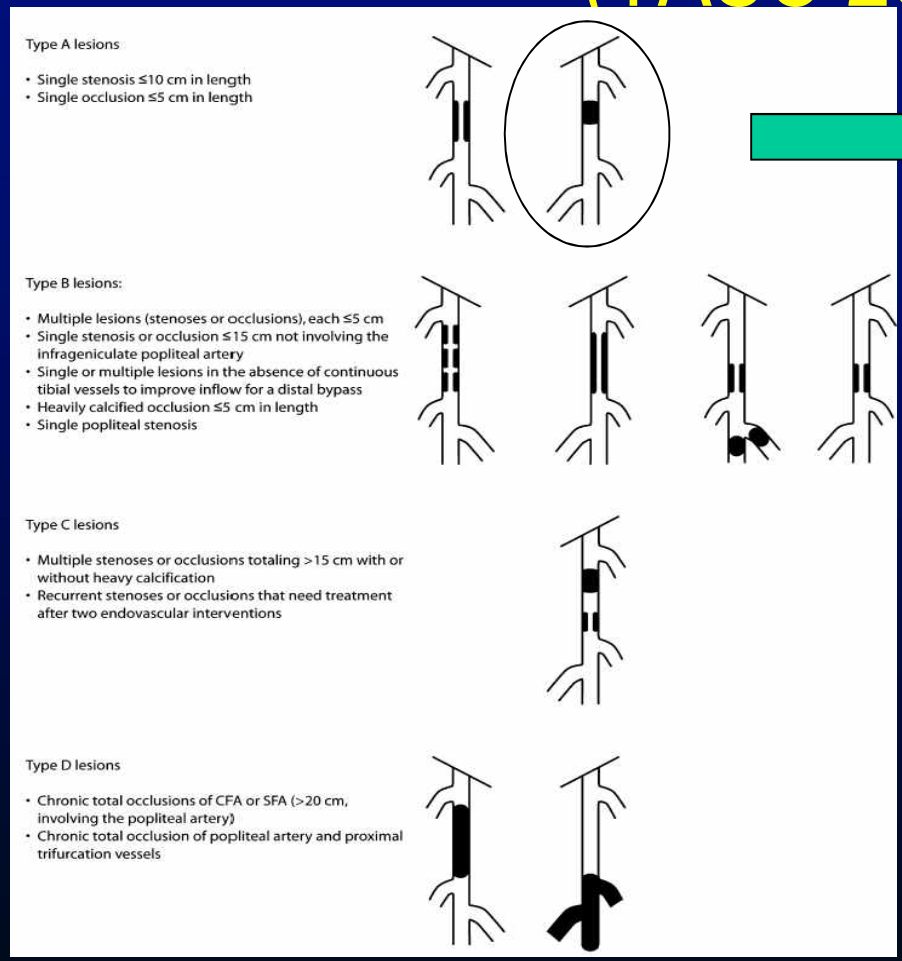
Luminexx (Bard, Inc, Murray Hill NJ)



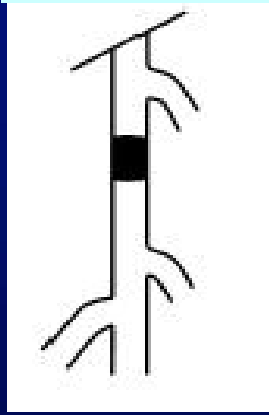
SMART control (Cordis Corp., Miami Lakes, FL)

Evidence shows that the advantage of nitinol stenting over angioplasty improves as lesion length increases.

TASC II classification of Femoro-Popliteal lesions (TASC 2006 documents)



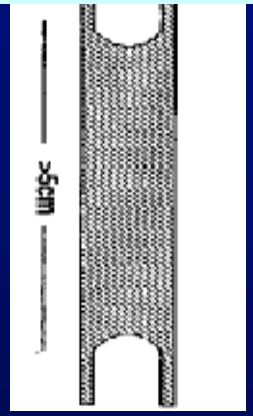
TASC 2006



TASC II A
CTO≦5cm

=

TASC 2000



TASC D
5cm ≦CTO

TASC II S 58
There is general agreement that for acute failure of PTA of an SFA lesion, stent placement is indicated. A recent randomized trial has demonstrated significantly higher primary patency rates of stenting vs.PTA of femoropopliteal artery lesions TASC A and B at 1-year follow up.

Mid-Term Clinical Outcome and Predictors of Vessel Patency after Femoropopliteal stenting with Self-Expanding Nitinol Stent

1) Table 1. Patient Characteristics

Patient Characteristics	
No. of Patients	511
Age (yrs)	72.0 ± 7.3
Male Gender (%)	361 (71)
Body Mass Index	22.3 ± 2.3
Hypertension (%)	451 (88)
Hyperlipidemia (%)	194 (38)
Diabetes (%)	313 (61)
Current Smoker (%)	126 (47)
Hemodialysis (%)	100 (20)
CVD (%)	145 (28)
CAD (%)	284 (56)
IC / CLI (%)	388 (76) / 123 (24)
Cilostazol (%)	319 (62)
Rutherford Classification	
II / III / IV / V / VI	133 / 255 / 42 / 68 / 13

Soga Y et al. JVS in press 2010

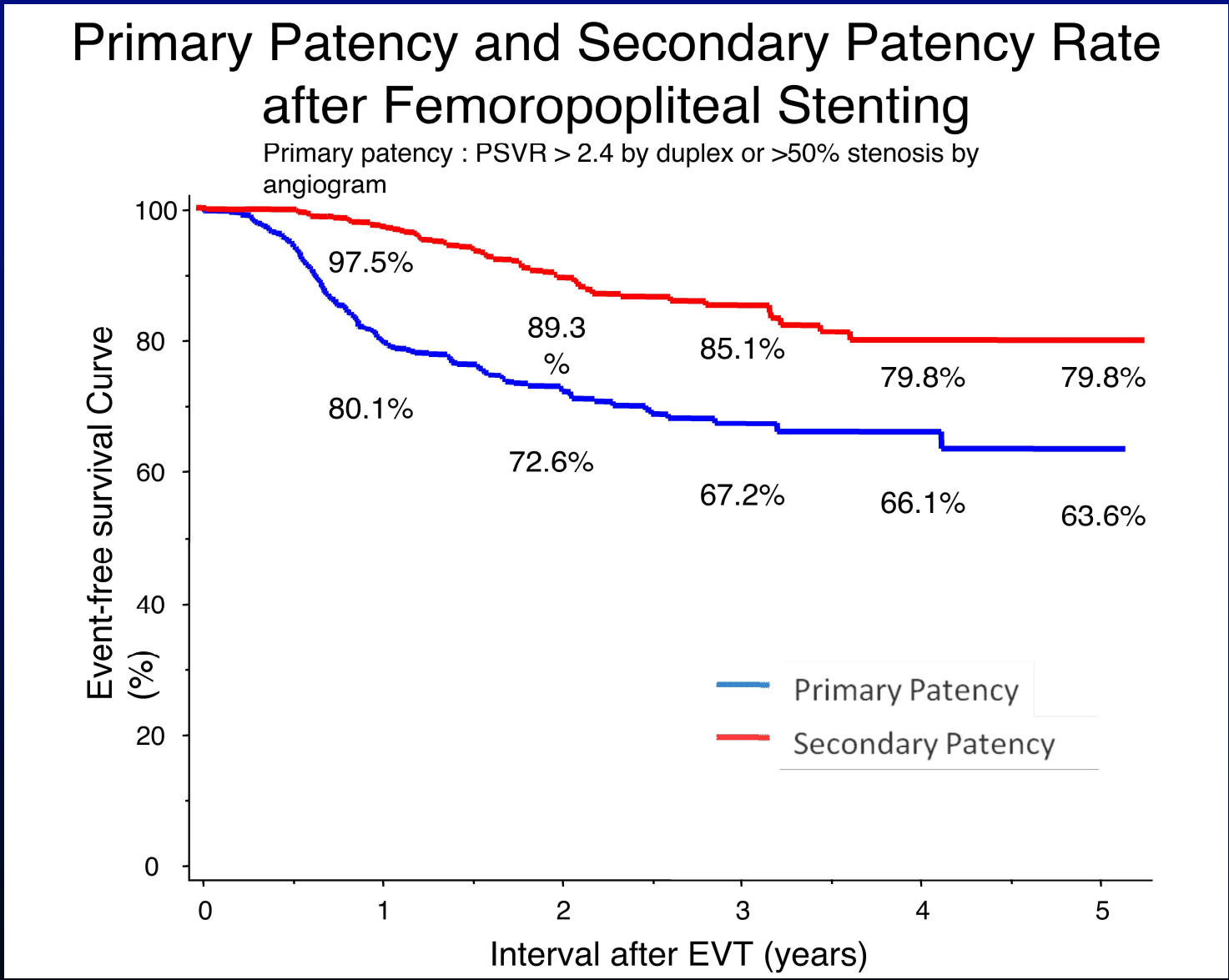
Mid-Term Clinical Outcome and Predictors of Vessel Patency after Femoropopliteal stenting with Self-Expanding Nitinol Stent

Table 2. Lesion Characteristics

Lesion Characteristics	
Number of Limbs	639
Approach	
Antegrade (%) / Retrograde (%)	486 (76) / 153 (24)
Lesion Length (mm)	150.5 ± 75.1
Reference Vessel Diameter (mm)	5.2 ± 0.5
Chronic Total Occlusion (%)	317 (50)
Calcified Lesion (%)	217 (34)
Pre-procedure ABI	0.57 ± 0.15
Post-procedure ABI	0.84 ± 0.15
Below-the-knee runoff	
0 / 1 / 2 / 3	45 / 163 / 217 / 214
Runoff Scores	5.6 ± 2.3
IC / CLI	5.0 ± 2.1 / 7.6 ± 2.4
Type of Nitinol Stent	
Luminexx (%)	135 (21)
S.M.A.R.T. (%)	504 (79)
Number of Stent	
per lesion / per patients	1.8 ± 0.8 / 2.3 ± 1.1
Stent Fracture (%)	88 (13.8)

Soga Y et al. JVS in press 2010

Mid-Term Clinical Outcome and Predictors of Vessel Patency after Femoropopliteal stenting with Self-Expanding Nitinol Stent



Soga Y et al. JVS in press 2010

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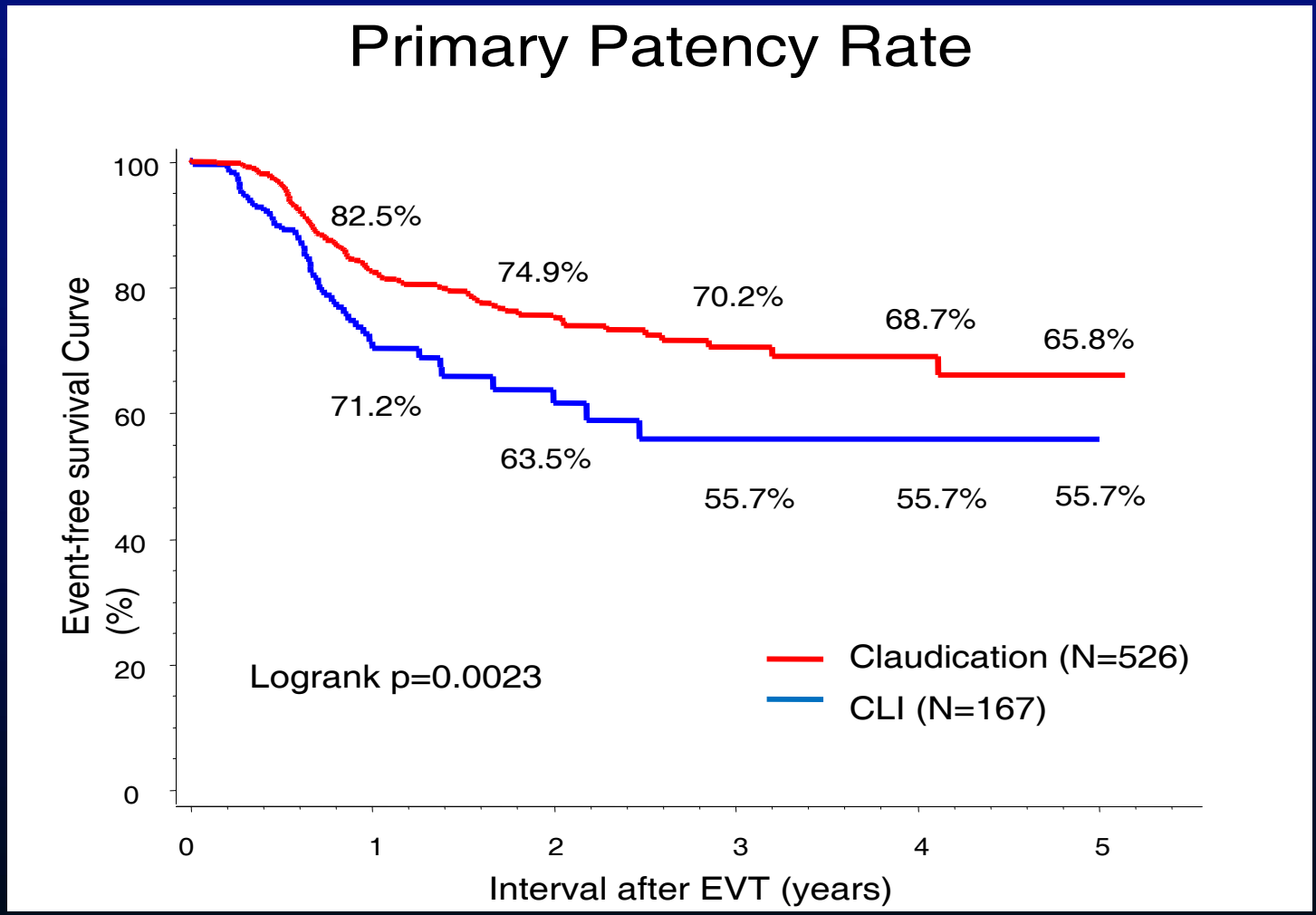
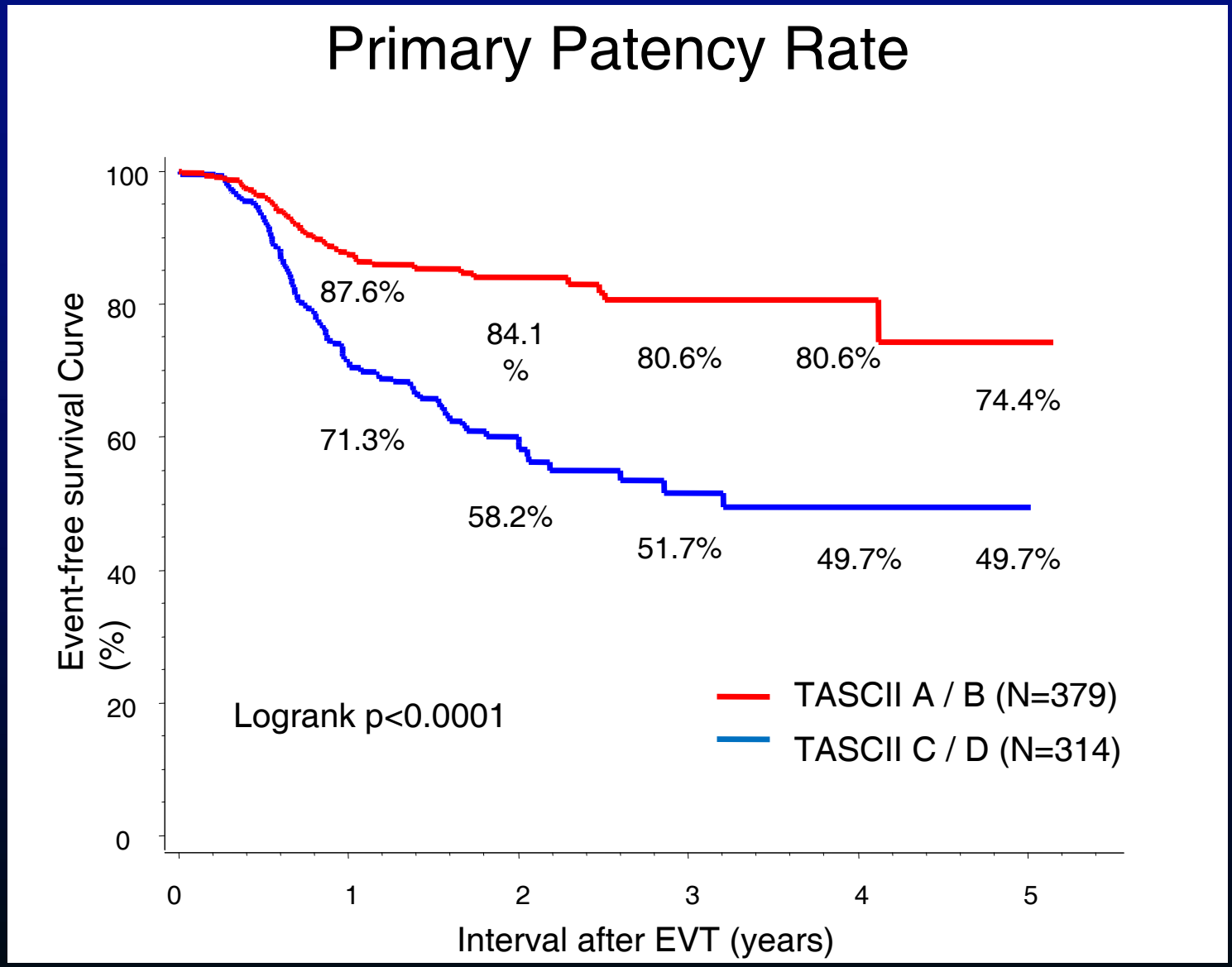


Soga Y et al. JVS in press 2010

Mid-Term Clinical Outcome and Predictors of Vessel Patency after Femoropopliteal stenting with Self-Expanding Nitinol Stent



Soga Y et al. JVS in press 2010

Multivariate Analysis of Primary Patency

Variables	HR	95% CI	P value
TASC II class C / D	2.39	1.68 – 3.40	< 0.0001
Hemodialysis	1.65	1.11 – 2.45	0.013
Stent Fracture	1.57	1.06 – 2.34	0.025
Cilostazol Administration	0.52	0.37 – 0.71	< 0.0001

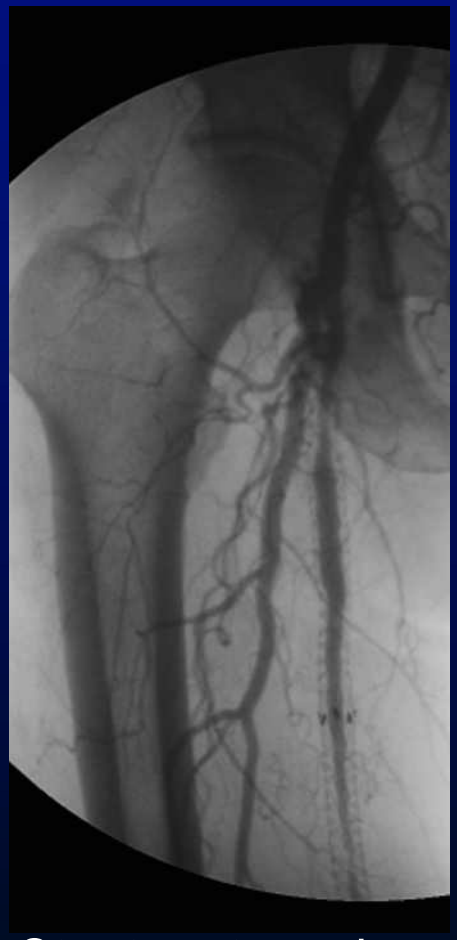
Soga Y et al. JVS in press 2010

SFA TASC D Lesions
Why are restenosis rates still higher?

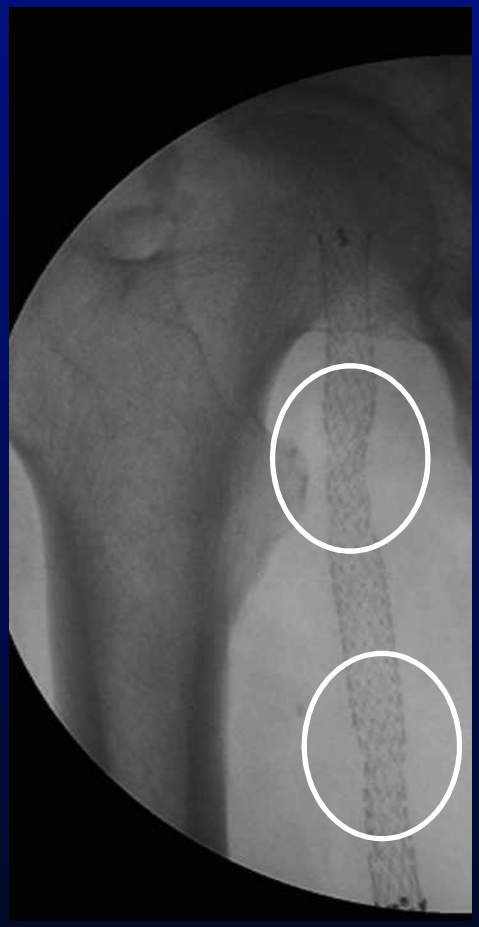
1) Stent Fracture

2) Intimal Hyperplasia

Stent fracture

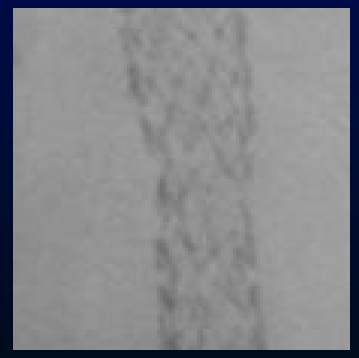


Stent restenosis



Stent fracture !!

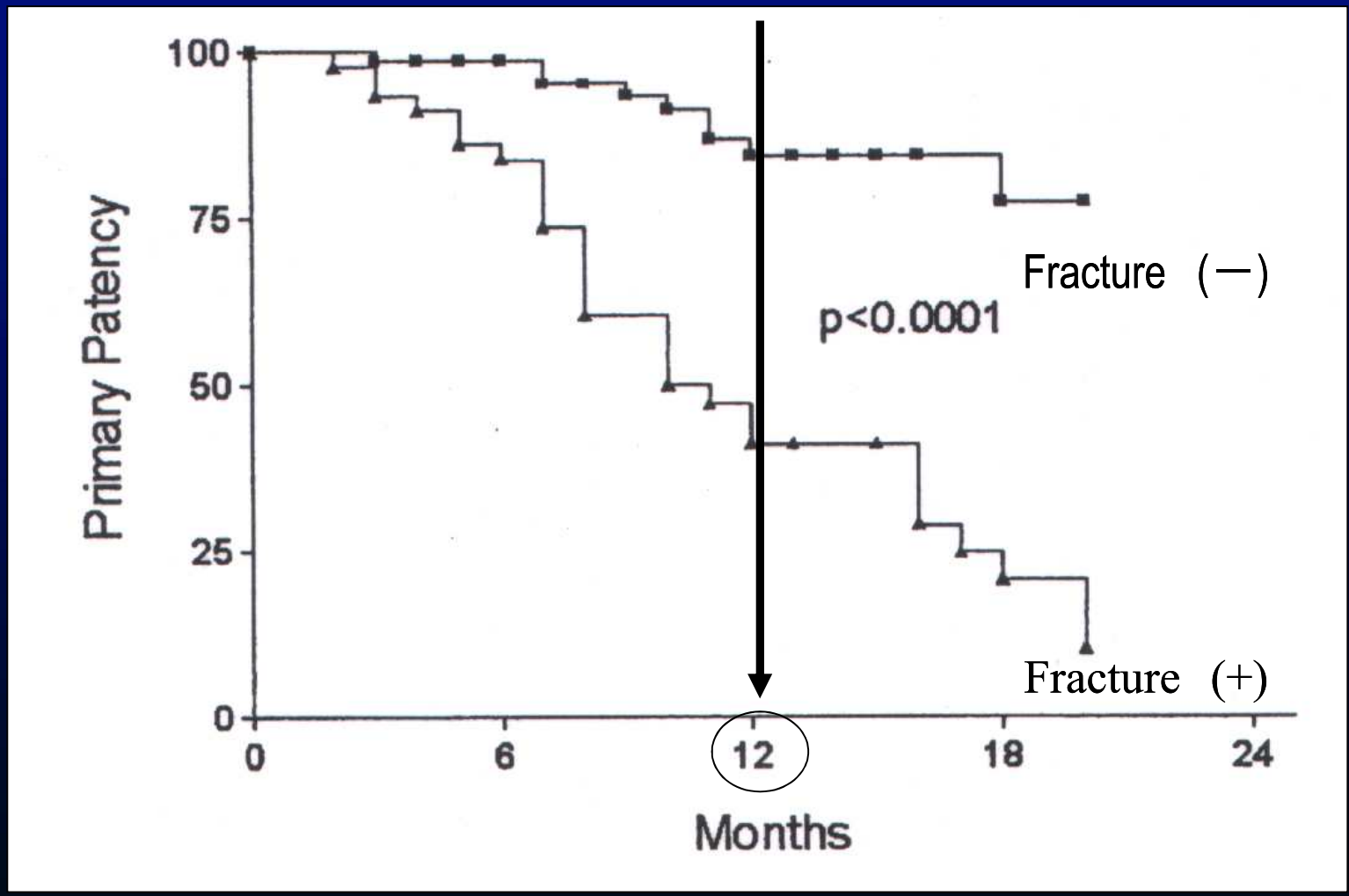
Type II stent fracture



Type II stent fracture

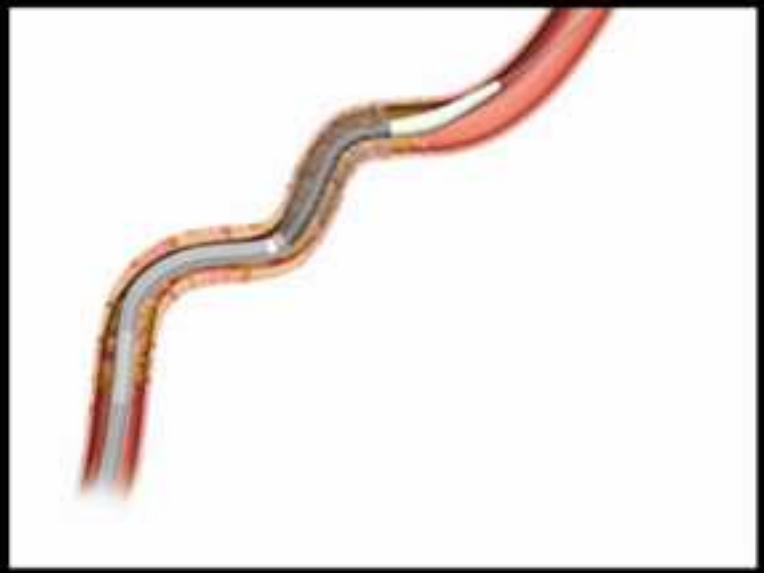
Type 2

The occurrence of stent fracture is associated with a reduction in overall patency rate.



Scheinert D, Biamino J et al. J Am Coll Cardiol. 2005;45:312-5

LifeStent NT



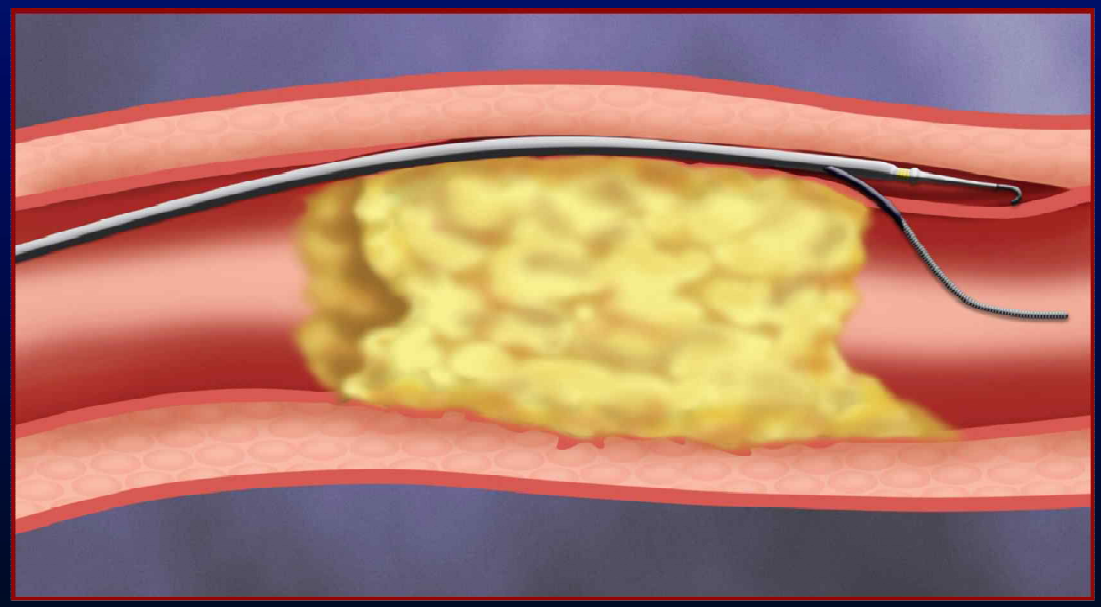
Single Hand Deployment

John Laird, Jr., MD

VIVA 05

True Lumen Return by Cross Point
- Pass Guide Wire -

Pass 0.014” extra-support guide wire (300cm) through CrossPoint needle into vessel lumen.



Progress of CTO-EVT in Japan

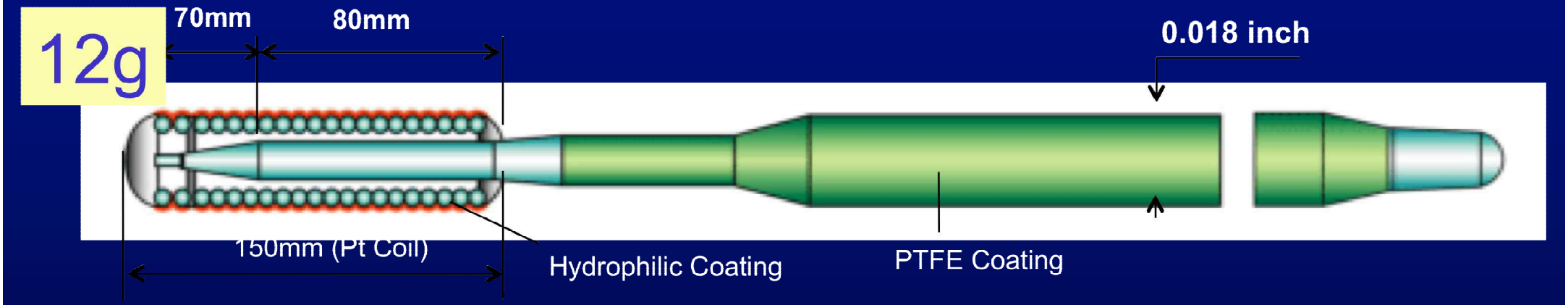
Factors contributing to progress in CTO-EVT

- Digital angiography
- Development of Japanese stiff-wire technology

  (Treasure wire, Aatato wire family)
- Retrograde Approach
- Ultrasound Guided (Surface Echo, IVUS)
- CTO wiring techniques from CTO-PCI

Treasure

From June 2004

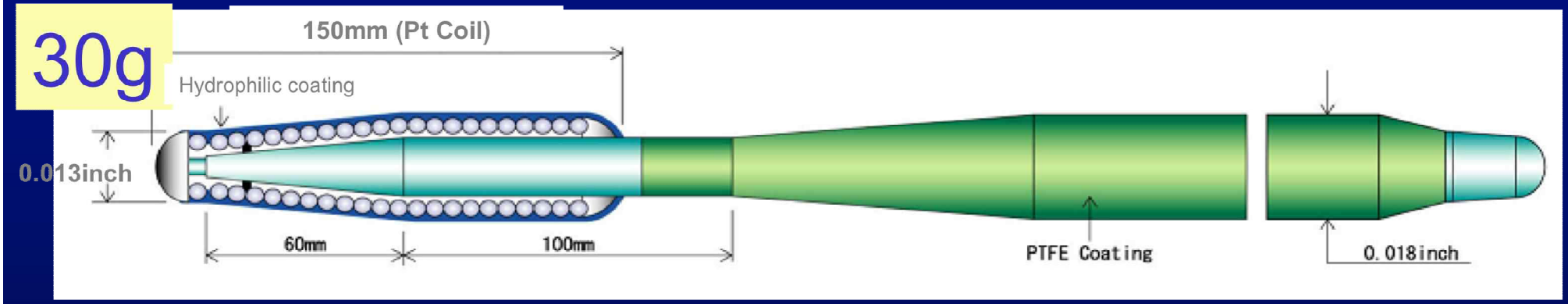


Treasure is a hydrophilic coated 0.018” PTA guidewire, which possesses superior torqueability due to its structure using thick stainless steel wires for the spring coil.

High torque performance
Good for controlled drilling

Astato

From August 2006

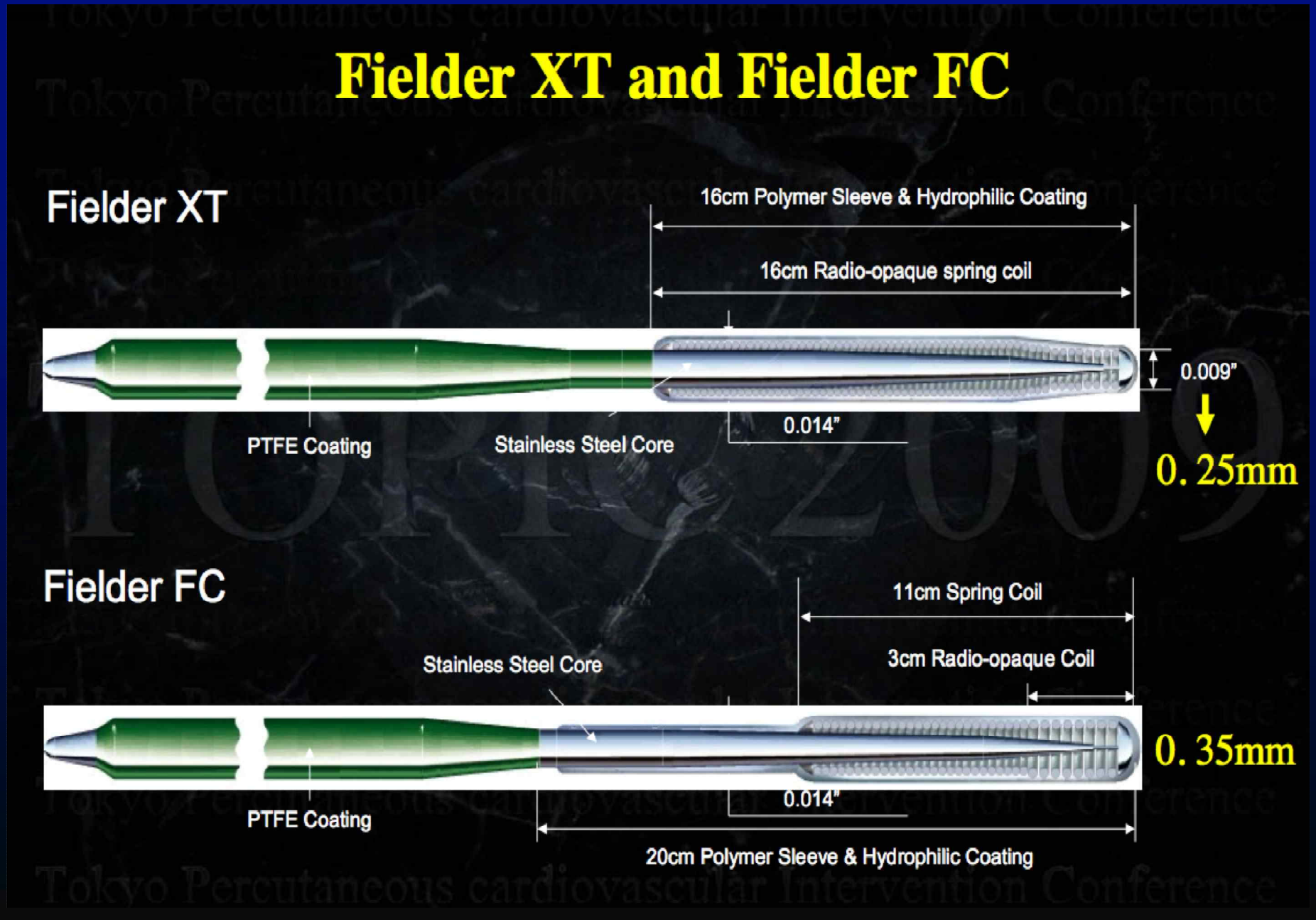


Astato is a 0.018” hydrophilic coated PTA guidewire, which possesses high penetration power with its 30g tip load and tapered design down to 0.013”.

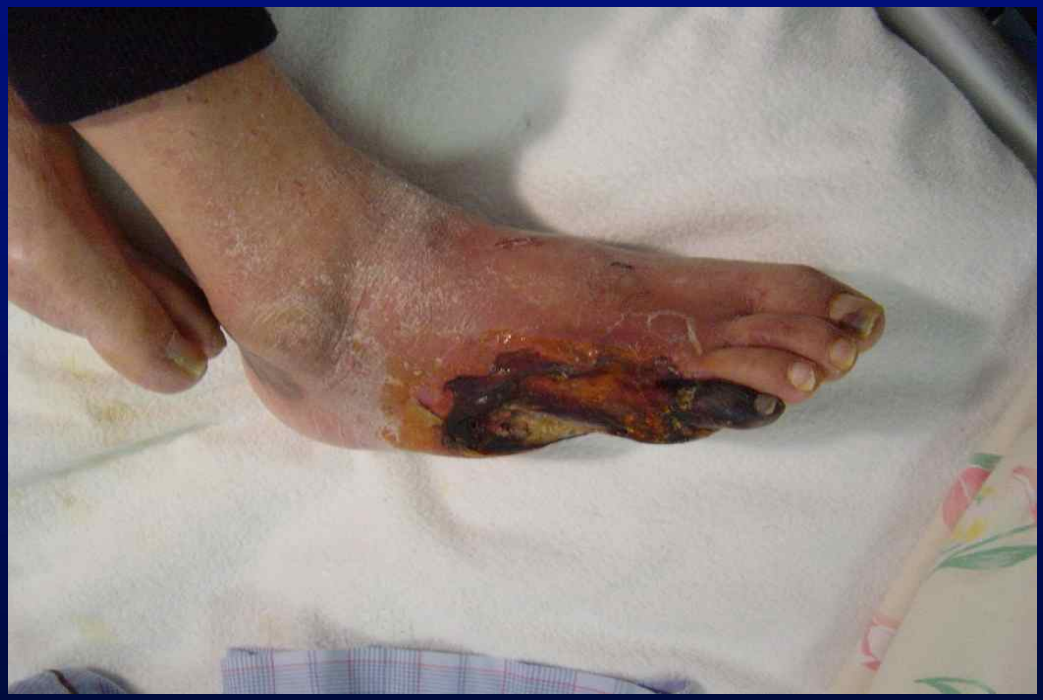
High penetration force
Good for penetration

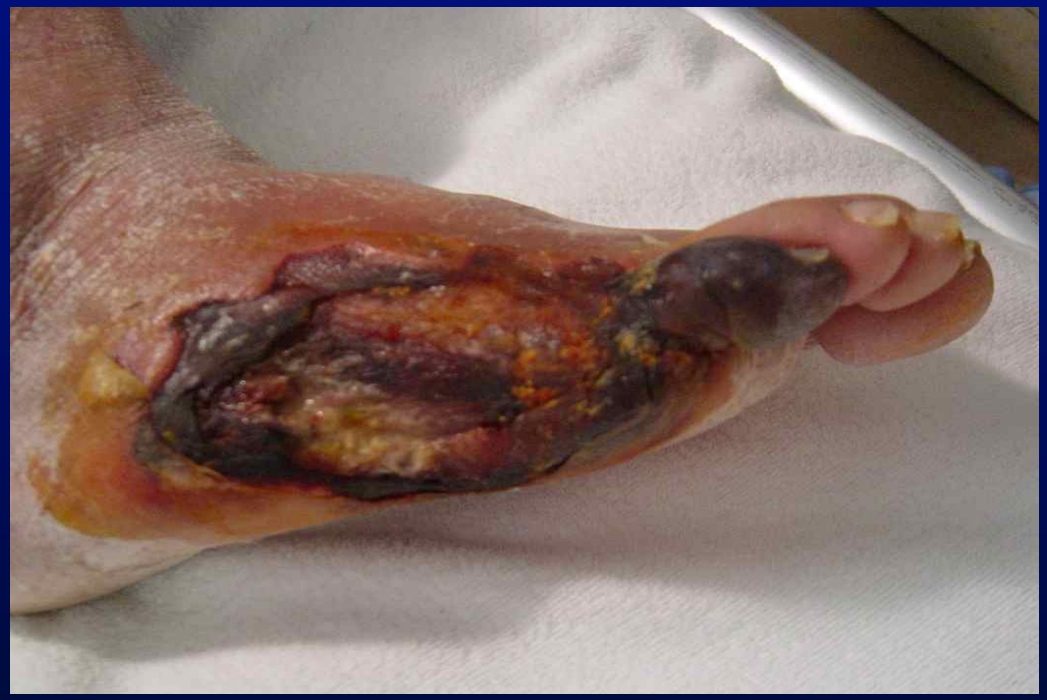
From 2009

Fielder XT and Fielder FC



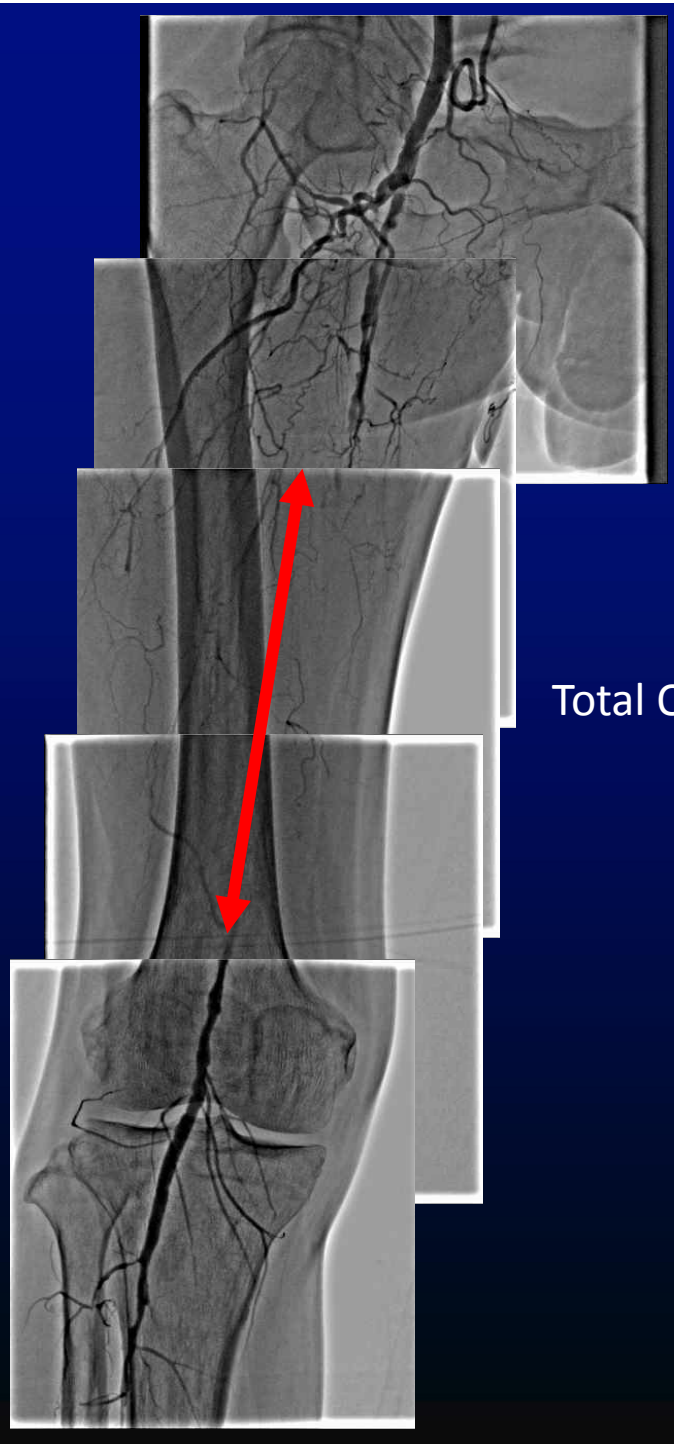
60 y.o. Male





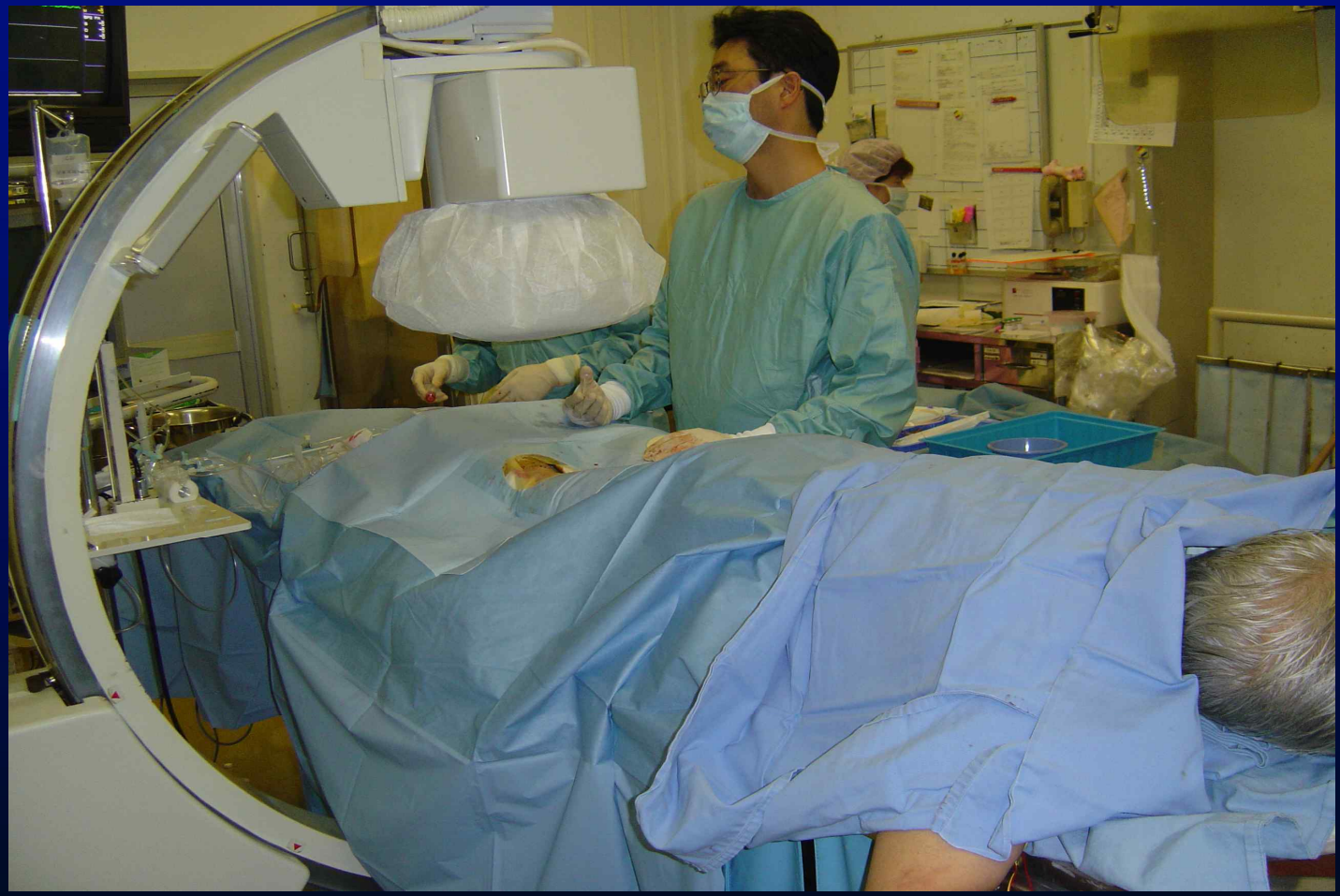
ABI : right 0.38, left 0.78

SPP : (right)plantar 59 mmHg, dorsal 20 mmHg

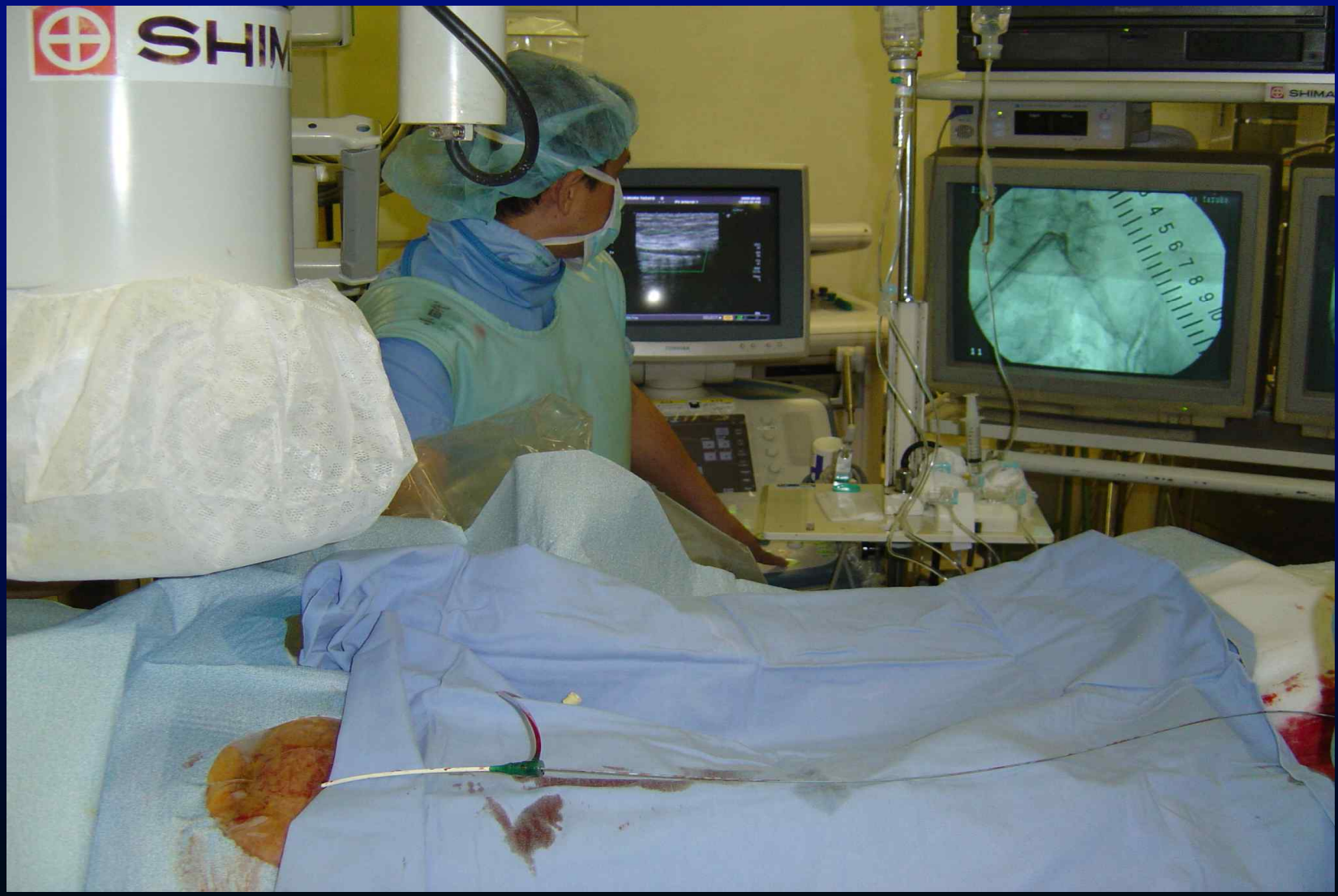


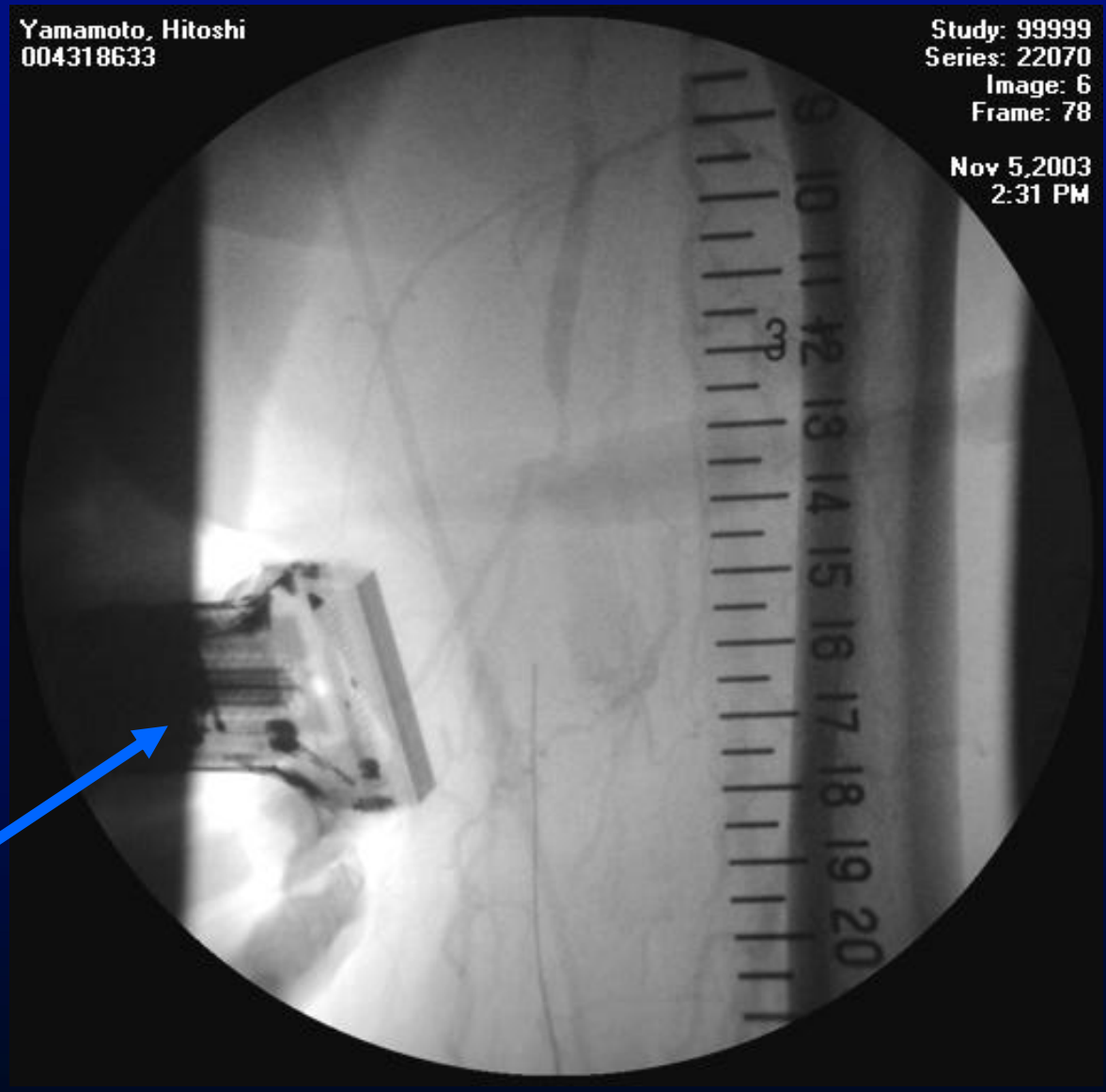
Total Occlusion

Bidirectional approach



Echo guided intervention



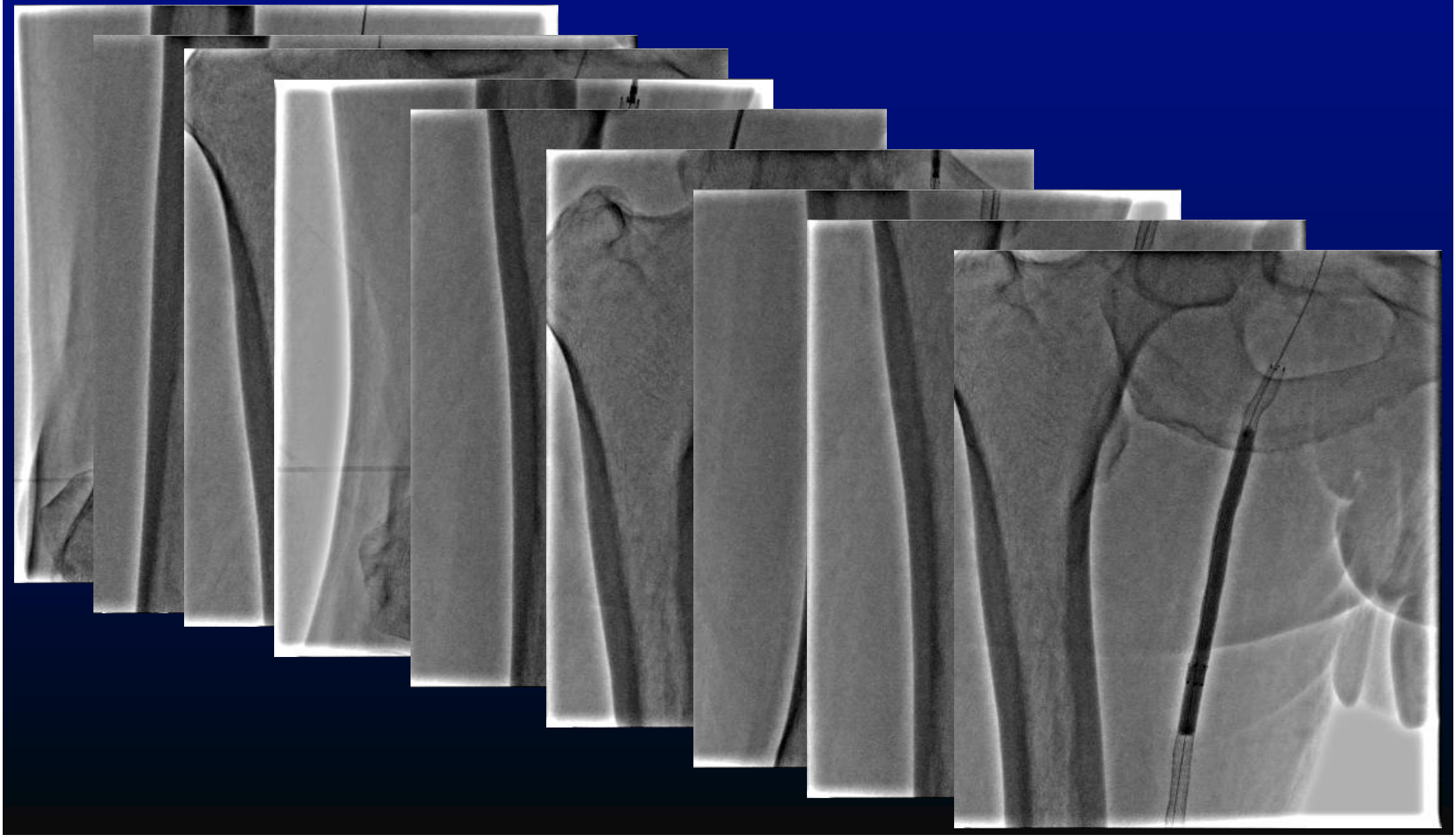


Probe

Echo-Guided GW Manipulation


TOSHIBA
BK:- -
O
SAPPORO HIGASHI MC
- -
PV Arterial1
0:04:29
2005/09/03
3:14:49 PM
13.9
13.9
cm/s
0
1
2
3
4
T
2DG
81
DR
65
CG
38
PRF
9.4k
Filter
7
11L5
T8.4
CF 4.4
14 fps
HDD:64% Free
Raw Memory:#0(0%)
SELECT

Balloon → Stent → Post-balloon



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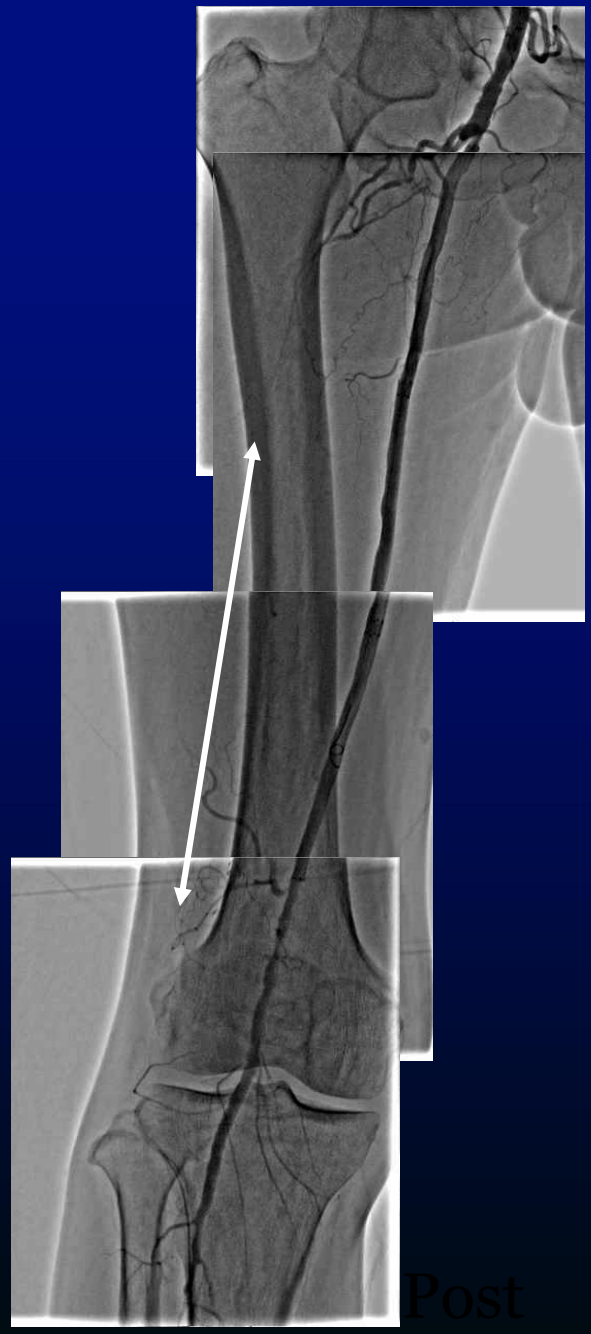


Post

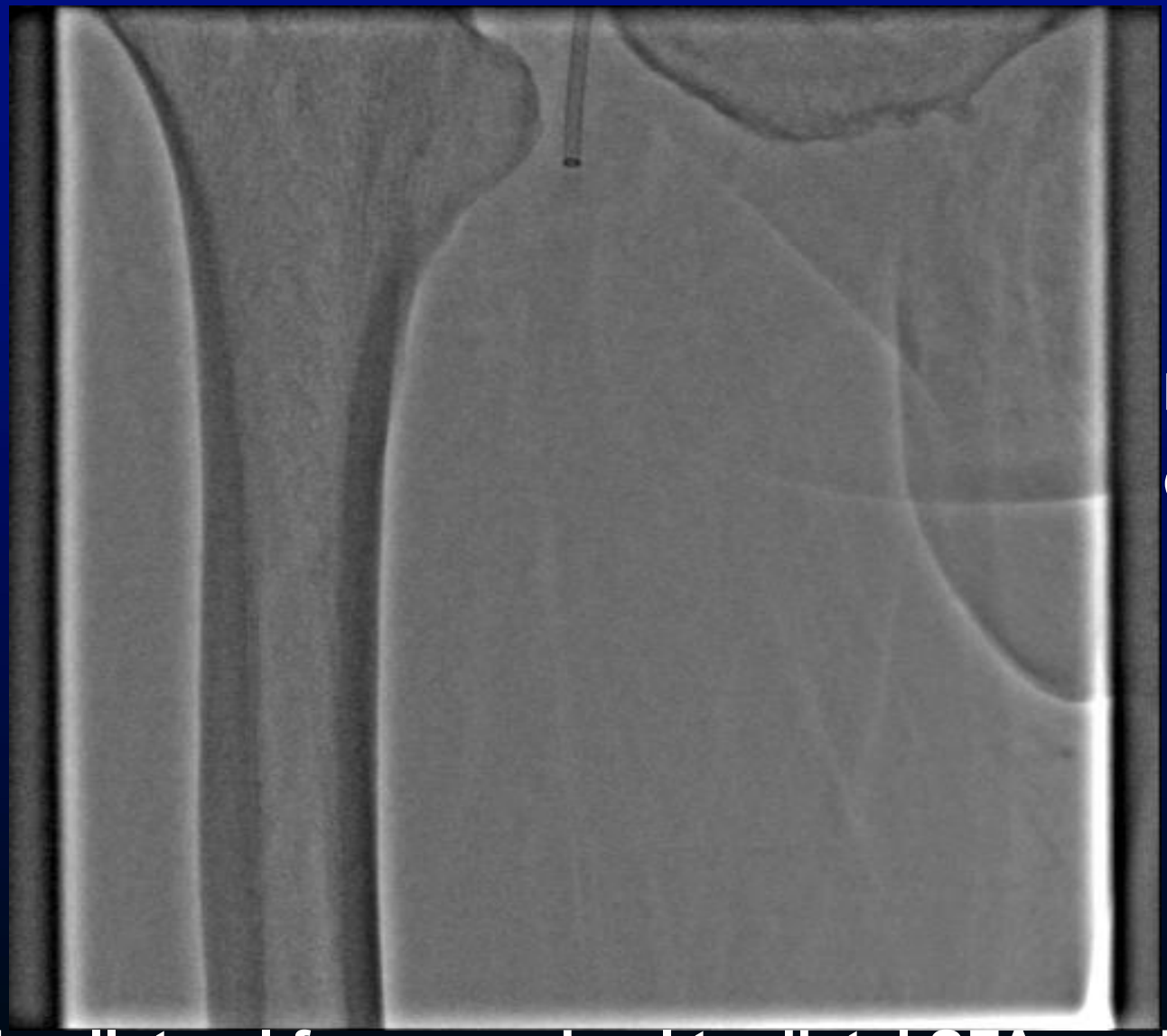
PPI for long SFA lesions (>10cm)

1 Y Primary Patency Rate

Jan 2001~Apr. 2004	56% (5/9)
May 2004~Aug. 2004 (Echo guided and lesion and zone specific stenting)	80% (12/15)

60y.o Male

EVT to rt SFA CTO

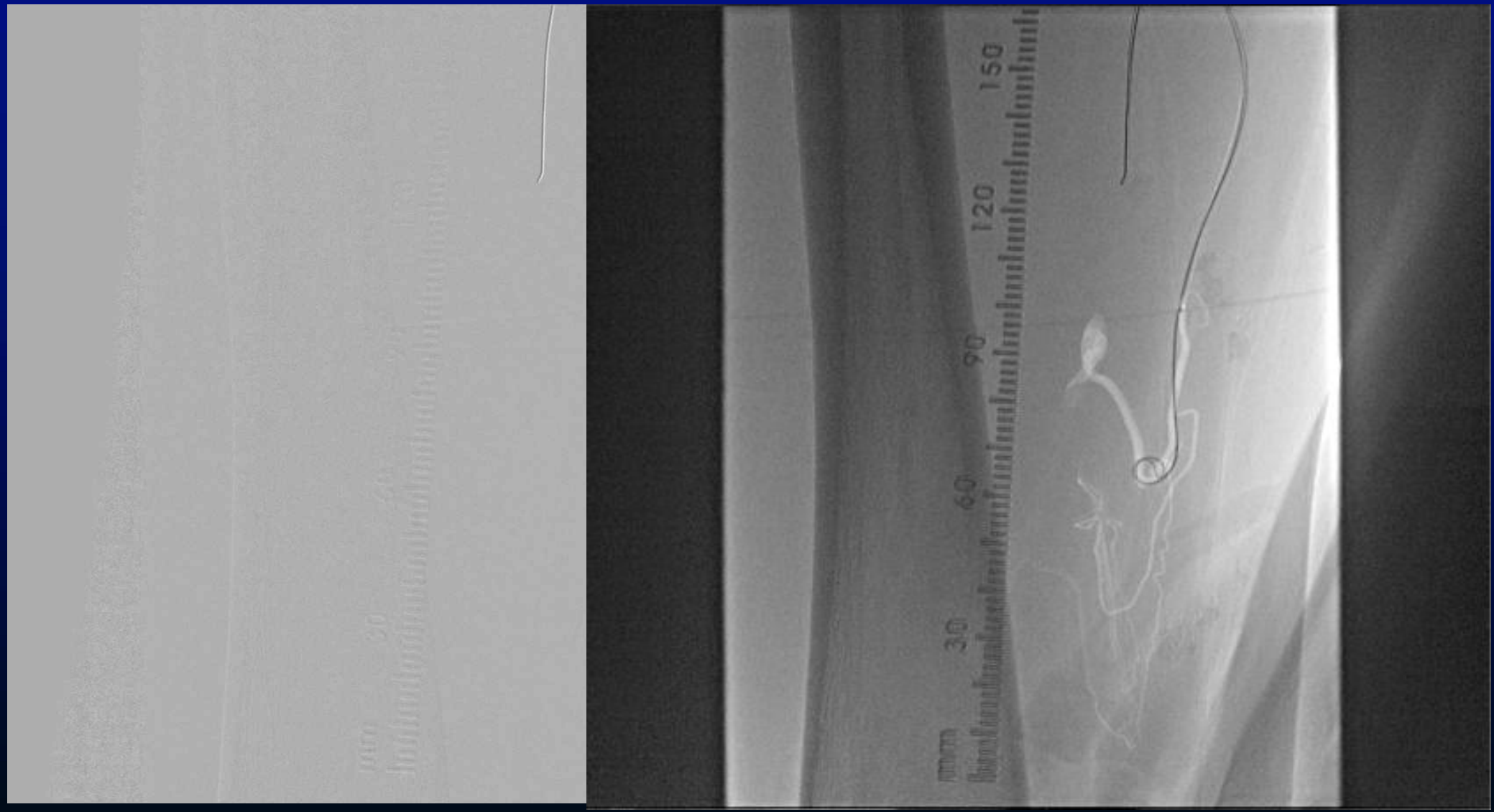


Lt femoral A approach

G.C destination 45cm 6F

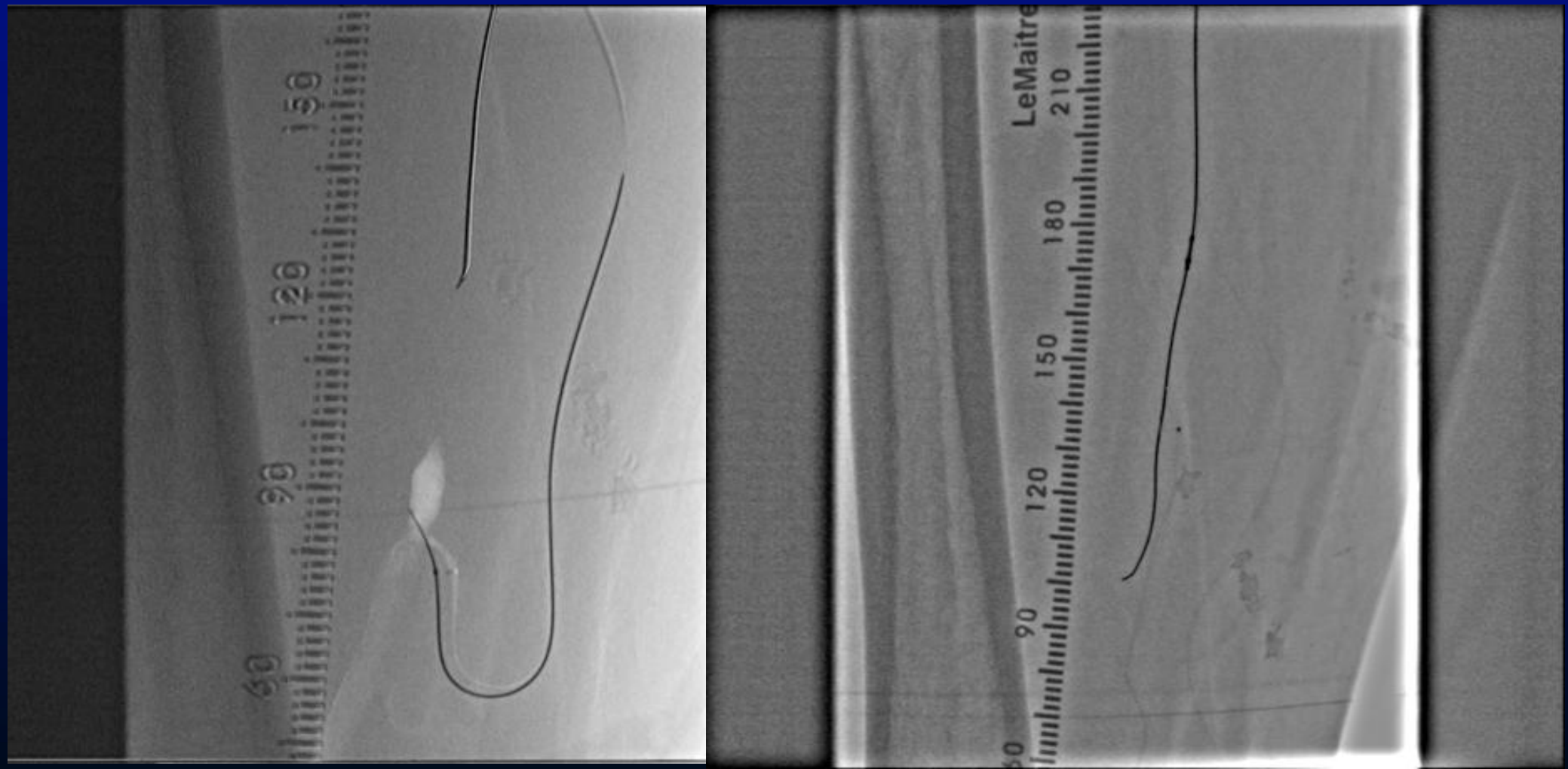
Good collateral from proximal to distal SFA, no BK lesion

60y.o Male

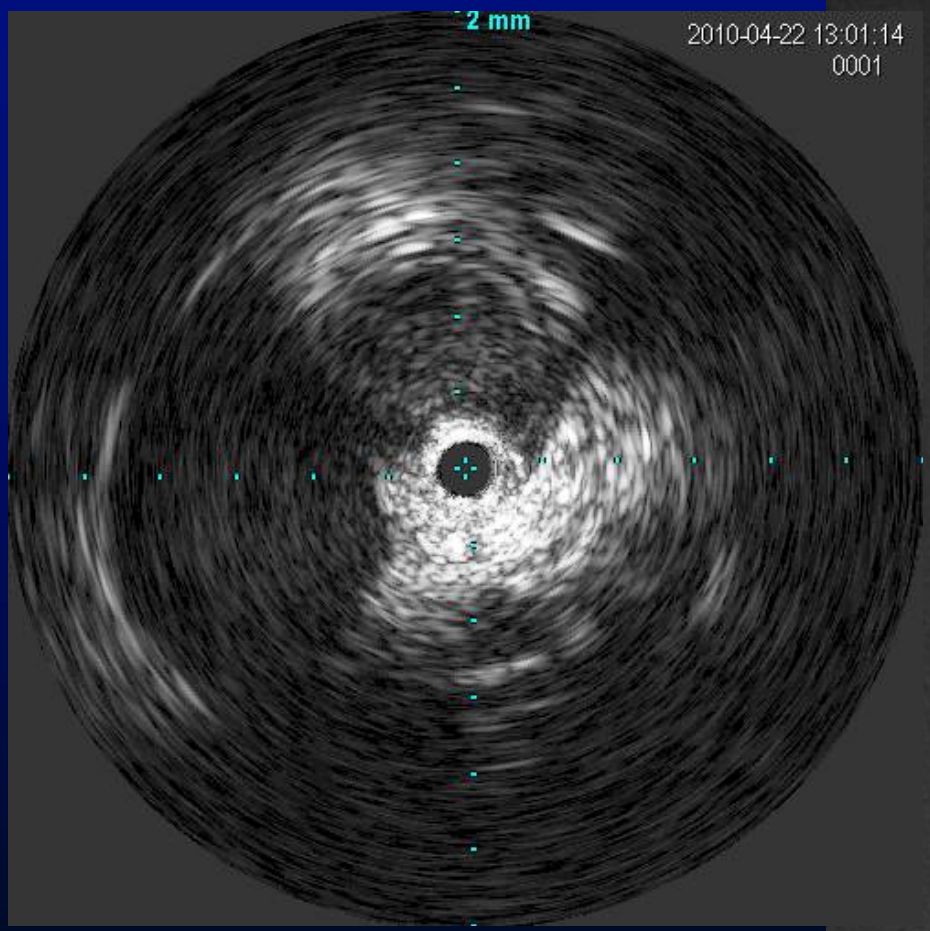


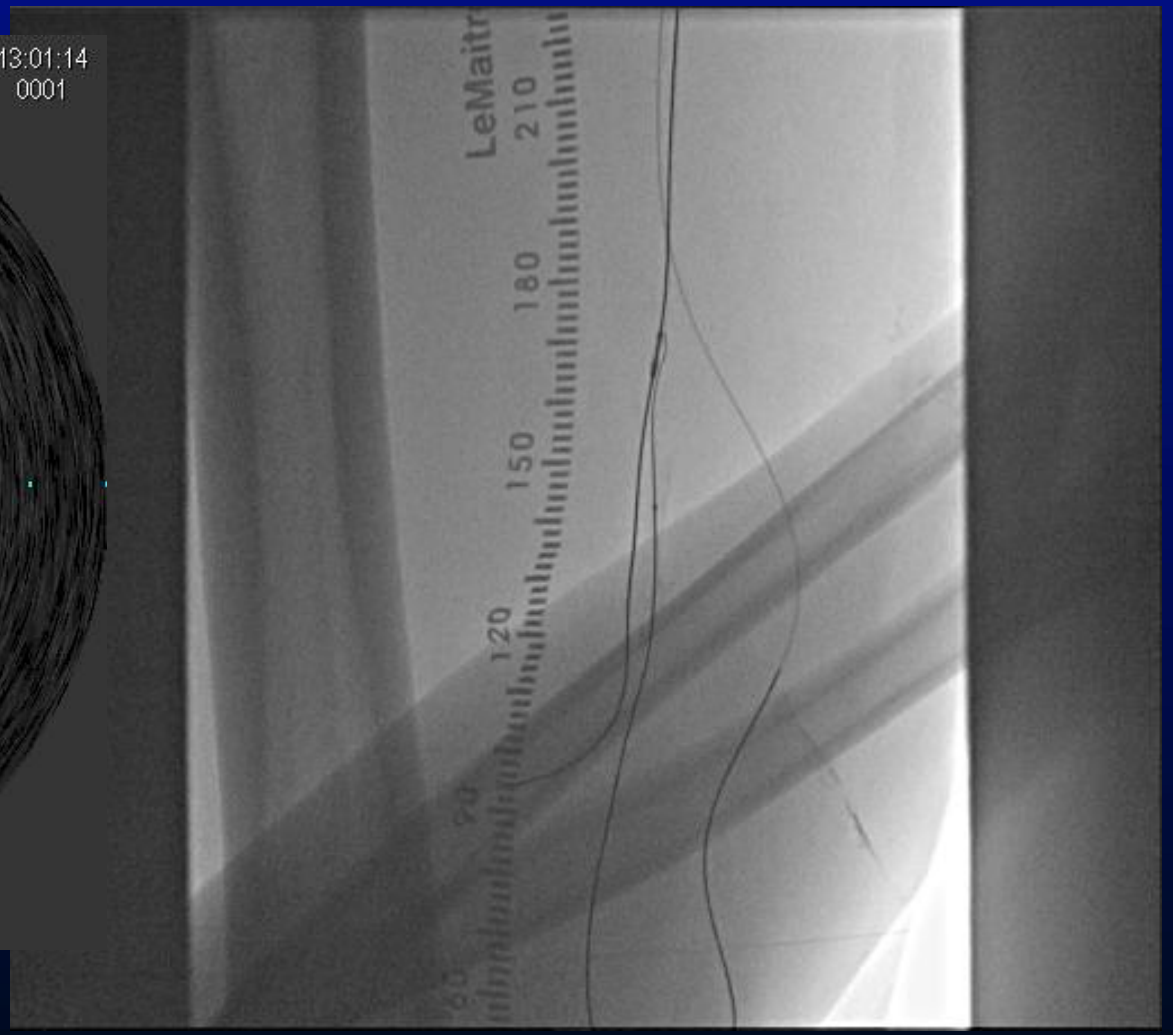
X-treme PV with Fine cross crossing collateral artery

60y.o Male



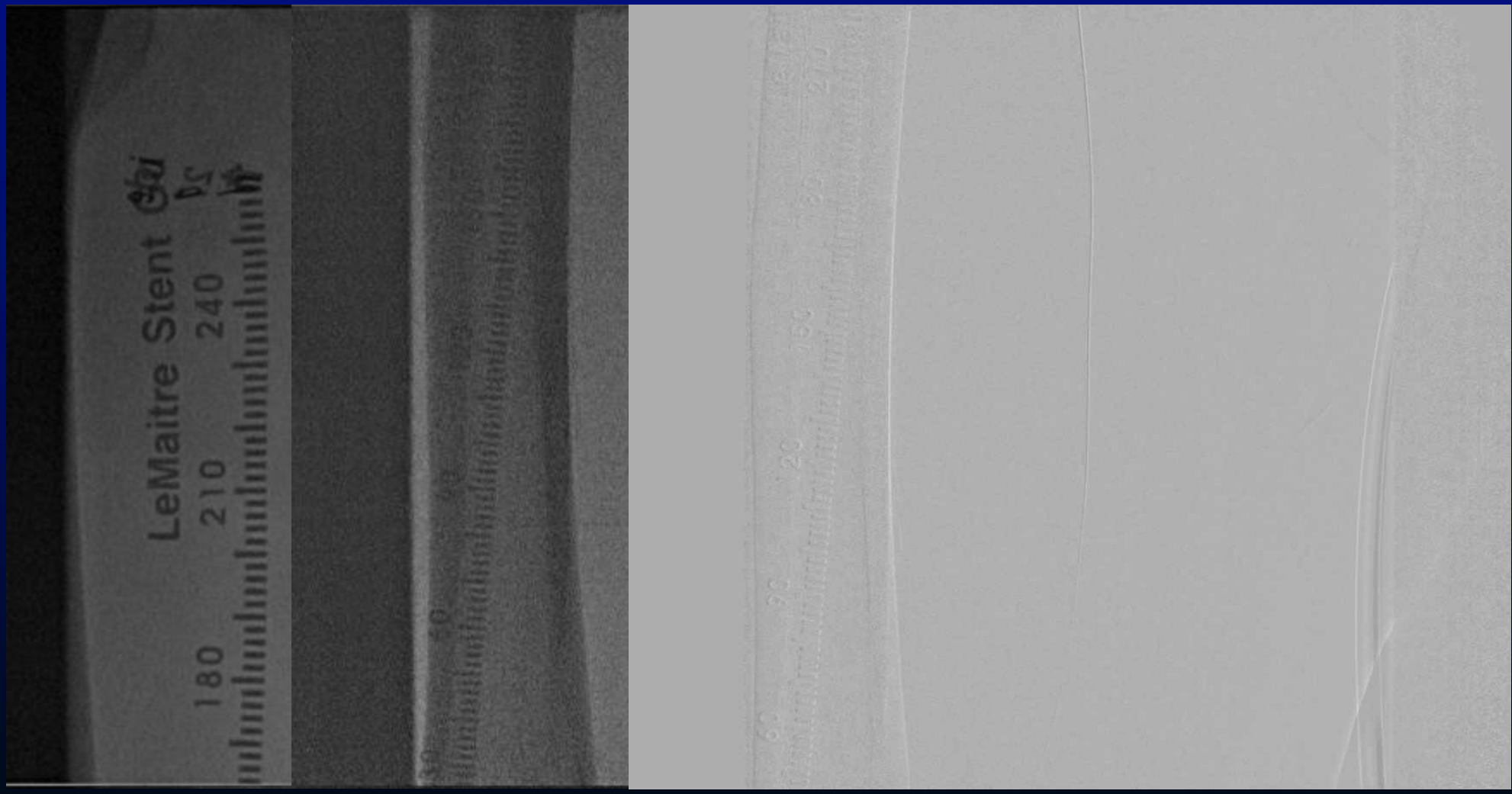
60y.o Male





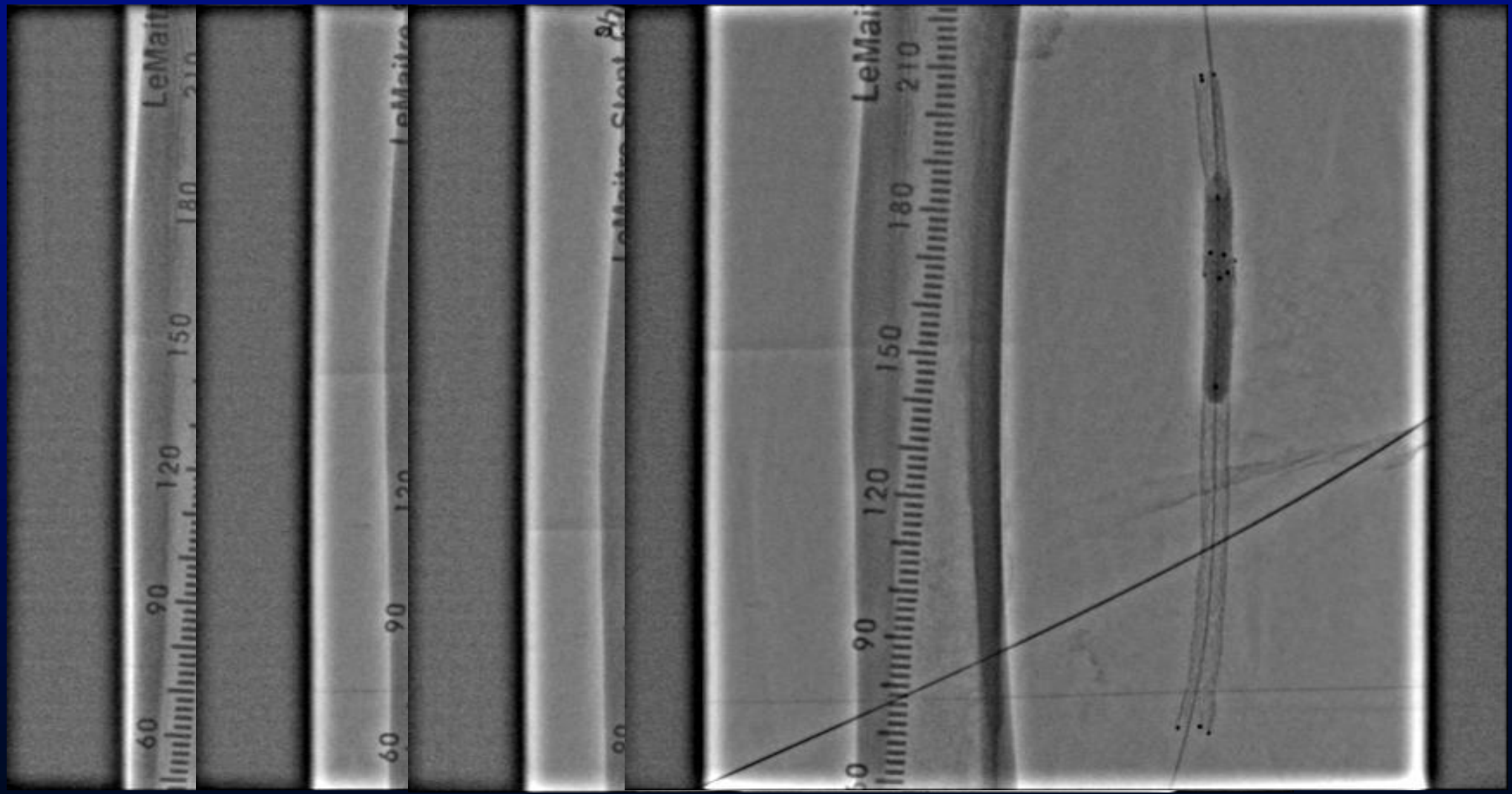
Retrograde wire crossing true lumen using IVUS

60y.o Male



Catching retrograde wire using snea

60y.o Male



Amphirion Deep

4/120

Misago

6/100

Misago

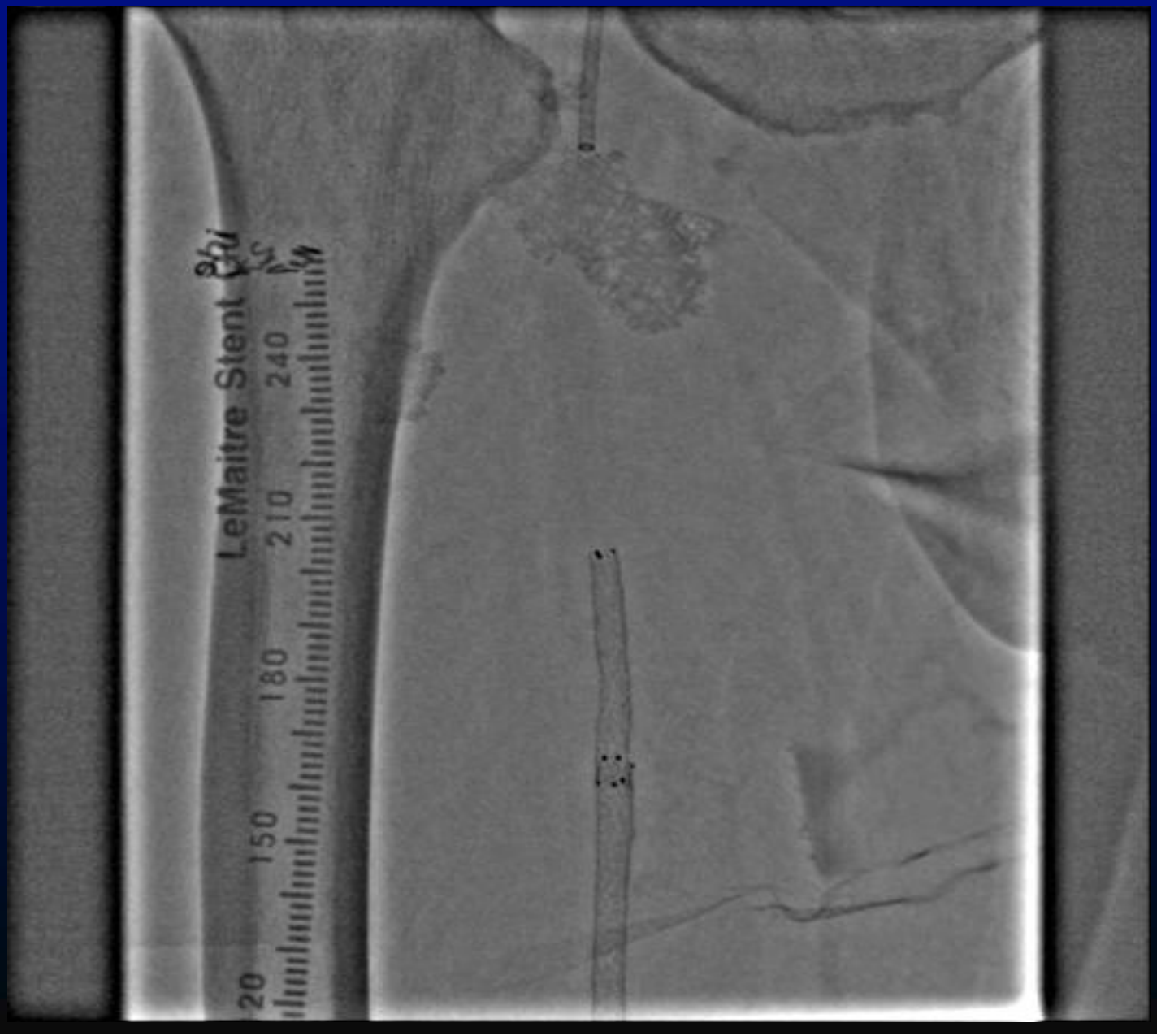
4/40

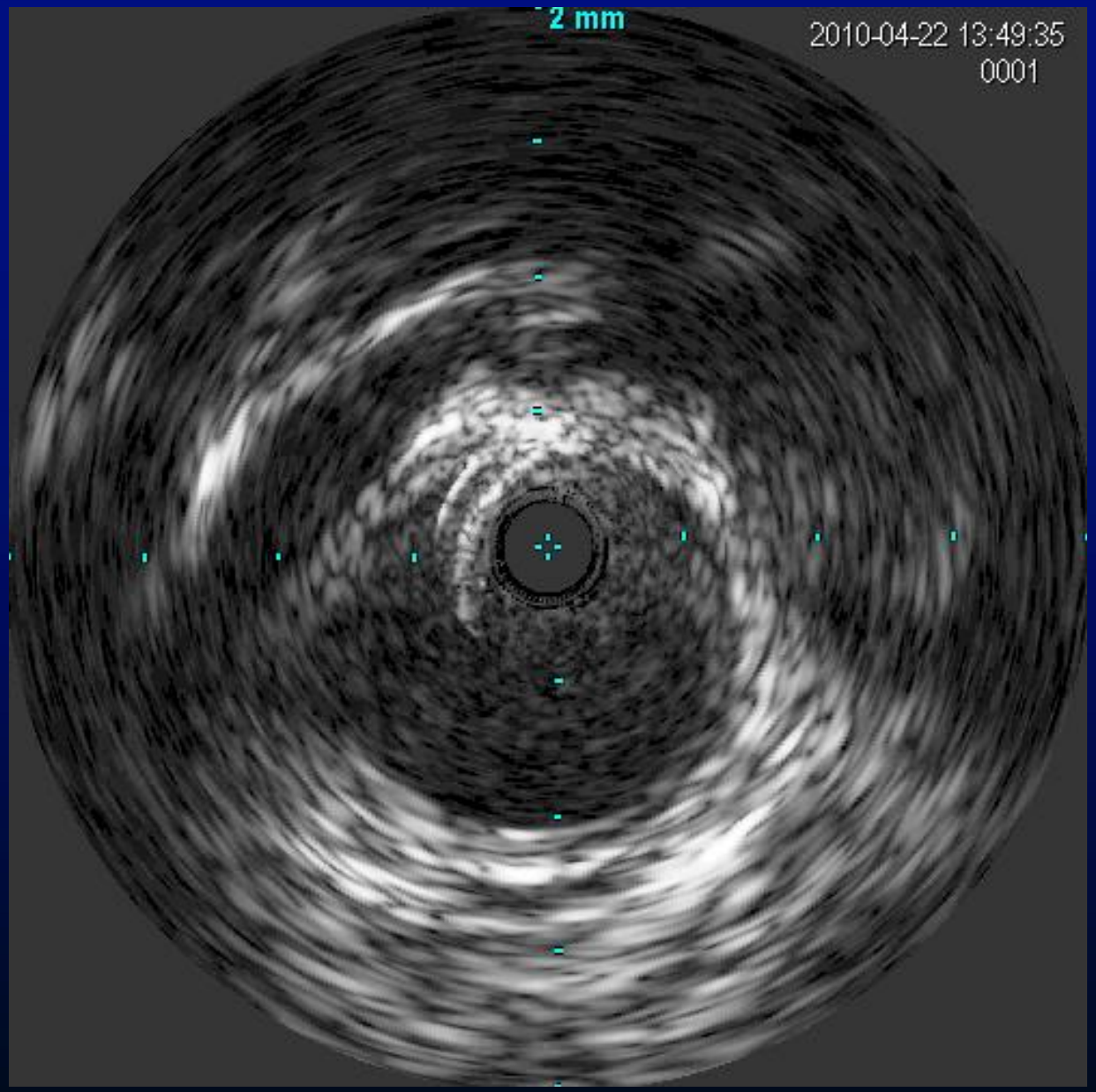
Shiden

5/40

60y.o Male

final

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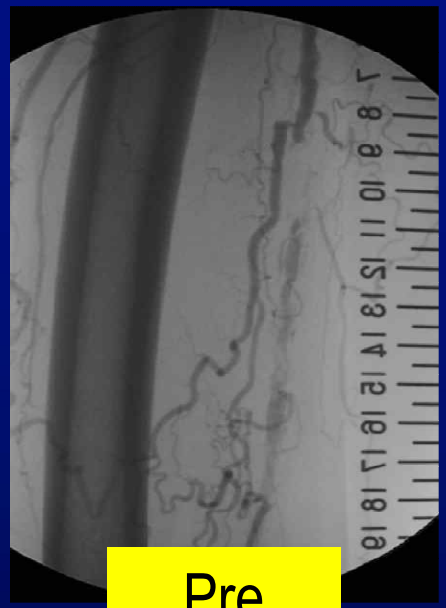
SFA TASC D Lesions
Why are restenosis rates still higher?

1) Stent Fracture

2) Intimal Hyperplasia



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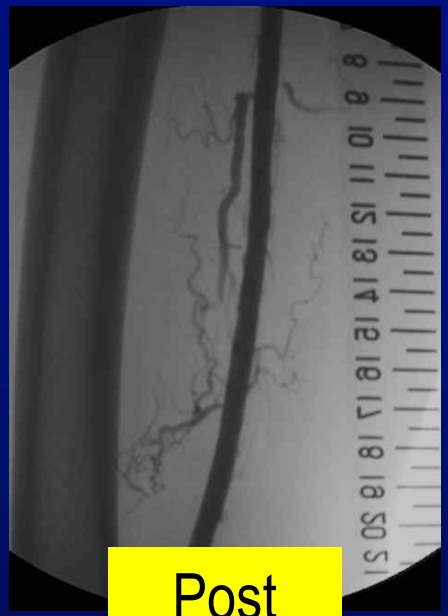
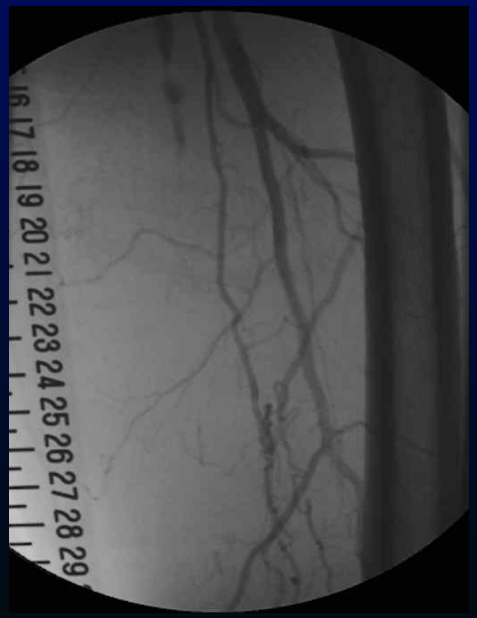
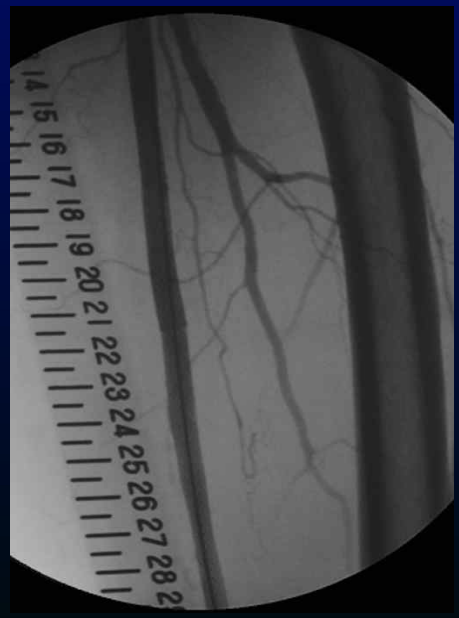


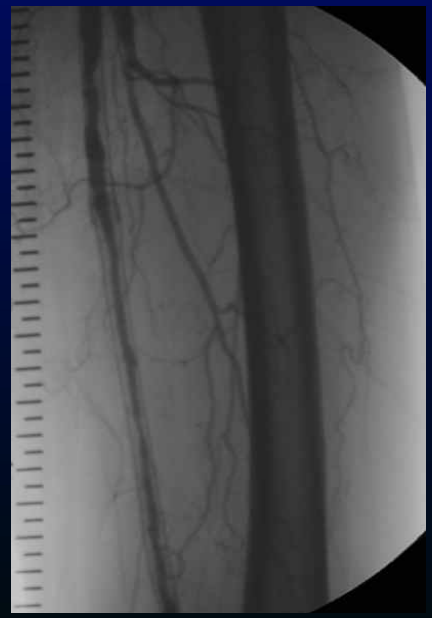
Post

1 year

With cilostazol

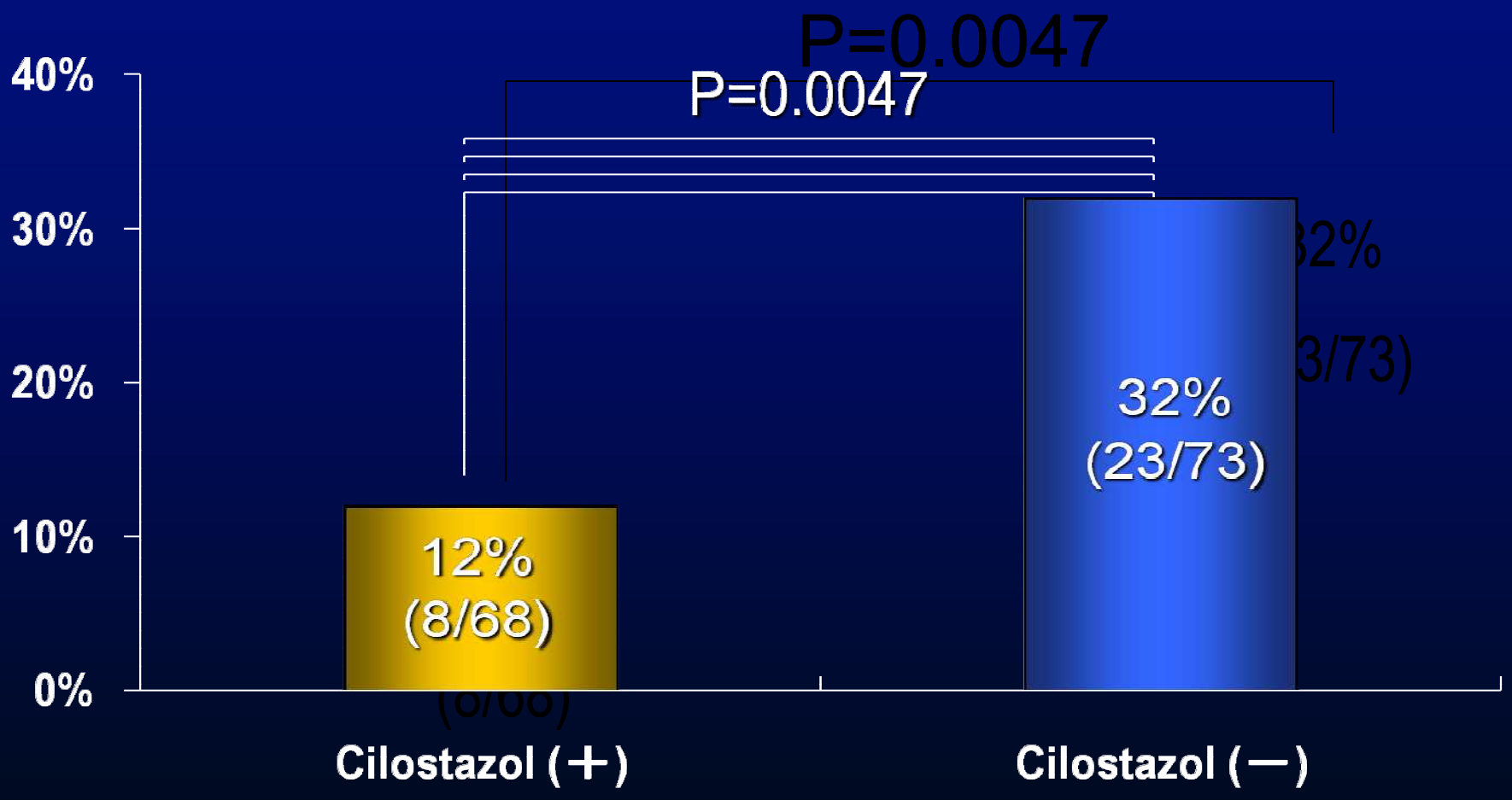






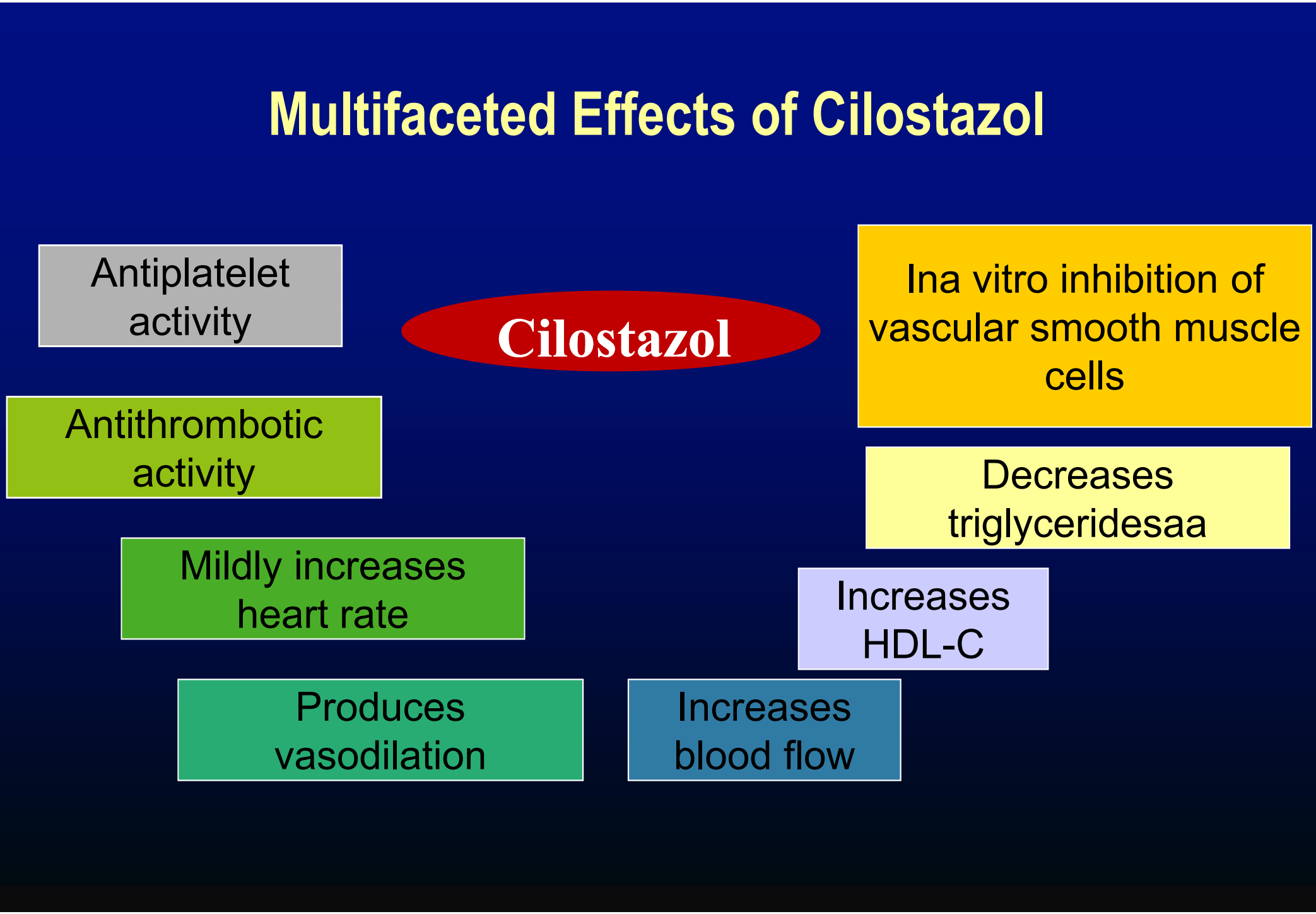
Without cilostazol

Target lesion revascularization was significantly reduced in the cilostazol-treated cilostazol (+) group.



Iida O et al. Circ J 2005; 69:1256-1259

Multifaceted Effects of Cilostazol



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ACC/AHA GUIDELINES

ACC/AHA Guidelines for the Management of Patients With Peripheral Arterial Disease (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic)

RECOMMENDATIONS

Class I

1. **Cilostazol (100 mg orally 2 times per day) is indicated as an effective therapy to improve symptoms and increase walking distance in patients with lower extremity PAD and intermittent claudication (in the absence of heart failure). *(Level of Evidence: A)***
2. **A therapeutic trial of cilostazol should be considered in all patients with lifestyle-limiting claudication (in the absence of heart failure). *(Level of Evidence: A)***

Cilostazol improves maximal walking distance by 40% to 60% after 12 to 24 weeks of therapy (56–60). Cilostazol increases ABI modestly, but the hemodynamic effect cannot account for the improvement in claudication (56,57,59,61). A meta-analysis indicates that cilostazol also improves walking ability and health-related quality of life (62). Cilostazol administered at 100 mg twice daily is more effective than 50 mg twice daily (58,60). Although no trials have found a significant increase in major cardiovascular events in patients treated with cilostazol, this medication should not be used in individuals with heart failure because of its potential adverse effect in this population as a phosphodiesterase type 3 inhibitor.

Pentoxifylline.

Produces vasodilation

Increases blood flow

1. **Cilostazol (100 mg orally 2 times per day) is indicated as an effective therapy to improve symptoms and increase walking distance in patients with lower extremity PAD and intermittent claudication (in the absence of heart failure). *(Level of Evidence: A)***
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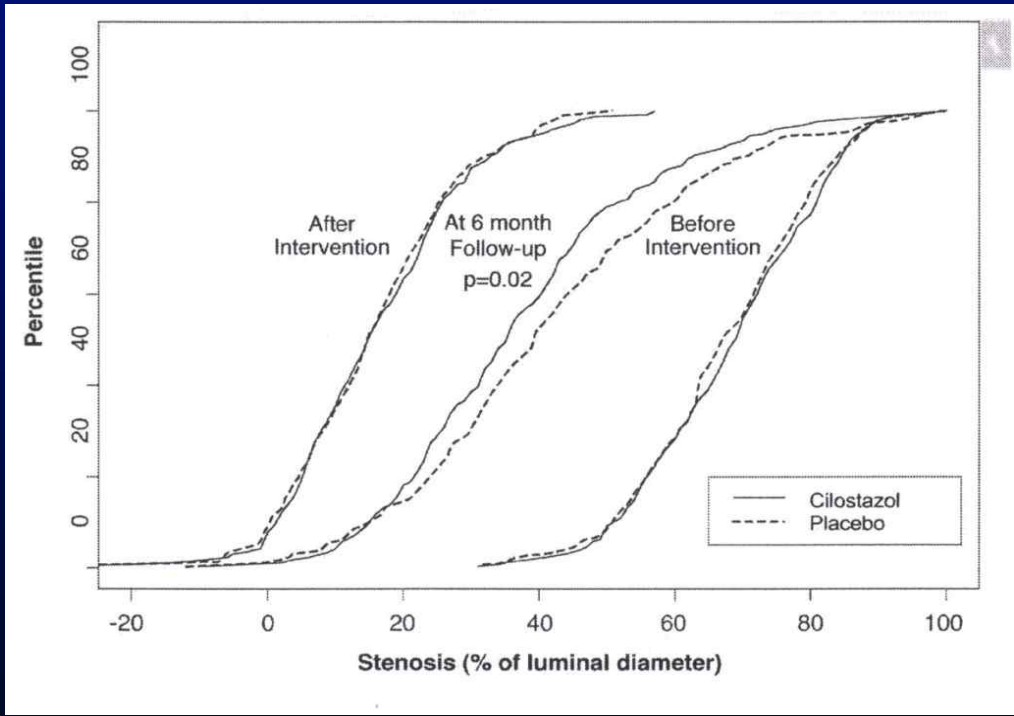
Hirsch et al. JACC Vol. xx, 2006
ACC/AHA Guidelines Management of PAD

Coronary Stent Restenosis in Patients Treated With Cilostazol

John S. Douglas, Jr, MD; David R. Holmes, Jr, MD; Dean J. Kereiakes, MD; Cindy L. Grines, MD;
Elizabeth Block, BS; Ziyad M.B. Ghazzal, MD; Douglas C. Morris, MD; Henry Liberman, MD;
Karen Parker, BS; Claudine Jurkovitz, MD; Nancy Murrah, BSN; Jovonne Foster, MS; Pamela Hyde, BSN;
G.B. John Mancini, MD; William S. Weintraub, MD;
for the Cilostazol for Restenosis Trial (CREST) Investigators*



inhibition of vascular smooth muscle cells

Circulation, Nov 2005; 112: 2826 - 2832.

Multifaceted Effects of Cilostazol

Reduced Restenosis after implantation of coronary artery stents
(Circulation, Nov 2005; 112: 2826 - 2832.)

Antiplatelet activity

Cilostazol

In vitro inhibition of vascular smooth muscle cells

Antithrombotic activity

Decreases triglycerides

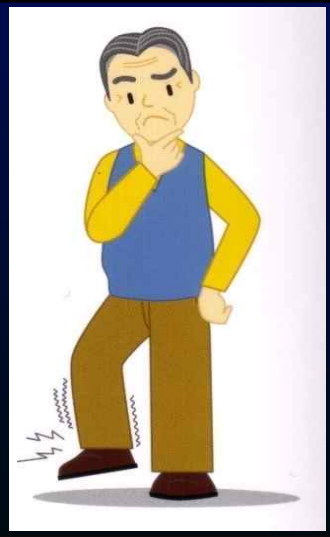
Mildly increases heart rate

Increases HDL-C

Produces vasodilation

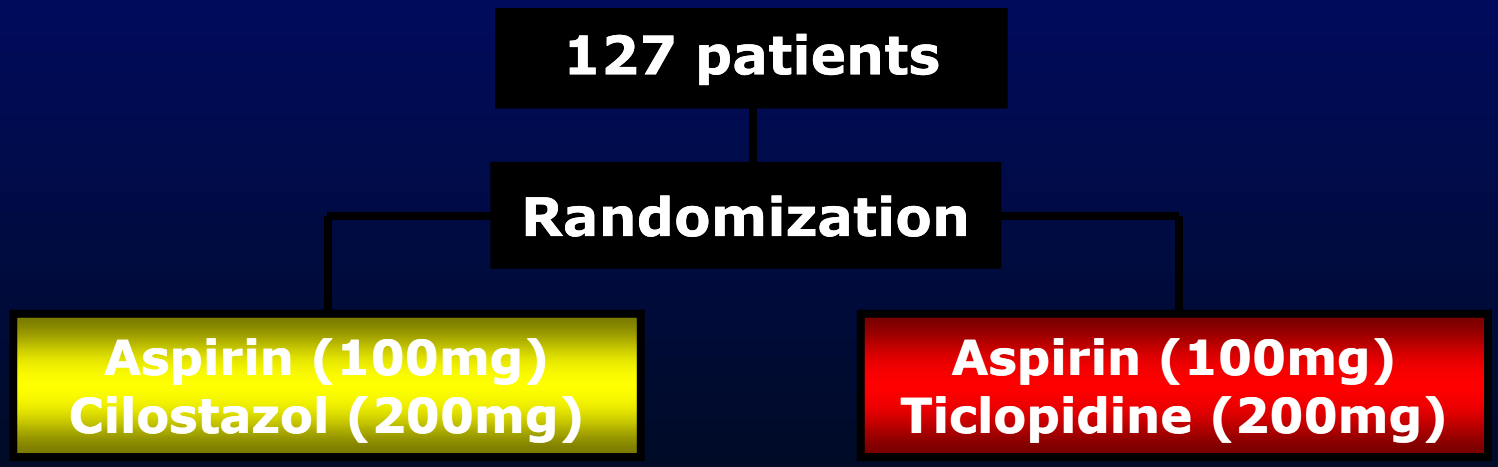
Increases blood flow

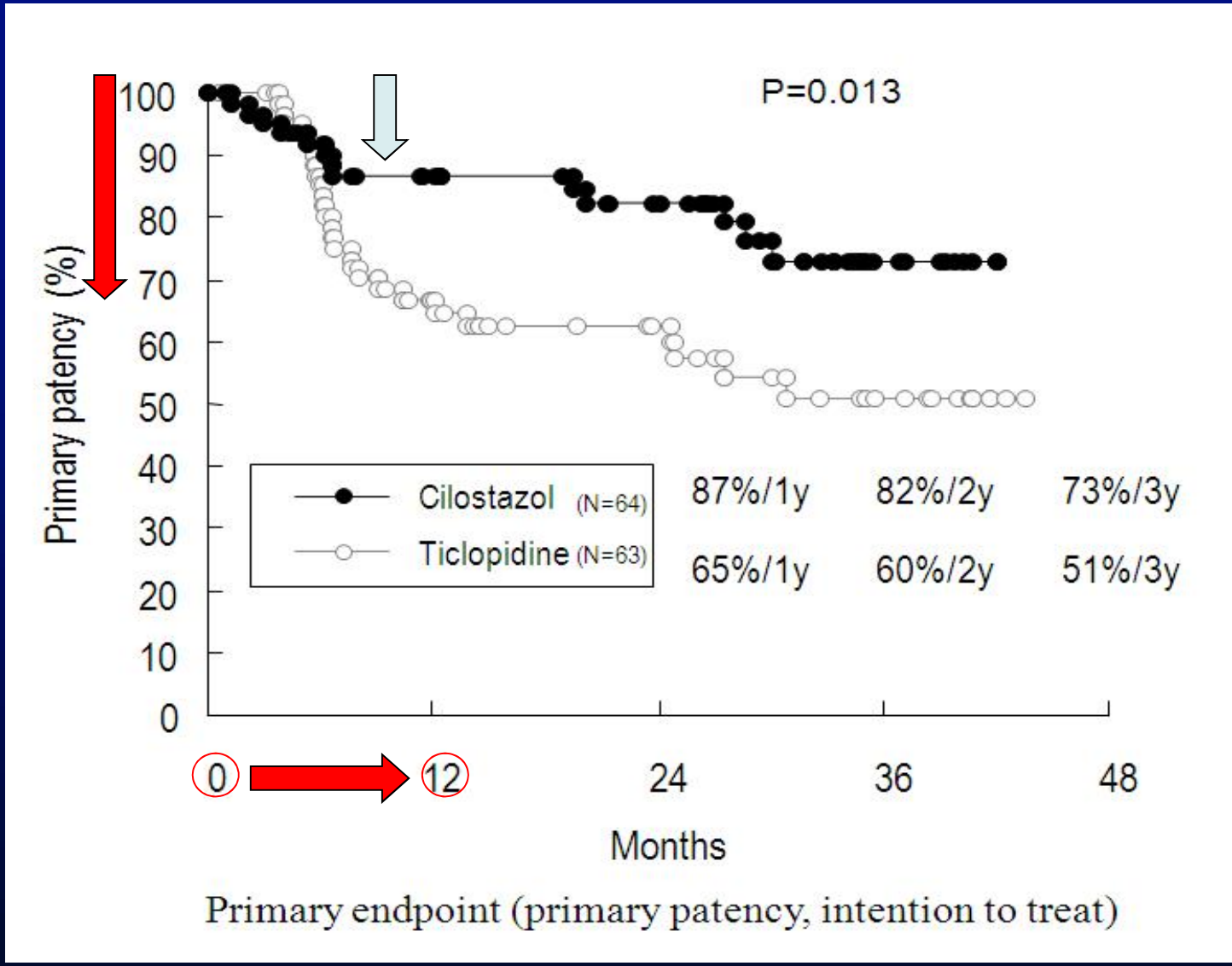
Improved of symptoms and walking distance
(Circulation.1998;98:678-68)



Methods

- **Study design; study populations**
  - Prospective, randomized, Single center trial
  - Between March, 2004, and June, 2005, 127 patients who had symptoms of leg ischemia in the FP lesion were enrolled.





As similar to the coronary intervention, the most essential issue is to prevent restenosis occurring during the first year following EVT. It should be noted that cilostazol reduced the restenosis during the first year and maintained the patency by continuing the medication.

Iida O et al. J Vasc Surg. 2008;48:144-9.

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Peripheral Vascular Disease

Efficacy of Cilostazol After Endovascular Therapy for Femoropopliteal Artery Disease in Patients With Intermittent Claudication

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Kitakyusyu, Kurume, Kagoshima, Miyakonojyo, and Saga, Japan

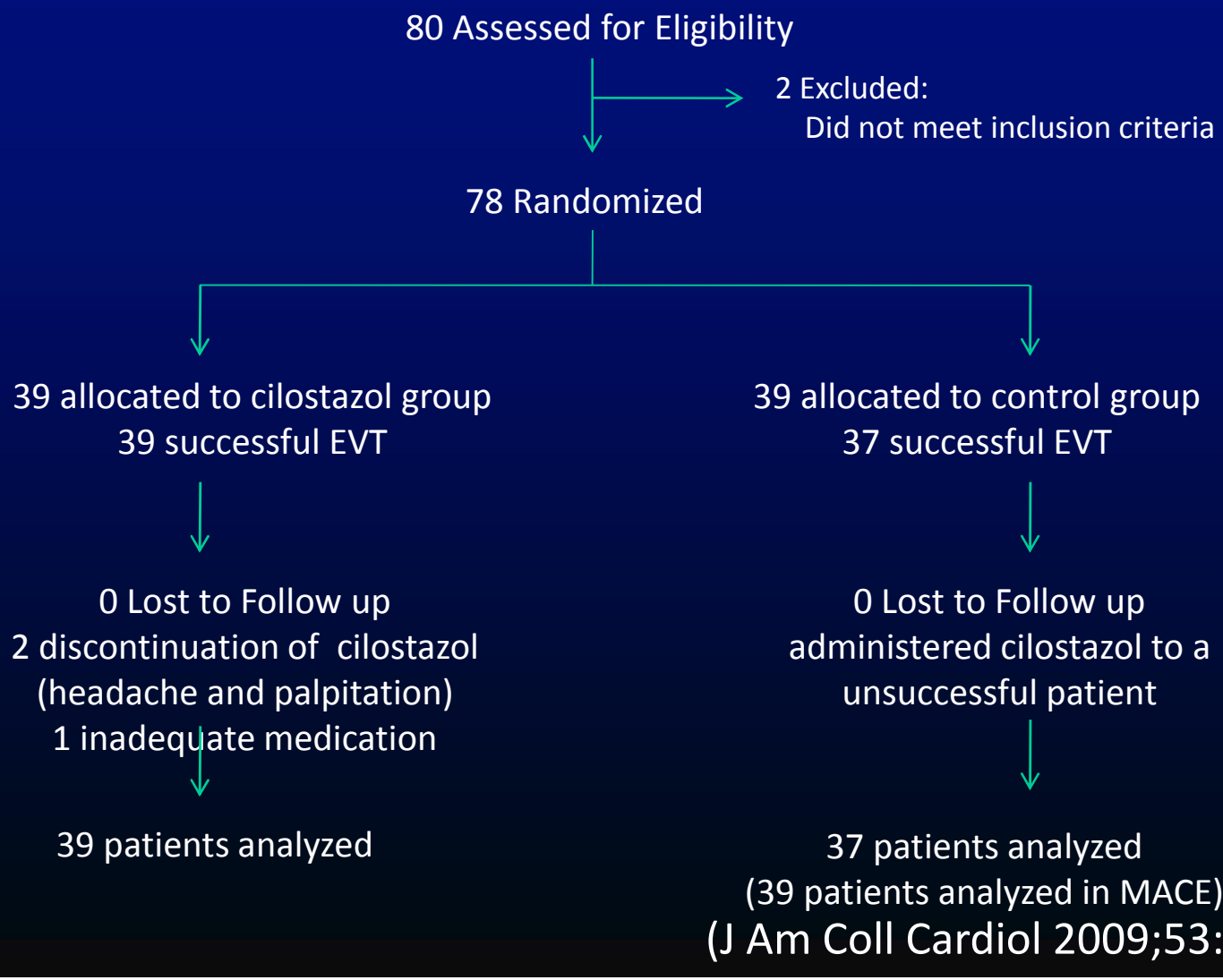
(J Am Coll Cardiol 2009;53:48–53)

Objectives The purpose of this study was to investigate whether cilostazol reduces restenosis and revascularization after endovascular therapy (EVT) for femoropopliteal lesions.

Background Cilostazol improves walking distance in patients with intermittent claudication and reduces restenosis after coronary intervention, but its efficacy remains unclear after EVT for femoropopliteal disease.

Methods This study was performed as a multicenter, randomized, open-label clinical trial. Eighty patients (mean age 70.7 ±

Participant Flow



(J Am Coll Cardiol 2009;53:48-53)

Patient Characteristics

Variables	Cilostazol Yes (n = 39)	Cilostazol No (n = 39)	p Value
Age (yrs)	69.8 ± 7.0	71.6 ± 8.1	0.30
> 75 years old (%)	12 (31)	17 (43)	0.24
Male Gender (%)	31 (79)	34 (87)	0.36
Diabetes Mellitus (%)	12 (31)	16 (41)	0.34
Hypertension (%)	19 (49)	19 (49)	0.99
Hypercholesterolemia (%)	15 (38)	11 (28)	0.34
Current Smoker (%)	13 (33)	17 (44)	0.35
Renal Failure (%)	8 (21)	7 (18)	0.77
Ischemic Heart Disease (%)	21 (54)	21 (54)	1.00
Previous Stroke (%)	9 (23)	8 (21)	0.78
Stent / CBA / BA	16 / 15 / 8	20 / 12 / 5	0.32
Use of Stent (%)	16 (41)	20 (51)	0.36
Luminexx / SMART / Wall	5 / 8 / 3	6 / 13 / 1	0.39
Use of Statins (%)	10 (26)	9 (23)	0.79
Use of β-Blockers (%)	7 (18)	4 (10)	0.33
Use of ACEI / ARB (%)	14 (36)	12 (31)	0.63
Pre-procedure ABI **	0.59 ± 0.12	0.64 ± 0.15	0.13
Post-procedure ABI	0.81 ± 0.18	0.84 ± 0.16	0.49

(J Am Coll Cardiol 2009;53:48-53)

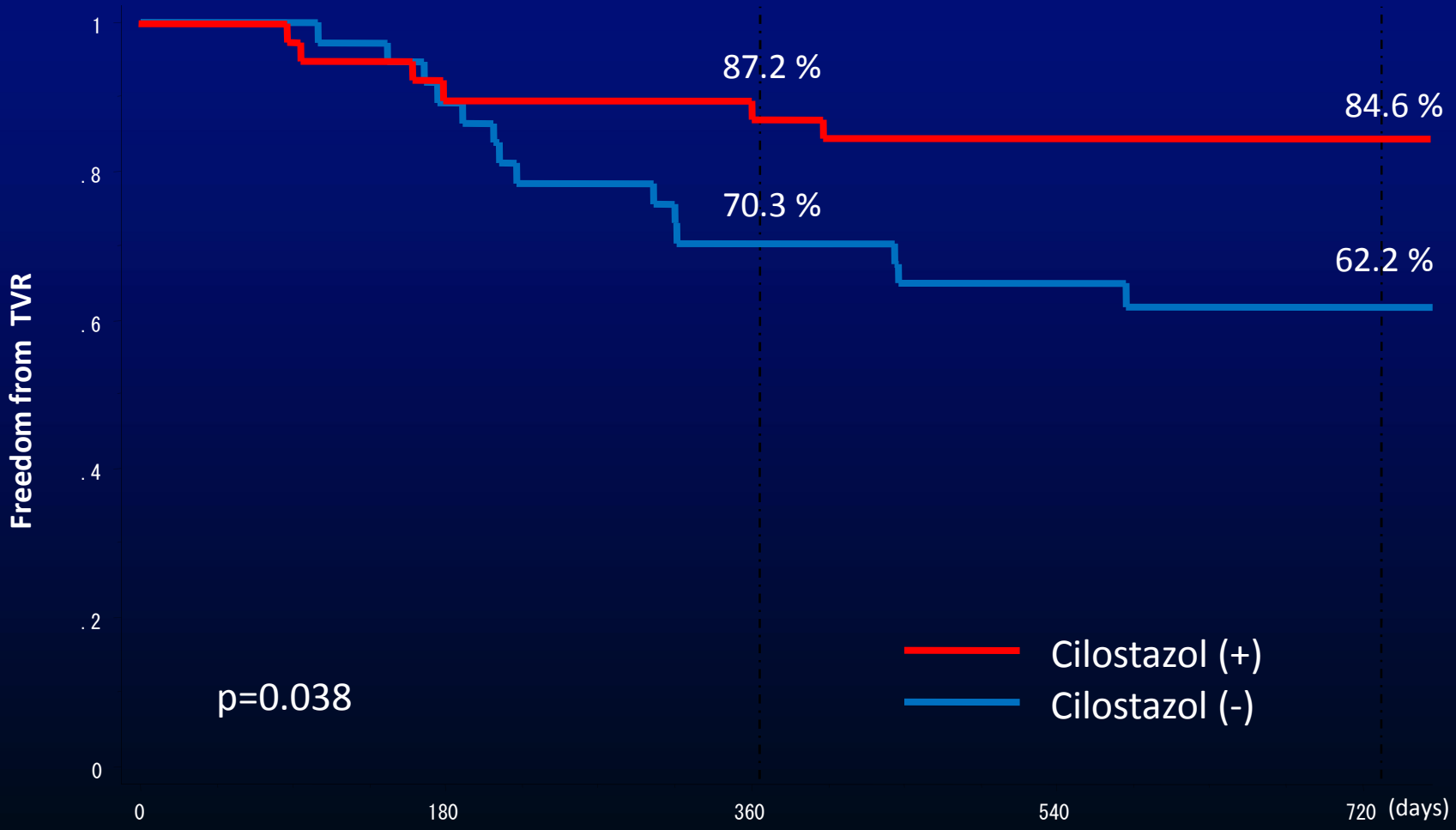
Lesion Characteristics

Variables	Cilostazol		
	Yes (n = 39)	No (n = 39)	p Value
Lesion Length (mm)	121.1 ± 67.3	131.5 ± 84.0	0.56
Pre Minimum Lumen Diameter (mm)	0.92 ± 0.74	0.94 ± 0.81	0.31
Pre Diameter Stenosis (%)	78.7 ± 18.1	78.8 ± 18.2	0.99
Pre Reference Diameter (mm)	4.77 ± 0.72	4.85 ± 0.81	0.65
Post Minimum Lumen Diameter (mm)	3.20 ± 0.98	3.27 ± 0.86	0.77
Post Diameter Stenosis (%)	28.0 ± 12.5	25.8 ± 12.1	0.46
Post Reference Diameter (mm)	4.78 ± 0.74	4.74 ± 0.91	0.85
TASC Ⅱ A / B / C / D	4 / 5 / 10/ / 20	5 / 3 / 14 / 17	0.68
Chronic Total Occlusion (%)	10 (26)	14 (36)	0.33
Calcified Lesion (%)	8 (21)	6 (15)	0.56
Stent Fracture at Follow-up (%)	1 / 16 (6)	2 / 20 (10)	0.69

**Calcified lesion defined as obvious densities noted within the apparent vascular wall in the angiogram.*

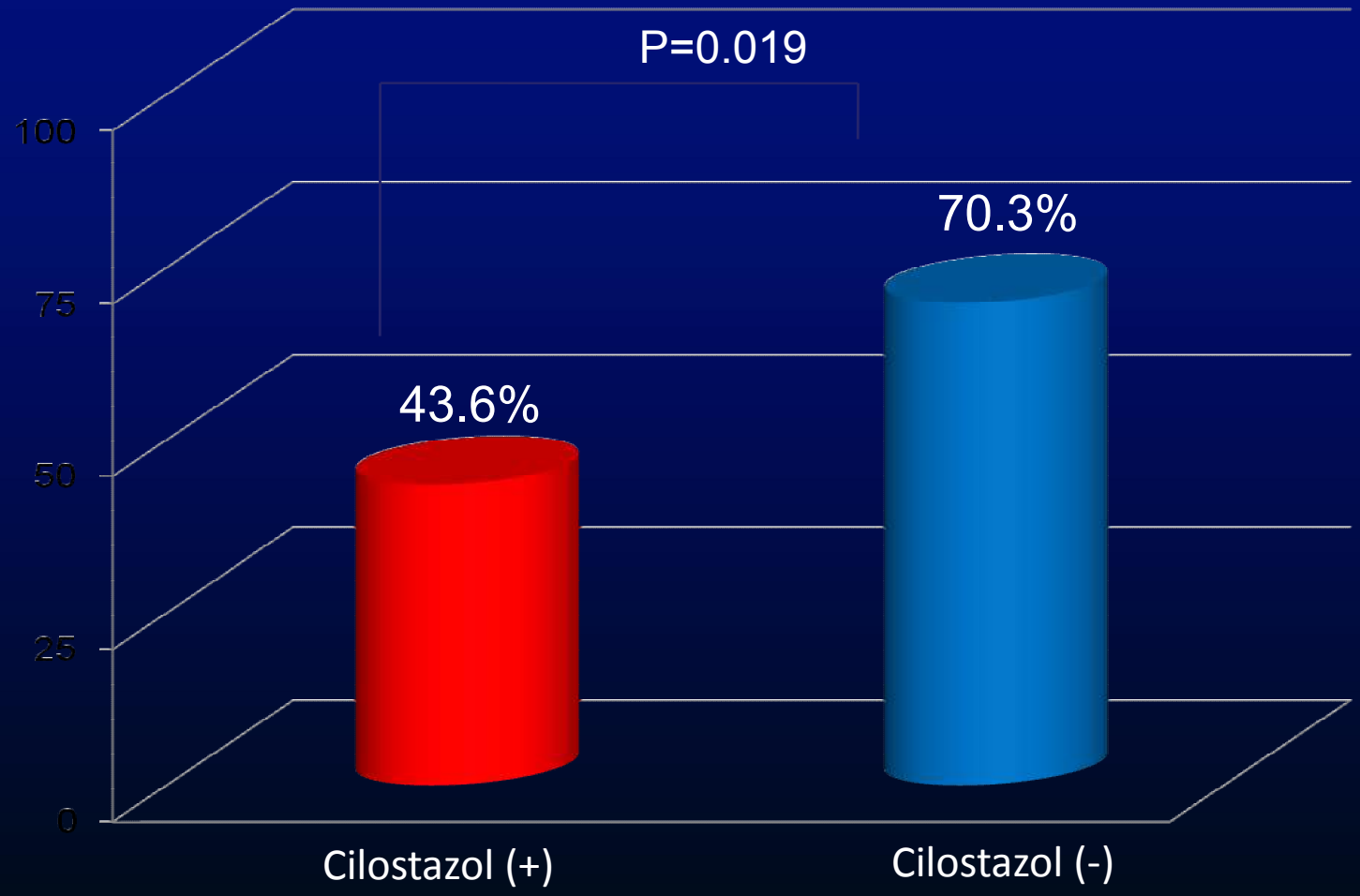
(J Am Coll Cardiol 2009;53:48-53)

Freedom from TVR



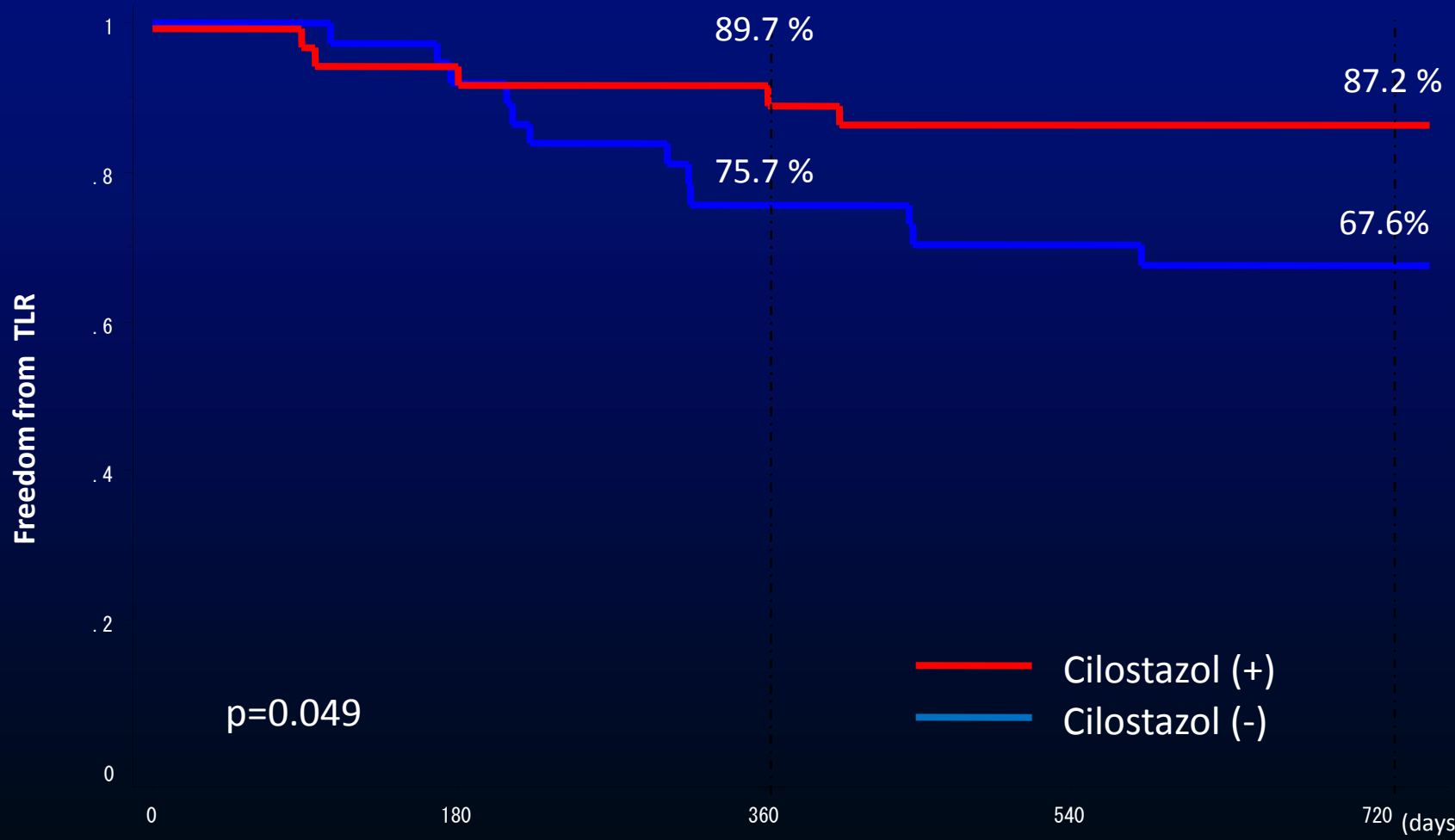
(J Am Coll Cardiol 2009;53:48-53)

Binary Restenosis Rate @ 24 mons



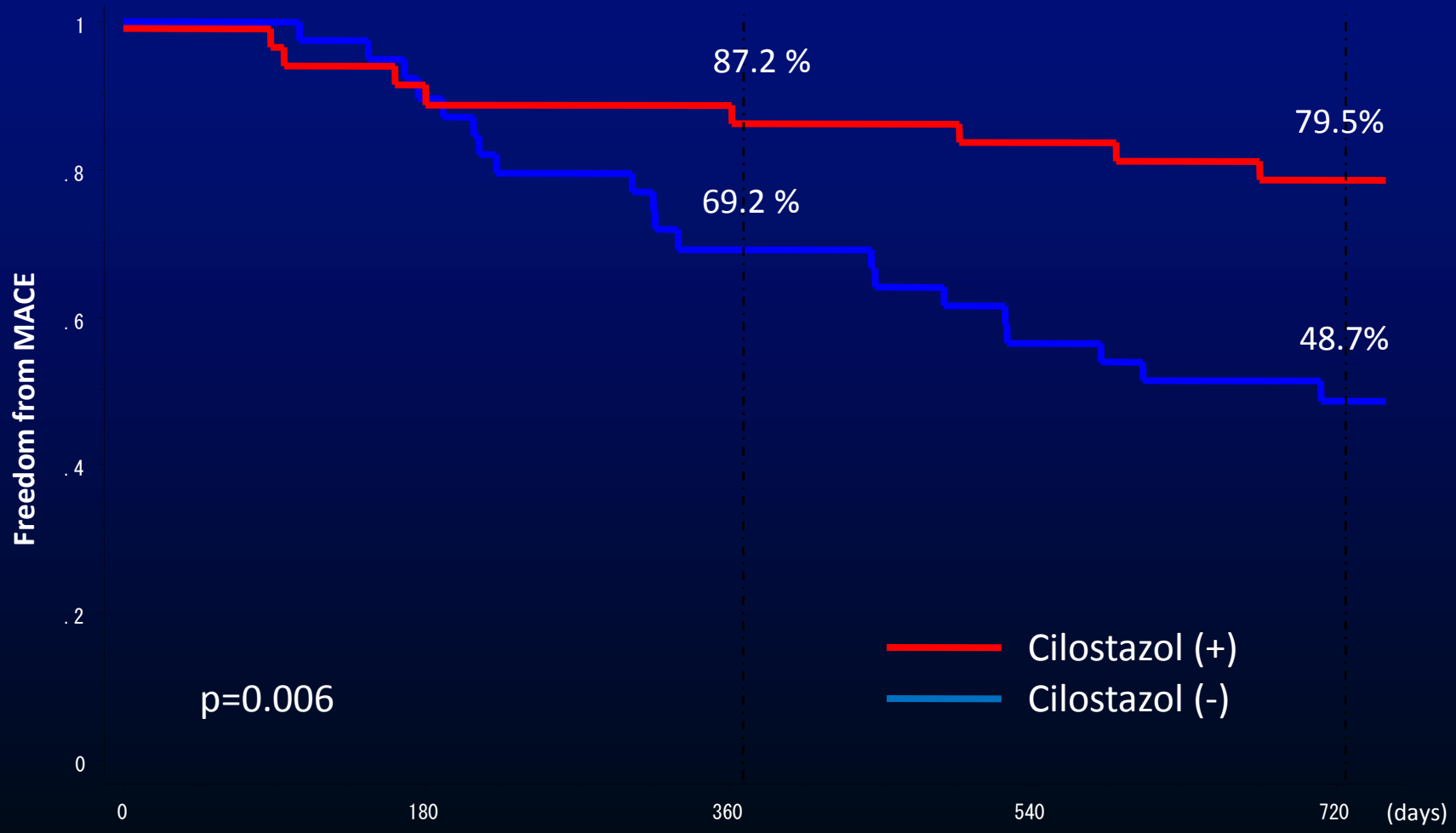
(J Am Coll Cardiol 2009;53:48-53)

Freedom from TLR



(J Am Coll Cardiol 2009;53:48-53)

Freedom from MACE



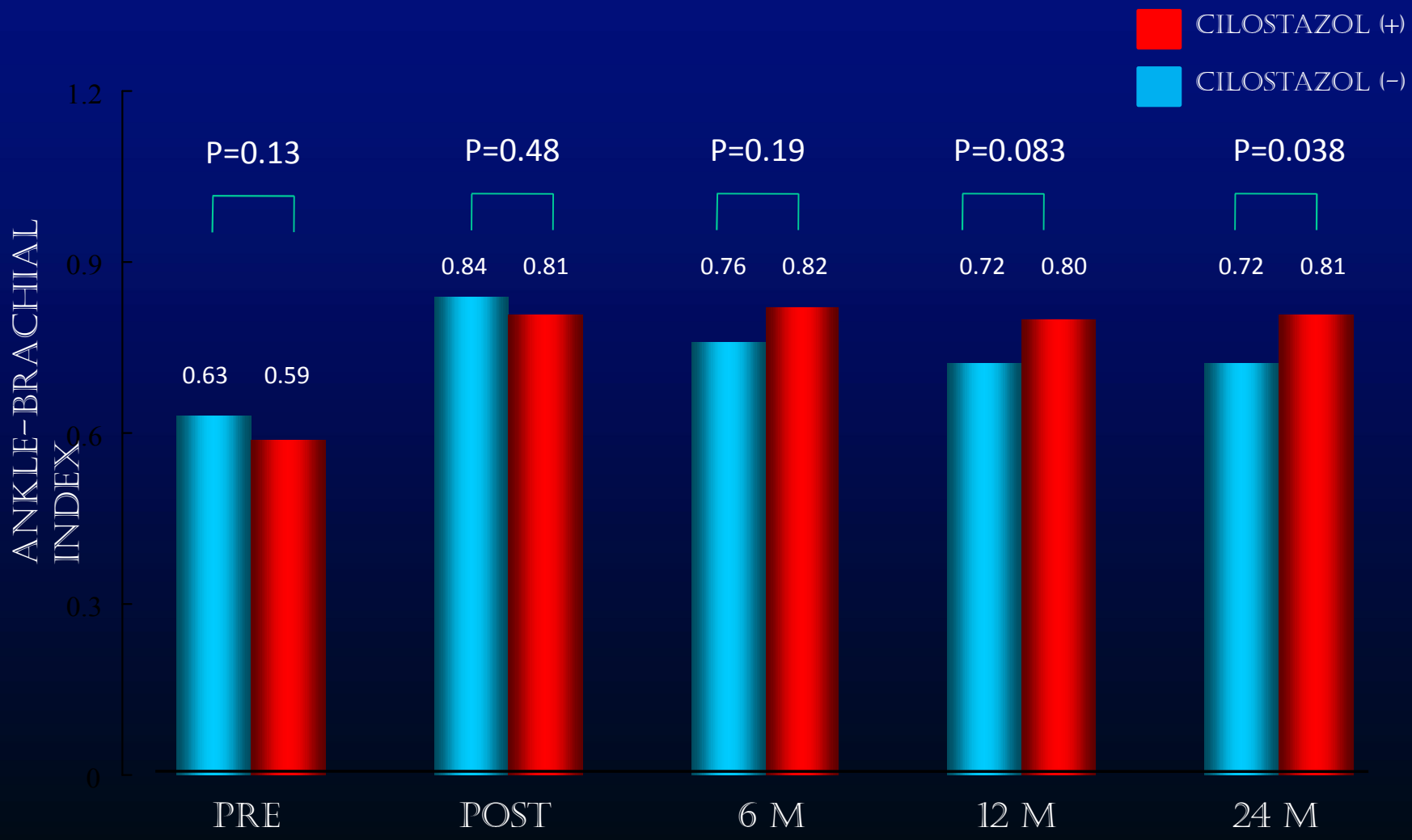
(J Am Coll Cardiol 2009;53:48-53)

Causes of MACE

MACE	Cilostazol			
	Total	(+) N=39	(-) N=39	p Value
All-cause Death (cardiac death)	3	1 (0)	2 (1)	0.60
Non-fatal MI*	0	0	0	0.99
Stroke	1	0	1	0.31
Repeat Revascularization	24	7	17	0.014
TLR**	17	5	12	
TVR***	20	6	14	
Surgical Revascularization	1	1	0	
Leg Amputation	0	0	0	0.99
Major Bleeding	0	0	0	0.99

(J Am Coll Cardiol 2009;53:48-53)

Resting Ankle-Brachial Index



(J Am Coll Cardiol 2009;53:48-53)

Cox Proportional Hazard Ratio Analysis of TVR Predictors

	Univariate			Multivariate		
Variables	**OR**	**95% CI**	**p Value**	**OR**	**95% CI**	**p Value**
Diabetes Mellitus	3.75	1.29 – 11.0	0.015	3.22	1.02 – 10.1	0.046
Chronic Total Occlusion	3.00	1.34 – 8.70	0.043	2.47	0.77 – 7.95	0.13
Hyperlipidemia	2.50	0.87 – 7.15	0.088	2.46	0.74 – 8.22	0.13
Use of Statins	1.97	0.65 - 6.04	0.23			
Calcified Lesion	1.74	0.51 – 6.01	0.38			
Current Smoker	1.36	0.49 - 3.84	0.49			
Hypertension	1.31	0.47 – 3.66	0.60			
Lesion Length	1.00	0.99 – 1.01	0.71			
Male Gender	1.23	0.30 – 5.02	0.77			
Age	0.99	0.92 – 1.06	0.69			
Reference Diameter	0.58	0.25 – 1.32	0.19			
Use of Stent	0.67	0.24 – 1.88	0.44			
Renal failure *	0.37	0.08 – 1.88	0.22			
Use of Cilostazol	0.23	0.07 - 0.73	0.012	0.29	0.09 - 0.97	0.045

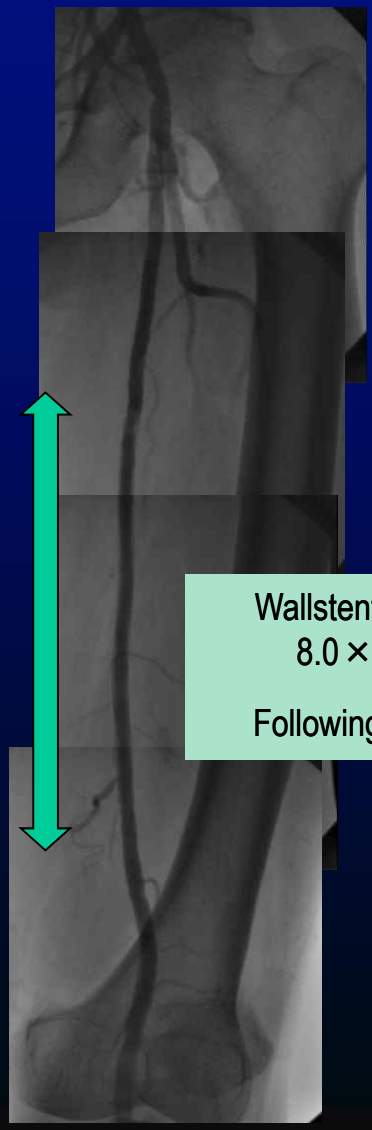
(J Am Coll Cardiol 2009;53:48-53)

Conclusion

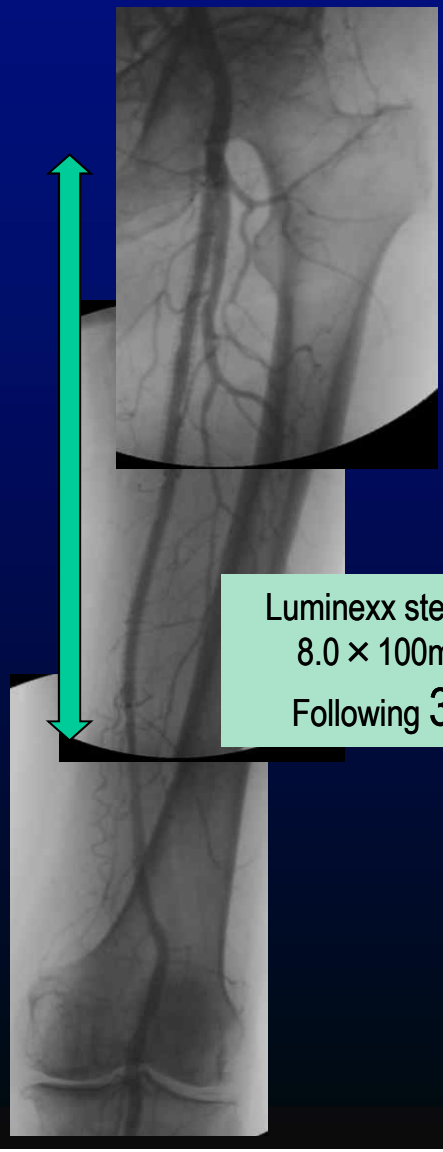
- Cilostazol reduces restenosis and repeat revascularization after endovascular therapy in patients with intermittent claudication for femoropopliteal disease.

(J Am Coll Cardiol 2009;53:48-53)

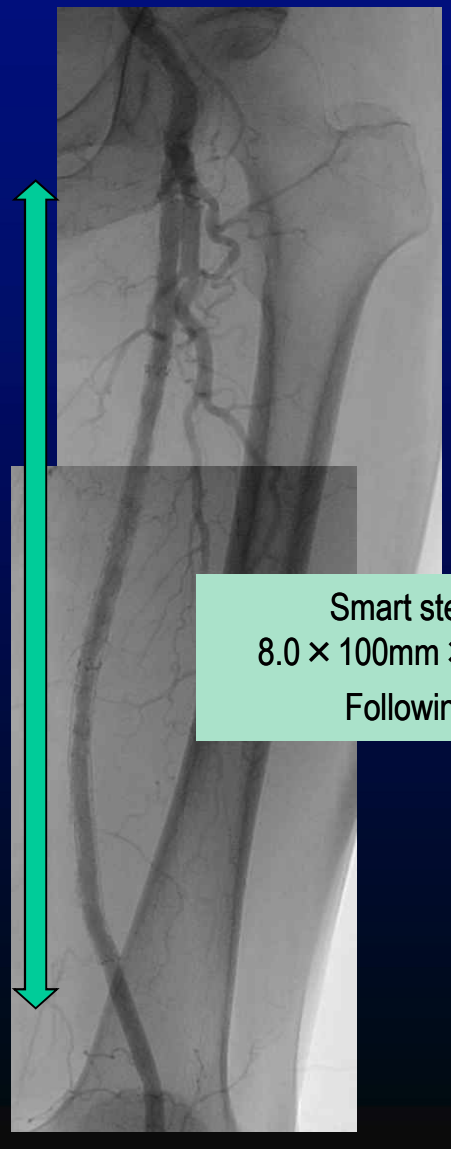
Cilostazol Reduces Restenosis Following Endovascular Therapy in Patients with Femoro-popliteal lesions



Wallstent (Boston)
8.0 × 66mm
Following 4 years



Luminexx stent (Bard)
8.0 × 100mm × 2
Following 3 years



Smart stent (Cordis)
8.0 × 100mm × 2, 8.0 × 60mm
Following 2 years

Take Home Messages
- EVT for Patients with SFA-CTO -

- Endovascular treatment using a new generation nitinol stent by ultrasound guided tapered wire manipulation with bidirectional approach is feasible for SFA-CTO.
- Cilostazol plays an important role in preventing long-term restenosis after EVT for SFA.
- Endovascular therapy with new generation nitinol stent and cilostazol may be an attractive alternative therapy to bypass surgery for patients with SFA-CTO