

Most Important Clinical Trials of the Past Decade in Vascular Intervention

Andrew J. P. Klein, MD, FACC, FSCAI
Interventional Cardiology
Vascular and Endovascular Medicine
Piedmont Heart Institute
Atlanta, GA

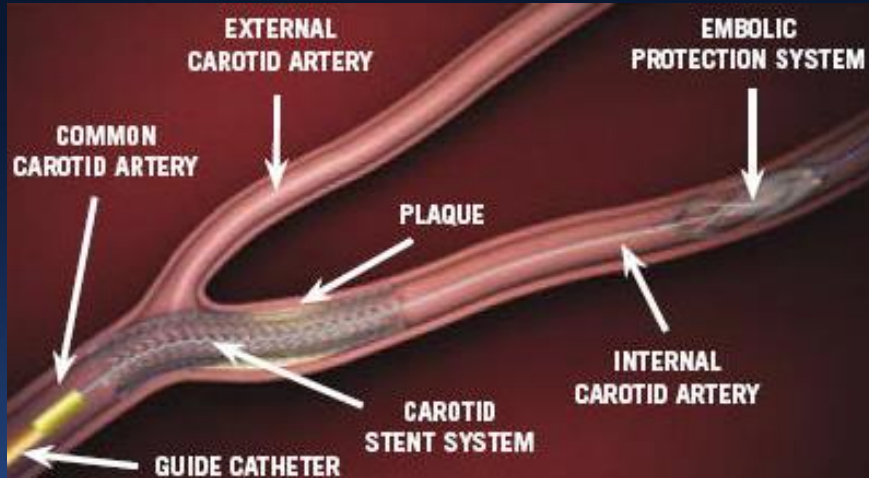
Disclosure Statement of Financial Interest

I, Andrew Klein DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

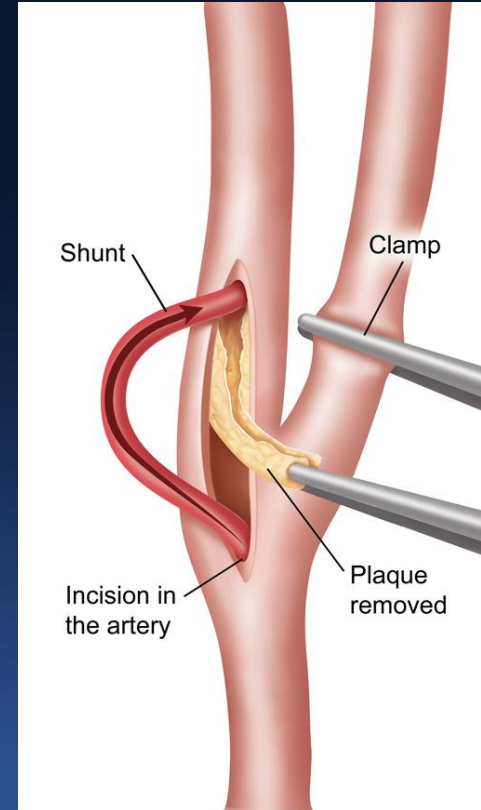
Most Important Vascular Intervention Trials 2007-2017



Most Important Vascular Intervention Trials #1



Vs.

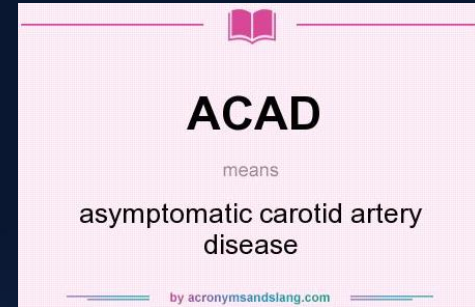
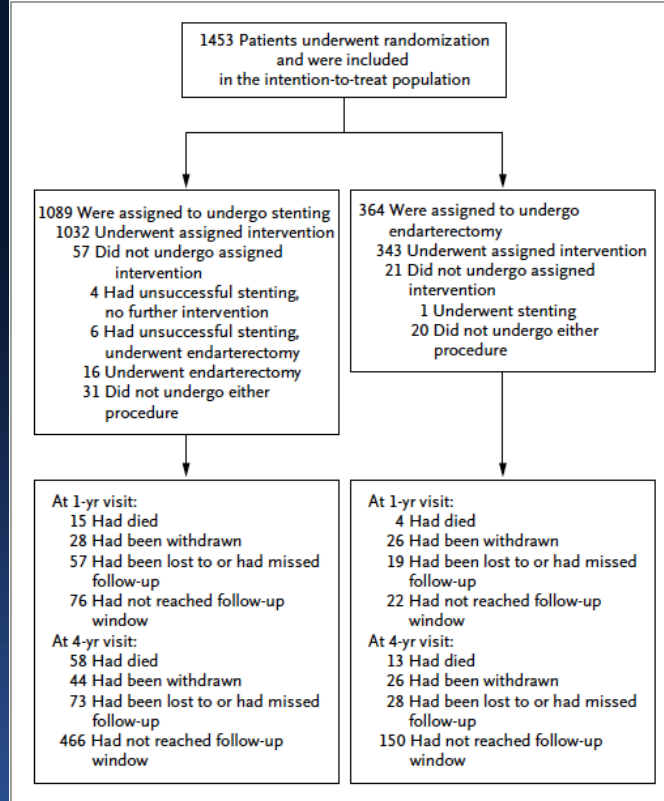


ACT TRIAL

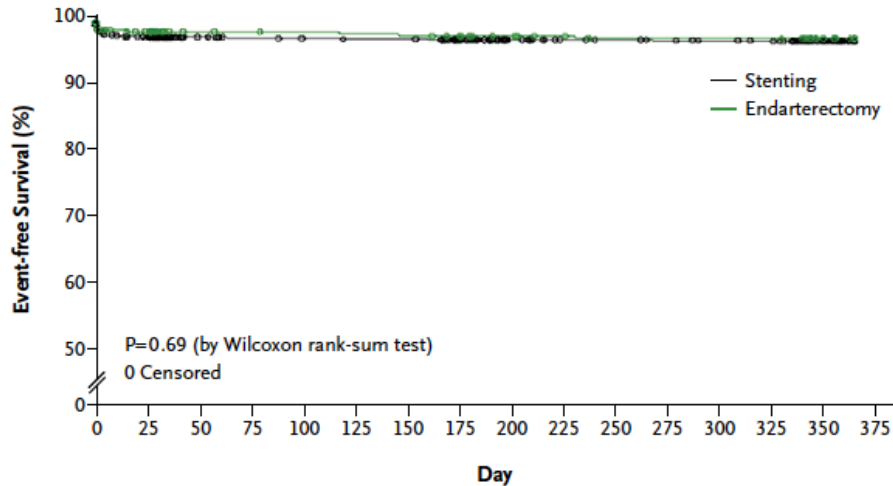
Randomized Trial of Stent versus Surgery for Asymptomatic Carotid Stenosis

Kenneth Rosenfield, M.D., M.H.C.D.S., Jon S. Matsumura, M.D., Seemant Chaturvedi, M.D., Tom Riles, M.D., Gary M. Ansel, M.D., D. Chris Metzger, M.D., Lawrence Wechsler, M.D., Michael R. Jaff, D.O., and William Gray, M.D., for the ACT I Investigators*

ACT Trial



ACT Trial



Days	0	1-30	31-180	181-365
Stenting (no. at risk)	1089	1067	1016	956
Endarterectomy (no. at risk)	364	354	325	309

Figure 2. Kaplan–Meier Analysis of Freedom from the Primary Composite End Point.

Shown is the Kaplan–Meier survival curve for freedom from death, stroke, and myocardial infarction within 30 days and from ipsilateral stroke within 365 days after the procedure in the intention-to-treat population.



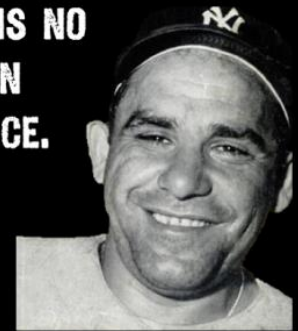
ACT Trial

Table 2. Death, Stroke, or Myocardial Infarction and Composite Measure of Complications within 30 Days after Index Procedure.*

Outcome	Stenting (N= 1089)	Endarterectomy (N= 364)	P Value†
	no. of patients/total no. (%)		
Death, stroke, or myocardial infarction	35/1072 (3.3)	9/348 (2.6)	0.60
Death or stroke	31/1072 (2.9)	6/348 (1.7)	0.33
Death or major stroke	6/1072 (0.6)	2/348 (0.6)	1.00
Death	1/1072 (0.1)	1/348 (0.3)	0.43
All stroke	30/1072 (2.8)	5/348 (1.4)	0.23
Major stroke	5/1072 (0.5)	1/348 (0.3)	1.00
Ipsilateral	4/1072 (0.4)	1/348 (0.3)	1.00
Nonipsilateral	1/1072 (0.1)	0/348	1.00
Minor stroke	26/1072 (2.4)	4/348 (1.1)	0.20
Ipsilateral	22/1072 (2.1)	4/348 (1.1)	0.36
Nonipsilateral	4/1072 (0.4)	0/348	0.58
Myocardial infarction	5/1072 (0.5)	3/348 (0.9)	0.41
Composite measure of complications	31/1089 (2.8)	17/364 (4.7)	0.13
Cranial-nerve injury	1/1089 (0.1)‡	4/364 (1.1)	0.02
Peripheral-nerve injury	0/1089	0/364	NA
Vascular injury	8/1089 (0.7)	3/364 (0.8)	1.00
Noncerebral bleeding	21/1089 (1.9)	6/364 (1.6)	0.83
Endarterectomy incision or puncture-site bleeding	3/1089 (0.3)	4/364 (1.1)	0.07
Other complications	0/1089	0/364	NA

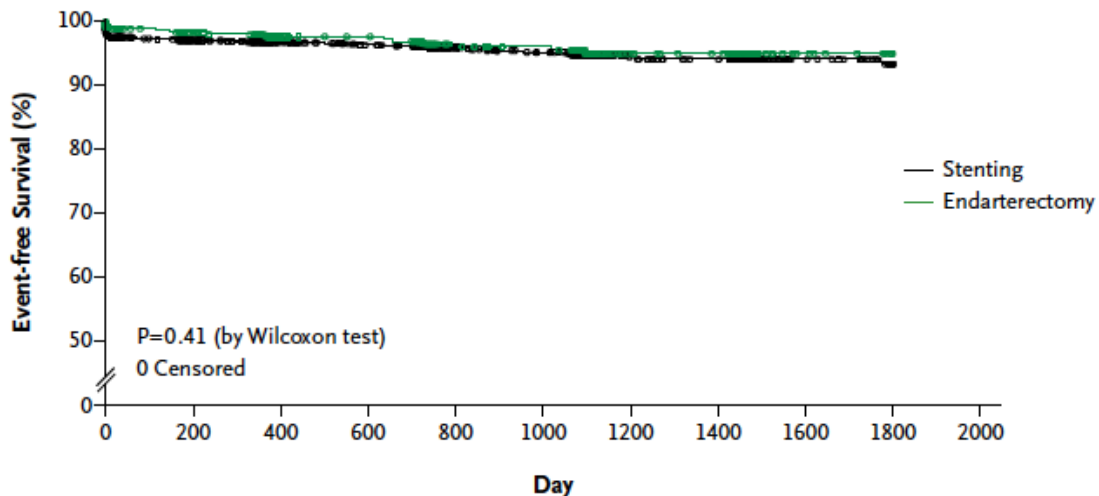
**“IN THEORY, THERE IS NO
DIFFERENCE BETWEEN
THEORY AND PRACTICE.
BUT IN PRACTICE,
THERE IS.”**

-YOGI BERRA



ACT Trial 5 Year Results

C Freedom from All Stroke through 5 Yr



Days	0	1-365	366-730	731-1095	1096-1460	1461-1825
Stenting (no. at risk)	1089	1068	865	730	541	363
Endarterectomy (no. at risk)	364	355	287	244	180	112

ACT Trial Take Home

Severe Asymptomatic Carotid Disease:

Stenting ~CEA

@5 years

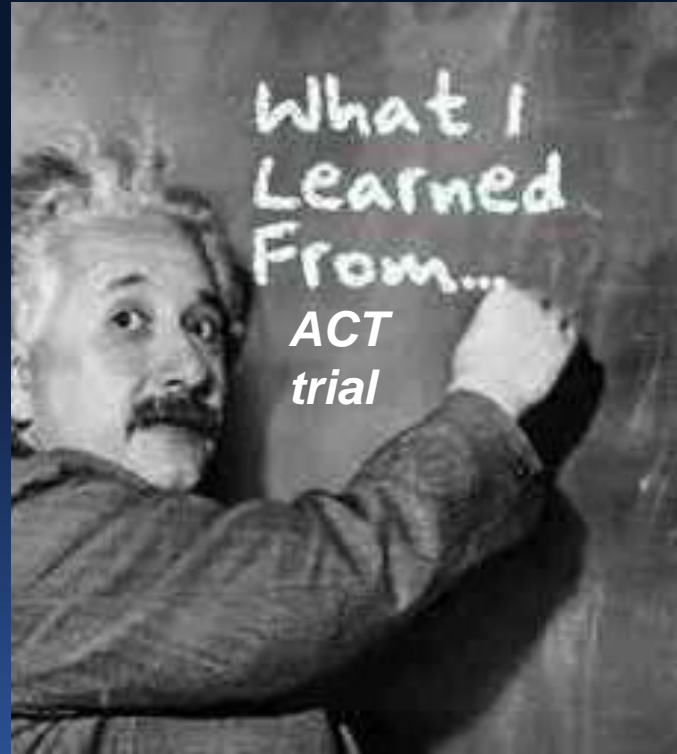
- Ipsilateral CVA*
- Stroke free survival*
- Death*

Upfront 30 d CVA risk

Stenting group: 2.9%

CEA: 1.7% (P = 0.33).

Need: EPD +Experience + OMT



Most Important Vascular Intervention Trials #2



CLEVER TRIAL

Supervised Exercise, Stent Revascularization, or Medical Therapy for Claudication Due to Aortoiliac Peripheral Artery Disease: A Randomized Clinical Trial

Timothy P. Murphy, MD^{*}, Donald E. Cutlip, MD^{†,‡}, Judith G. Regensteiner, PhD[§], Emile R. Mohler III, MD^{||}, David J. Cohen, MD, MSc[¶], Matthew R. Reynolds, MD[‡], Joseph M. Massaro, PhD^{‡,#}, Beth A. Lewis, PhD^{**}, Joselyn Cerezo, MD^{*}, Niki C. Oldenburg, DrPH^{††}, Claudia C. Thum, MA[‡], Michael R. Jaff, DO^{‡‡}, Anthony J. Comerota, MD^{§§}, Michael W. Steffes, MD^{††}, Ingrid H. Abrahamson, MS[‡], Suzanne Goldberg, MSN^{|||}, and Alan T. Hirsch, MD^{††}

CLEVER

Design

DESIGN:

111 patients with aortoiliac PAD randomly assigned to receive optimal medical care (OMC), OMC plus supervised exercise (SE), or OMC plus stent revascularization (ST)

OBJECTIVE:

Assess the 18-month efficacy of supervised exercise compared with stenting and optimal medical care

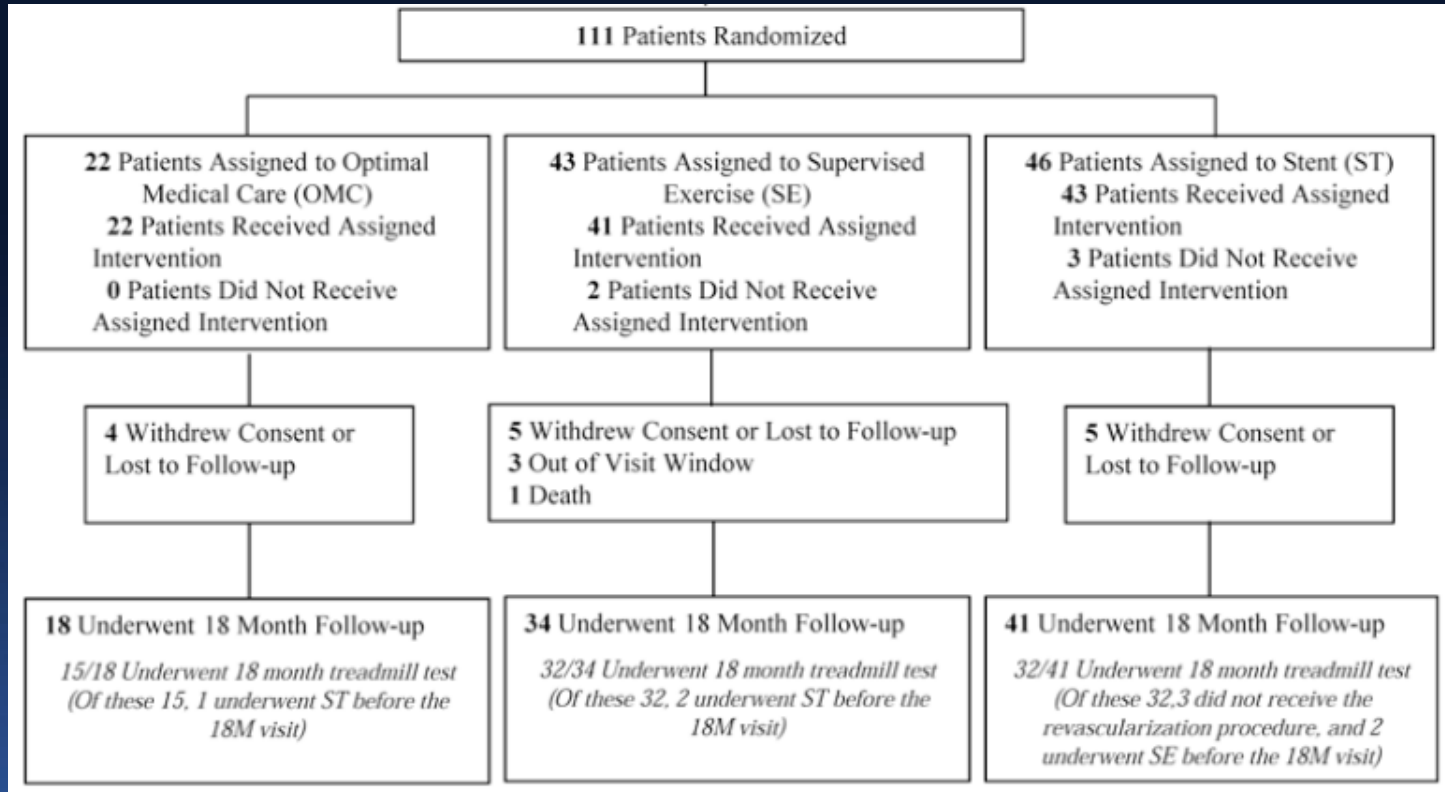
PRIMARY OUTCOME

Objective treadmill-based walking performance and subjective quality of life.

PRINCIPAL INVESTIGATOR

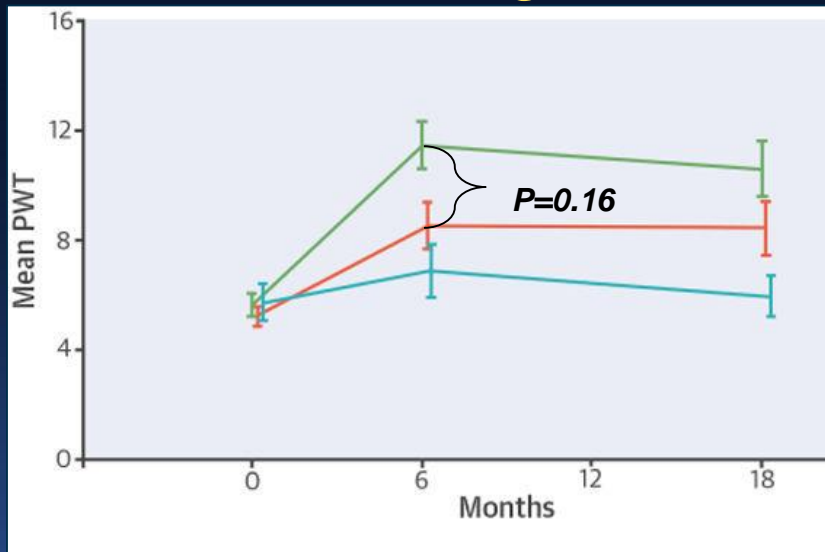
Timothy Murphy, MD
Rhode Island Hospital

CLEVER

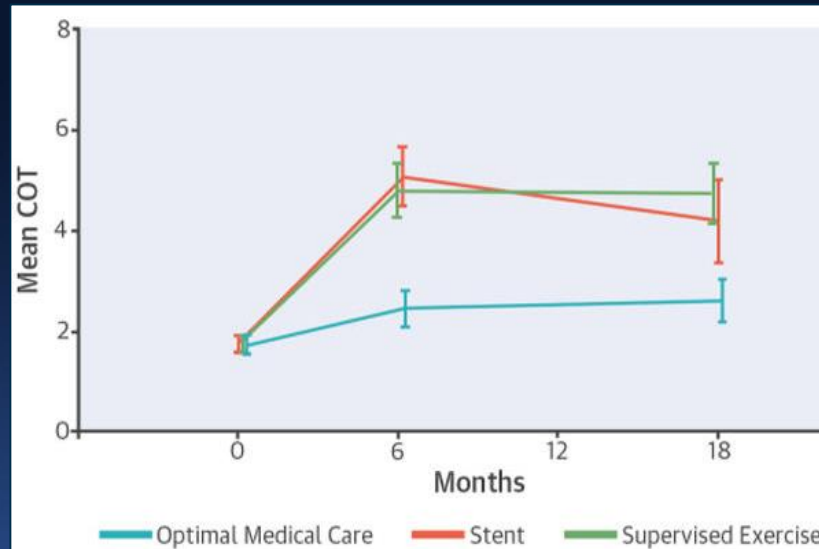


CLEVER

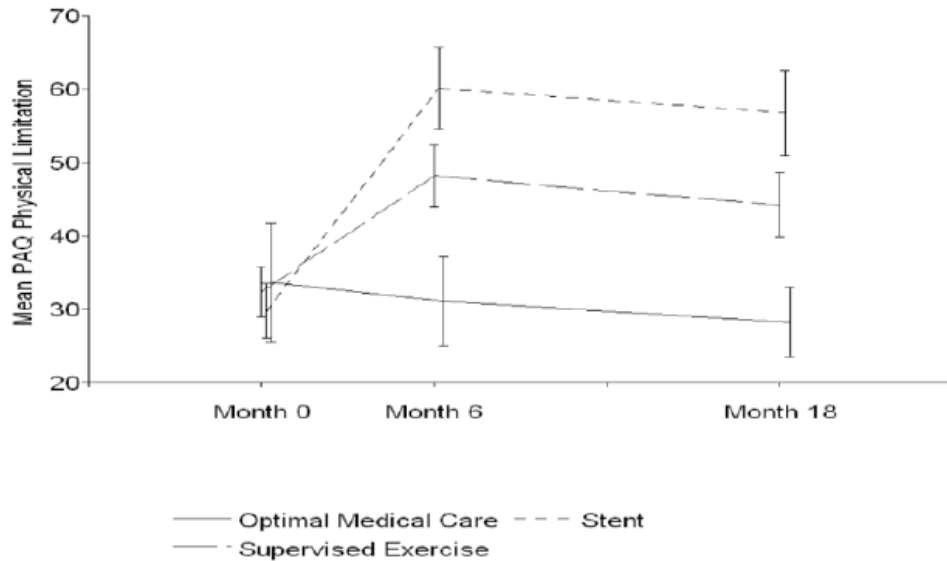
Δ Peak Walking Time



Δ Claudication Onset Time



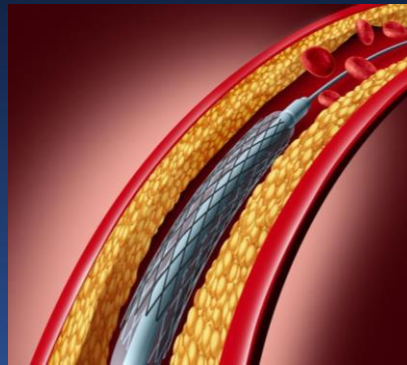
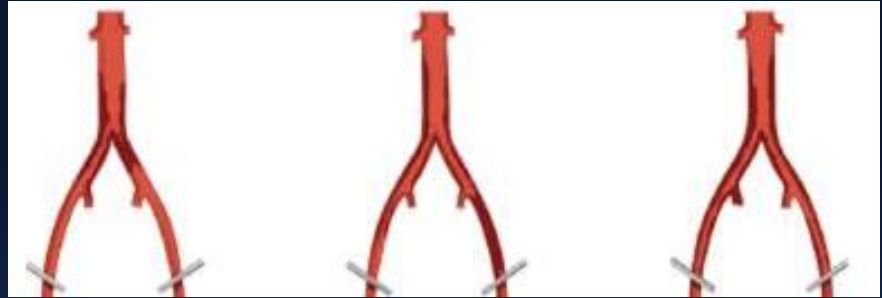
Quality of Life Scores



CLEVER

Take Home

- **Peak Walking Time: 0-18 months**
 - SET vs. EVT: No difference
 - OMC: Not effective
- **Many QOL indicators favor Stenting**



Or
?



Most Important Vascular Intervention Trials #3



ERASE TRIAL

Original Investigation

Endovascular Revascularization and Supervised Exercise for Peripheral Artery Disease and Intermittent Claudication A Randomized Clinical Trial

Farzin Fakhry, MD; Sandra Spronk, PhD; Lijckle van der Laan, MD, PhD; Jan J. Wever, MD, PhD; Joep A. W. Teijink, MD, PhD; Wolter H. Hoffmann, MD, PhD; Taco M. Smits, MD, PhD; Jerome P. van Brussel, MD, PhD; Guido N. M. Stultiens, MD; Alex Derom, MD; P. Ted den Hoed, MD, PhD; Gwan H. Ho, MD, PhD; Lukas C. van Dijk, MD, PhD; Nicole Verhofstad, PhD; Mariella Orsini, MSc; Andre van Petersen, MD; Kristel Woltman, MD; Ingrid Hulst, MA, ANP; Marc R. H. M. van Sambeek, MD, PhD; Dimitris Rizopoulos, PhD; Ellen V. Rouwet, MD, PhD; M. G. Myriam Hunink, MD, PhD

ERASE TRIAL

Design

DESIGN: 212 Claudicants randomly allocated to either endovascular revascularization (EVT) + supervised exercise (SET) or supervised exercise (SET) only.

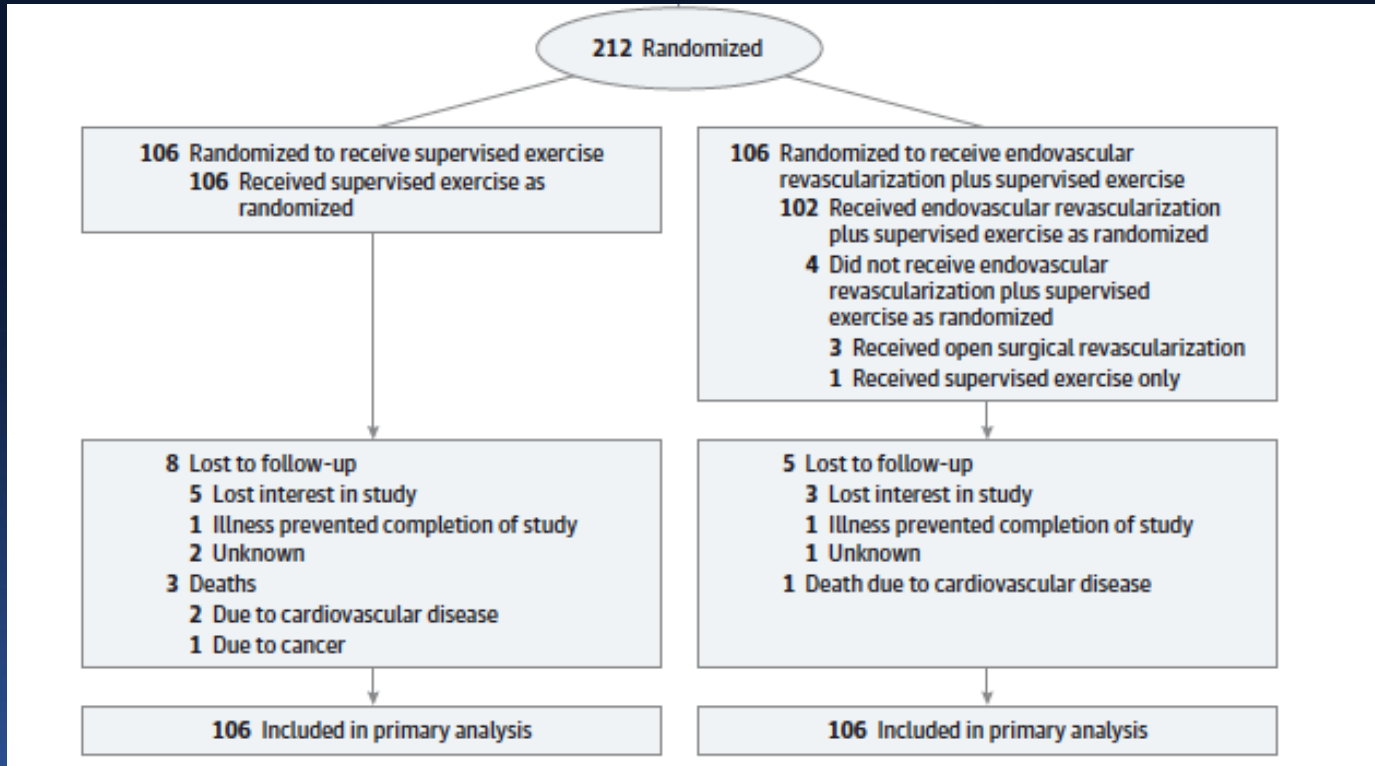
OBJECTIVE: To assess the effectiveness of EVT + SET VS. SET alone in claudication

1° ENDPOINT: Difference in maximum treadmill walking distance at 12 months between the groups

PRINCIPAL INVESTIGATOR

Myriam Hunink, MD, PhD,
Erasmus University Medical Center

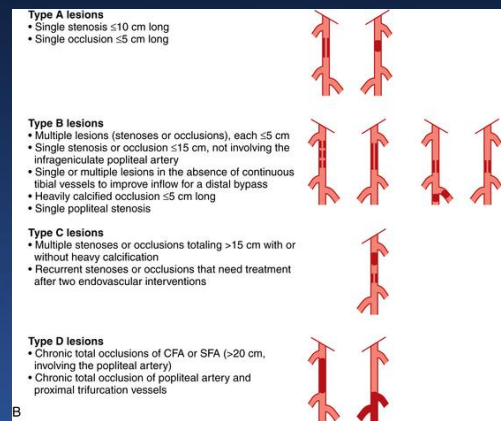
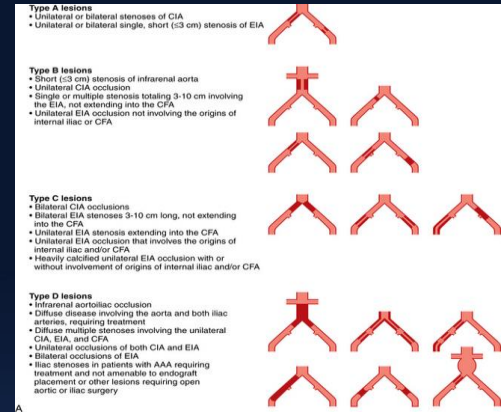
ERASE Trial



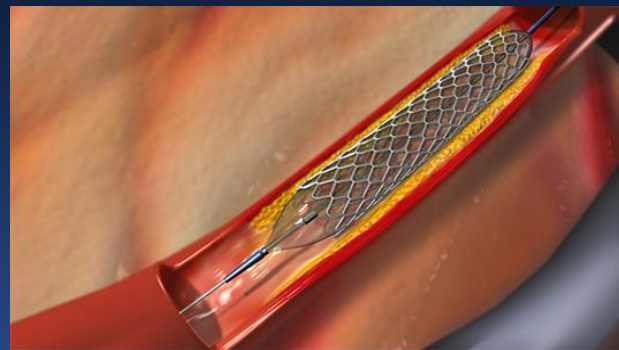
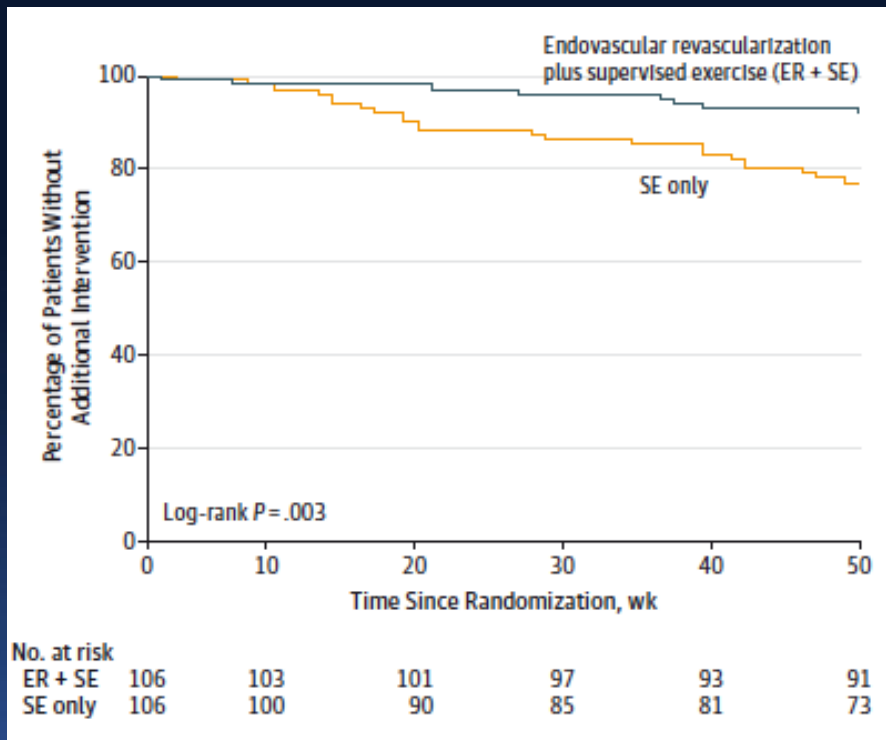
ERASE

Table 2. Functional Performance Measures

Functional Performance Measures	Mean (99% CI)		Between-Group Difference	P Value ^a
	Supervised Exercise (n = 106)	Endovascular Revascularization Plus Supervised Exercise (n = 106)		
Maximum walking distance, m				
At baseline	285 (244 to 326)	264 (228 to 300)		
1 mo	438 (282 to 595) ^b	1004 (835 to 1174) ^b	566 (358 to 774)	<.001
6 mo	851 (683 to 1018) ^b	1260 (1076 to 1444) ^b	409 (183 to 636)	<.001
12 mo	955 (786 to 1124) ^b	1237 (1058 to 1418) ^b	282 (60 to 505)	.001
Pain-free walking distance, m				
At baseline	135 (113 to 157)	117 (96 to 138)		
1 mo	181 (23 to 339) ^b	724 (561 to 886) ^b	543 (340 to 744)	<.001
6 mo	542 (378 to 707) ^b	1071 (900 to 1243) ^b	529 (315 to 743)	<.001
12 mo	712 (549 to 876) ^b	1120 (948 to 1293) ^b	408 (195 to 622)	<.001
Ankle brachial index at rest^c				
At baseline	0.68 (0.64 to 0.72)	0.71 (0.67 to 0.76)		
1 mo	-0.02 (-0.07 to 0.02) ^b	0.19 (0.15 to 0.23) ^b	0.21 (0.15 to 0.27)	<.001
6 mo	0.04 (-0.01 to 0.09) ^b	0.16 (0.11 to 0.20) ^b	0.12 (0.05 to 0.17)	<.001
12 mo	0.03 (-0.02 to 0.08) ^b	0.16 (0.11 to 0.21) ^b	0.13 (0.06 to 0.19)	<.001
Ankle brachial index after exercise^c				
At baseline	0.40 (0.34 to 0.46)	0.43 (0.38 to 0.48)		
1 mo	0.03 (-0.02 to 0.09) ^b	0.36 (0.30 to 0.42) ^b	0.33 (0.25 to 0.40)	<.001
6 mo	0.12 (0.06 to 0.18) ^b	0.33 (0.27 to 0.39) ^b	0.21 (0.13 to 0.29)	<.001
12 mo	0.11 (0.05 to 0.18) ^b	0.33 (0.27 to 0.40) ^b	0.22 (0.13 to 0.31)	<.001



ERASE



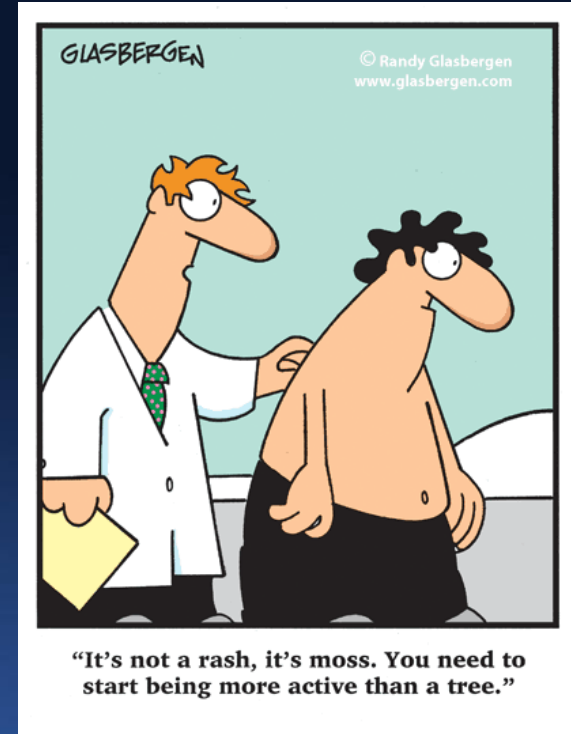
ERASE

Quality-of-Life Measures	Supervised Exercise (n = 106)	Endovascular Revascularization Plus Supervised Exercise (n = 106)	Between-Group Difference	P Value ^a
VascuQoL score^b				
At baseline	4.51 (4.25 to 4.77)	4.48 (4.25 to 4.71)		
1 mo	0.27 (0.04 to 0.50) ^c	1.52 (1.29 to 1.76) ^c	1.25 (0.94 to 1.56)	<.001
6 mo	0.62 (0.37 to 0.88) ^c	1.41 (1.16 to 1.66) ^c	0.79 (0.45 to 1.13)	<.001
12 mo	0.73 (0.43 to 1.03) ^c	1.34 (1.04 to 1.64) ^c	0.62 (0.20 to 1.03)	<.001
Rating score^d				
At baseline	64.9 (60.4 to 69.4)	67.9 (63.4 to 72.4)		
1 mo	1.1 (-3.9 to 6.2) ^c	9.9 (5.1 to 14.7) ^c	8.7 (2.4 to 15.1)	<.001
6 mo	-0.5 (-5.5 to 4.5) ^c	10.1 (5.2 to 15.0) ^c	10.6 (4.3 to 17.0)	<.001
12 mo	1.4 (-3.5 to 6.3) ^c	7.9 (3.0 to 12.8) ^c	6.5 (0.2 to 12.7)	.008
SF-36 physical functioning^e				
At baseline	52.7 (47.4 to 58.0)	51.4 (47.3 to 55.5)		
1 mo	4.0 (-0.7 to 8.6) ^c	27.3 (22.7 to 31.8) ^c	23.3 (17.3 to 29.4)	<.001
6 mo	12.7 (7.7 to 17.7) ^c	27.2 (22.3 to 32.2) ^c	14.6 (7.9 to 21.2)	<.001
12 mo	12.6 (6.3 to 18.9) ^c	22.4 (16.3 to 28.5) ^c	9.8 (1.4 to 18.2)	.002

SF-36 physical role functioning score^e				
At baseline	53.4 (43.2 to 63.7)	59.2 (49.1 to 69.3)		
1 mo	2.6 (-7.2 to 12.3) ^c	19.7 (10.0 to 29.4) ^c	17.1 (4.5 to 29.7)	<.001
6 mo	5.9 (-4.4 to 16.1) ^c	18.9 (8.8 to 28.9) ^c	13.0 (-0.1 to 26.1)	.01
12 mo	5.0 (-6.4 to 16.5) ^c	19.0 (7.8 to 30.2) ^c	14.0 (-0.8 to 28.7)	.02
SF-36 bodily pain, mo^e				
At baseline	53.1 (47.9 to 58.3)	52.7 (48.3 to 57.1)		
1 mo	-3.1 (-8.1 to 2.0) ^c	22.7 (17.7 to 27.8) ^c	25.8 (19.2 to 32.4)	<.001
6 mo	6.6 (1.2 to 11.9) ^c	21.0 (15.7 to 26.3) ^c	14.4 (7.4 to 21.5)	<.001
12 mo	10.4 (4.3 to 16.5) ^c	17.9 (12.0 to 23.9) ^c	7.6 (-0.6 to 15.7)	.02
SF-36 general health perceptions, mo^e				
At baseline	53.9 (48.9 to 59.0)	59.3 (55.4 to 63.2)		
1 mo	-0.6 (-4.7 to 3.5) ^c	5.0 (0.8 to 9.1) ^c	5.6 (0.1 to 11.0)	.009
6 mo	1.6 (-2.8 to 5.9) ^c	5.8 (1.5 to 10.1) ^c	4.2 (-1.6 to 9.9)	.06
12 mo	-2.4 (-7.3 to 2.5) ^c	1.7 (-3.1 to 6.5) ^c	4.1 (-2.4 to 10.6)	.11

ERASE Take Home

- Endovascular Therapy + Supervised Exercise Therapy provides the best results!
- Revascularization followed by exercise



Most Important Vascular Intervention Trials # 4



Zilver PTX

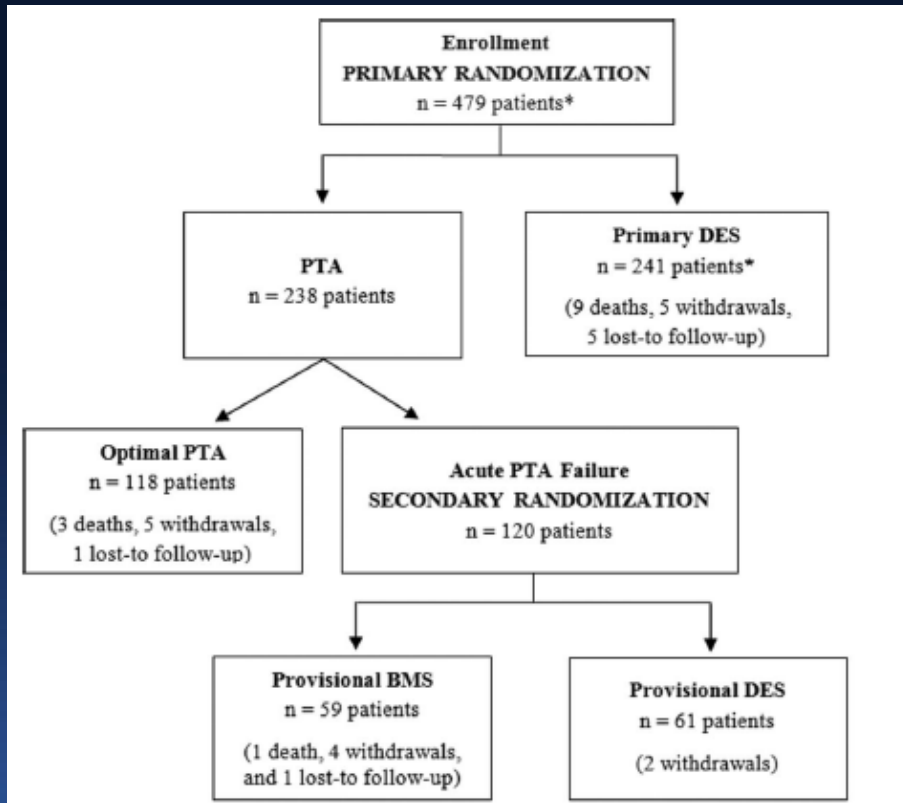
Paclitaxel-Eluting Stents Show Superiority to Balloon Angioplasty and Bare Metal Stents in Femoropopliteal Disease

Twelve-Month Zilver PTX Randomized Study Results

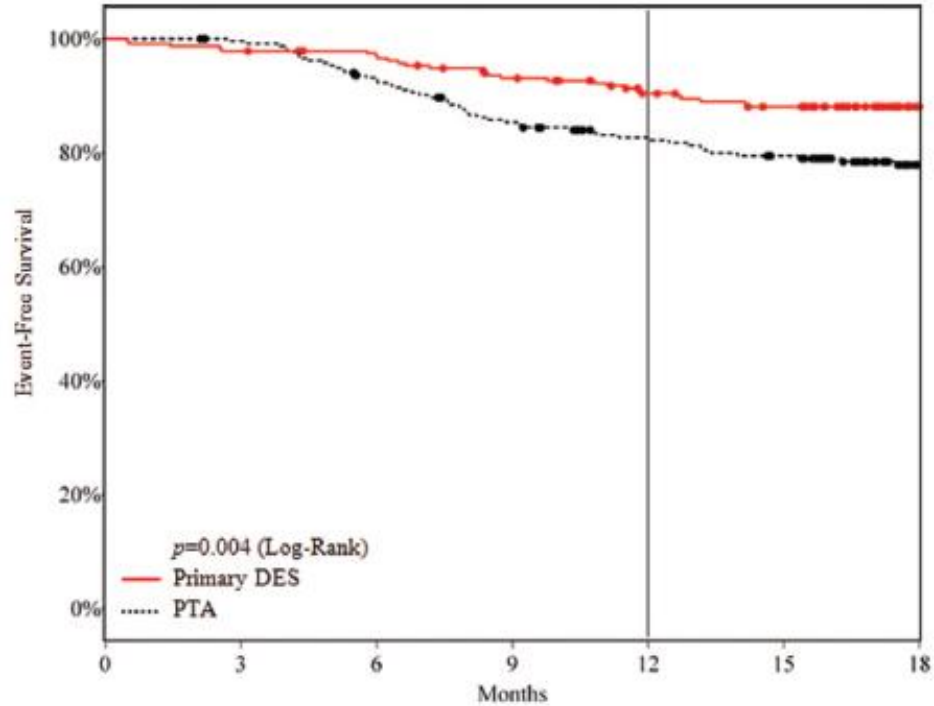
Michael D. Dake, MD; Gary M. Ansel, MD; Michael R. Jaff, DO; Takao Ohki, MD;
Richard R. Saxon, MD; H. Bob Smouse, MD; Thomas Zeller, MD; Gary S. Roubin, MD;
Mark W. Burket, MD; Yazan Khatib, MD; Scott A. Snyder, PhD; Anthony O. Ragheb, PhD;
J. King White, MD; Lindsay S. Machan, MD; on behalf of the Zilver PTX Investigators



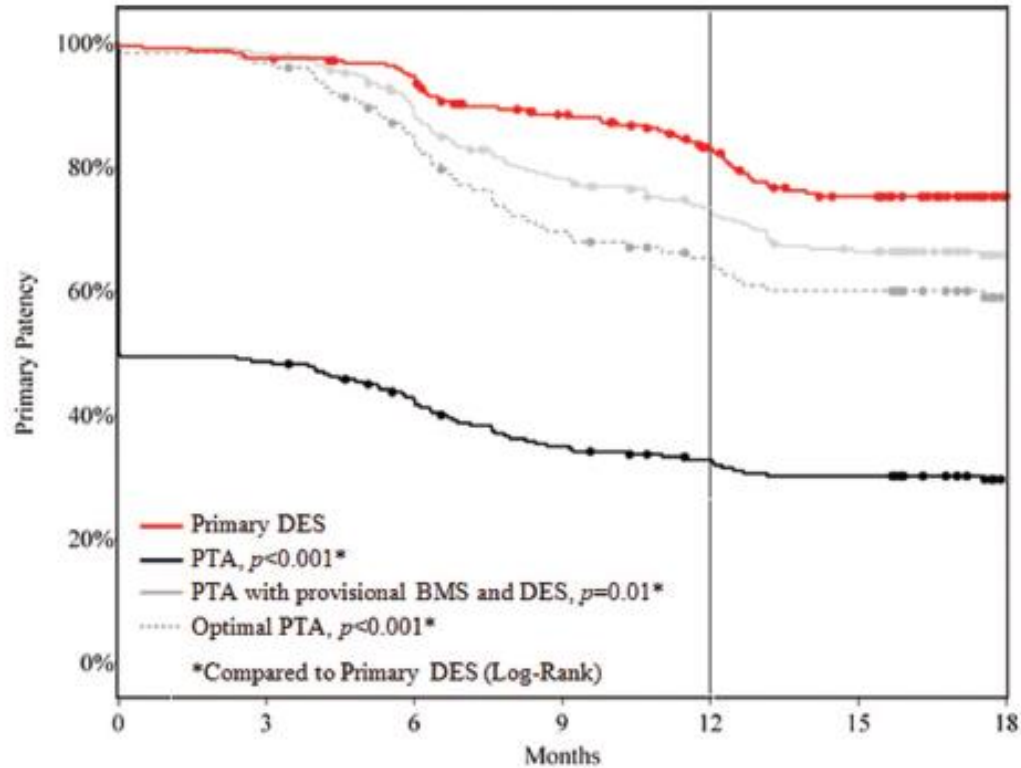
ZILVER PTX



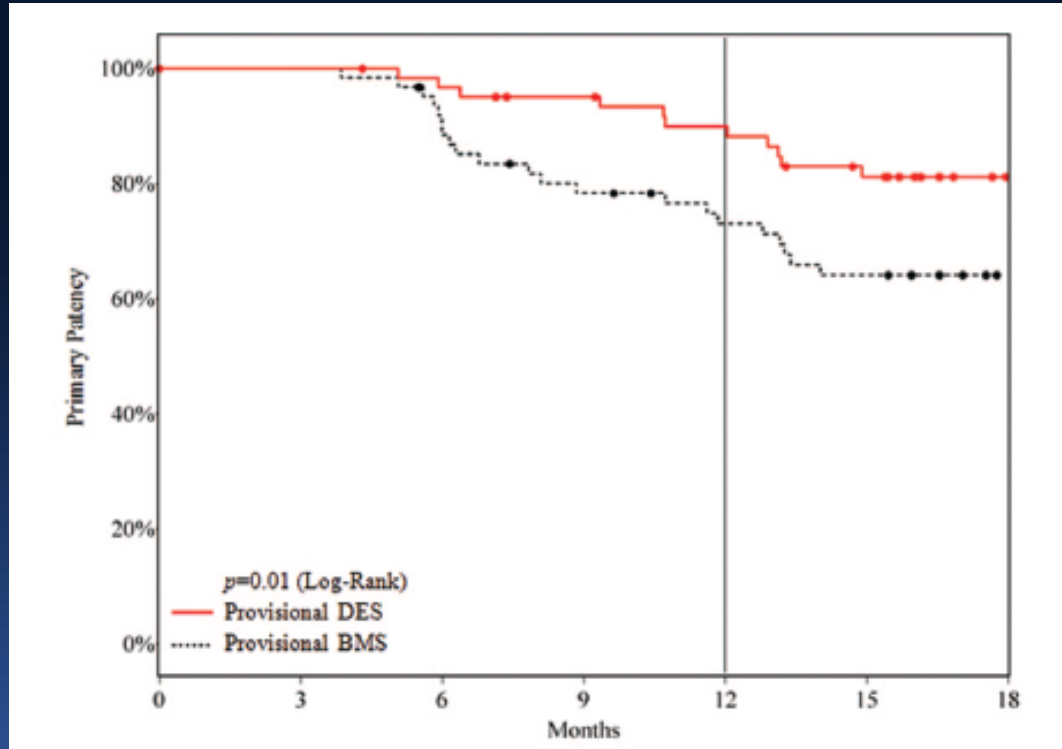
Zilver PTX 1° DES vs. PTA



Zilver PTX



Zilver PTX pDES vs. pBMS



Zilver PTX 5 Year Data

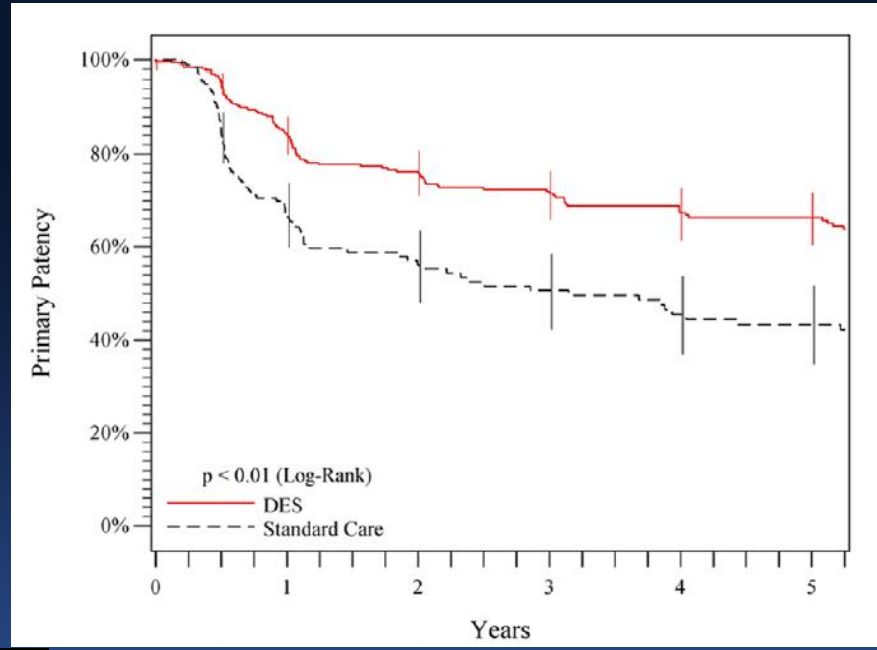
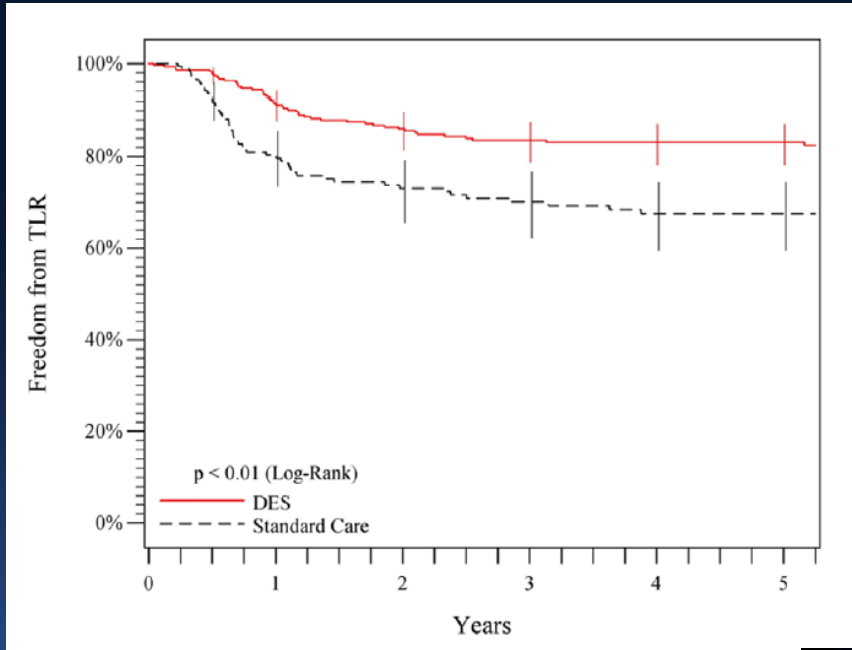
Durable Clinical Effectiveness With Paclitaxel-Eluting Stents in the Femoropopliteal Artery 5-Year Results of the Zilver PTX Randomized Trial

Michael D. Dake, MD; Gary M. Ansel, MD; Michael R. Jaff, DO; Takao Ohki, MD;
Richard R. Saxon, MD; H. Bob Smouse, MD; Lindsay S. Machan, MD;
Scott A. Snyder, PhD; Erin E. O'Leary, PhD; Anthony O. Ragheb, PhD; Thomas Zeller, MD;
on behalf of the Zilver PTX Investigators



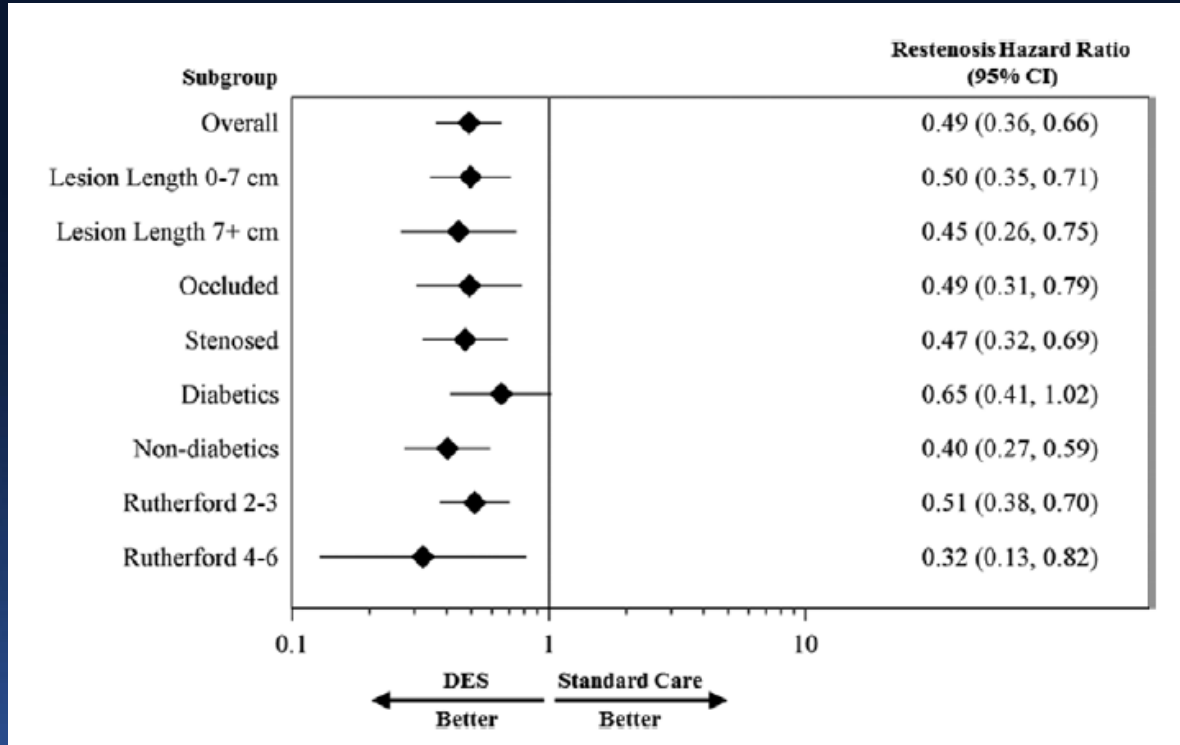
5 year Data Zilver PTA

1°DES+pDES vs. BMS + pPTA

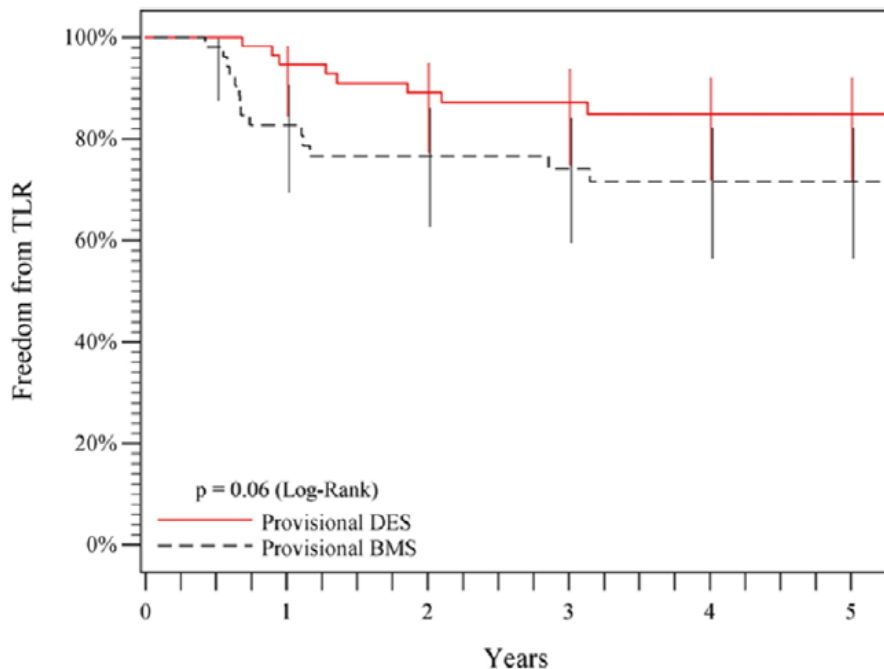


5
YEARS

5 year Data Zilver PTA



5 year Data Zilver PTA pDES vs. pPTA



ZILVER PTX TAKE HOME

Femoropopliteal disease:

-DES is better than PTA

-DES Is better than BMS

-5 Year outcomes

-only DES available



Most Important Vascular Intervention Trials # 5



IN PACT Trial

Drug-Coated Balloon Versus Standard Percutaneous Transluminal Angioplasty for the Treatment of Superficial Femoral and Popliteal Peripheral Artery Disease 12-Month Results From the IN.PACT SFA Randomized Trial

2 Gunnar Tepe, MD; John Laird, MD; Peter Schneider, MD; Marianne Brodmann, MD;
Prakash Krishnan, MD; Antonio Micari, MD; Christopher Metzger, MD; Dierk Scheinert, MD;
Thomas Zeller, MD; David J. Cohen, MD, MSc; David B. Snead, PhD;
Beaux Alexander, MBA; Mario Landini, MS; Michael R. Jaff, DO;
for the IN.PACT SFA Trial Investigators*

J
C
D
for the IN.PACT SFA Trial Investigators

IN.PACT Trial

Design

DESIGN: 331 patients with symptomatic (Rutherford 2 to 4) femoropopliteal lesions up to 18 cm randomly assigned in a 2:1 ratio to treatment with DCB or PTA

OBJECTIVE: Paclitaxel-eluting DCB vs. PTA for femoropopliteal lesions

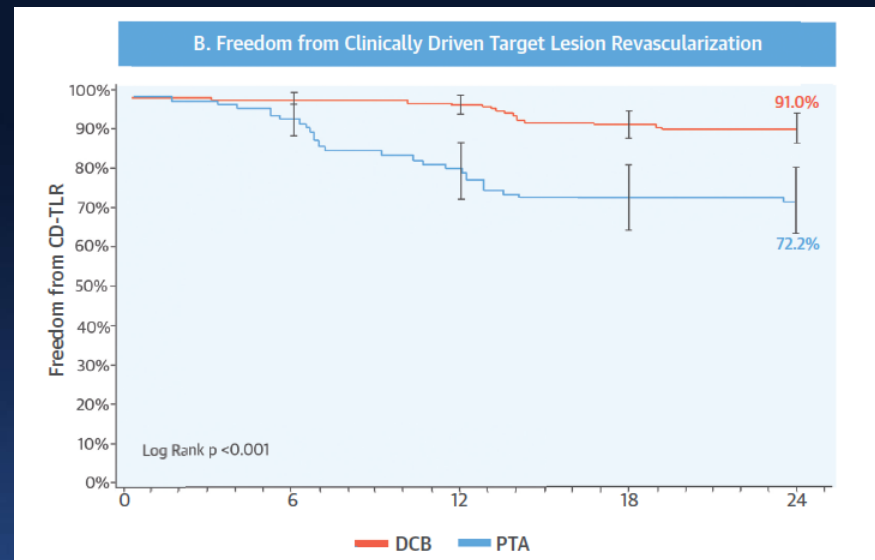
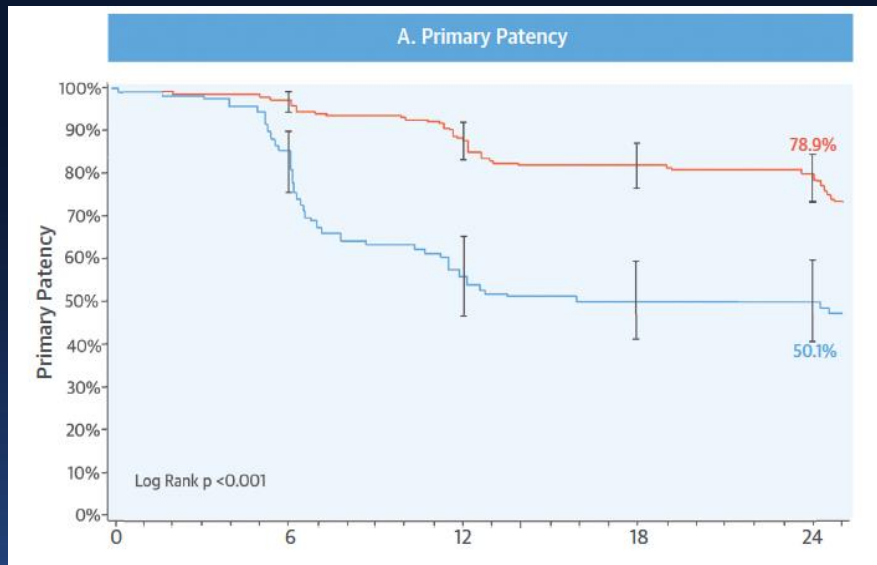
1° ENDPOINT: Primary patency, freedom from clinically driven target lesion revascularization (CD-TLR), major adverse events, and quality of life and functional outcomes as assessed by the EuroQOL-5D quality-of-life questionnaire, walking impairment questionnaire, and 6-min walk test

PRINCIPAL INVESTIGATOR:

John Laird, MD

UC Davis

IN.PACT Results-24 month



IN. PACT Results-24 month

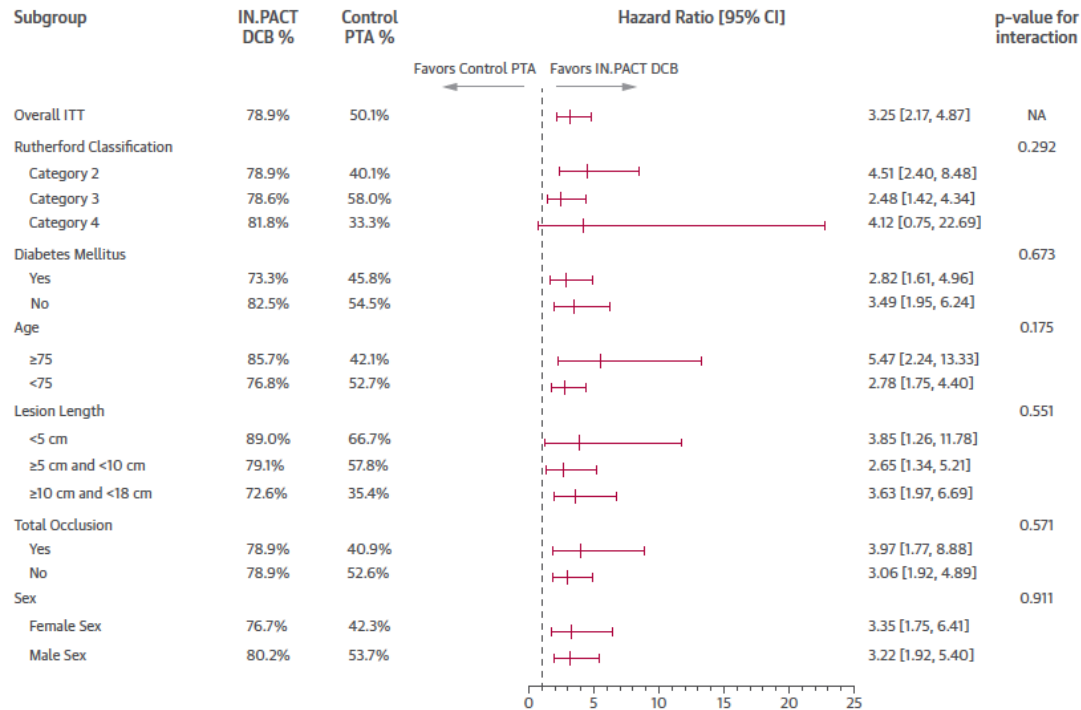
TABLE 2 Effectiveness Outcomes at 24 Months

	IN.PACT (n = 220)	PTA (n = 111)	p Value*
Primary patency†	78.9 (42)	50.1 (54)	<0.001‡
CD-TLR§	9.1 (18/198)	28.3 (30/106)	<0.001
Time to first CD-TLR, days	351.9 ± 165.9	261.7 ± 139.0	0.049
All TLR	10.1 (20/198)	29.2 (31/106)	<0.001
Primary sustained clinical improvement¶	76.9 (133/173)	59.2 (61/103)	0.003
ABI/TBI#	0.924 ± 0.261	0.938 ± 0.184	0.611



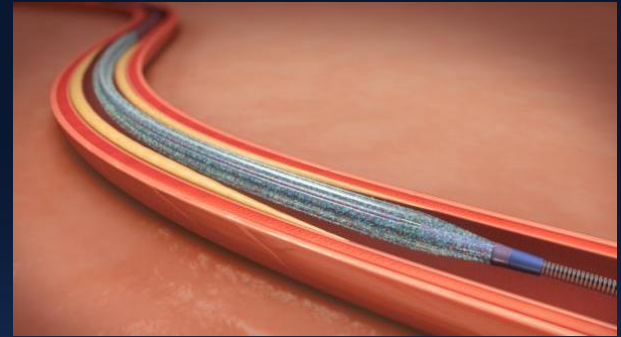
IN.PACT Results-24 Month

FIGURE 1 Subgroup Analysis of Primary Patency at 24 Months



IN.PACT Take Home

- DCB: Higher 1° patency vs. PTA
78.9% vs. 50.1%; $p < 0.001$
- DCB CD-TLR 9.1% vs. PTA 28.3% ($p < 0.001$)
- 58% fewer re-interventions in DCB arm
@2 years



Most Important Vascular Intervention Trials # 5



ACHILLES TRIAL

A Prospective Randomized Multicenter Comparison of Balloon Angioplasty and Infrapopliteal Stenting With the Sirolimus-Eluting Stent in Patients With Ischemic Peripheral Arterial Disease

1-Year Results From the ACHILLES Trial

Dierk Scheinert, MD,* Konstantinos Katsanos, MD, PHD,† Thomas Zeller, MD,‡
Renate Koppensteiner, MD,§ Philip Commeau, MD, PHD,|| Marc Bosiers, MD,¶
Hans Krankenberg, MD,# Iris Baumgartner, MD,** Dimitris Siablis, MD, PHD,†
Johannes Lammer, MD,§ Mariella Van Ransbeeck,†† Ayesha C. Qureshi, MBBS, PHD,††
Hans-Peter Stoll, MD,‡‡ on behalf of the ACHILLES Investigators

*Leipzig, Bad Krozingen, and Hamburg, Germany; Patras, Greece; Vienna, Austria; Ollioules, France;
Dendermonde and Waterloo, Belgium; Bern, Switzerland*

ACHILLES TRIAL

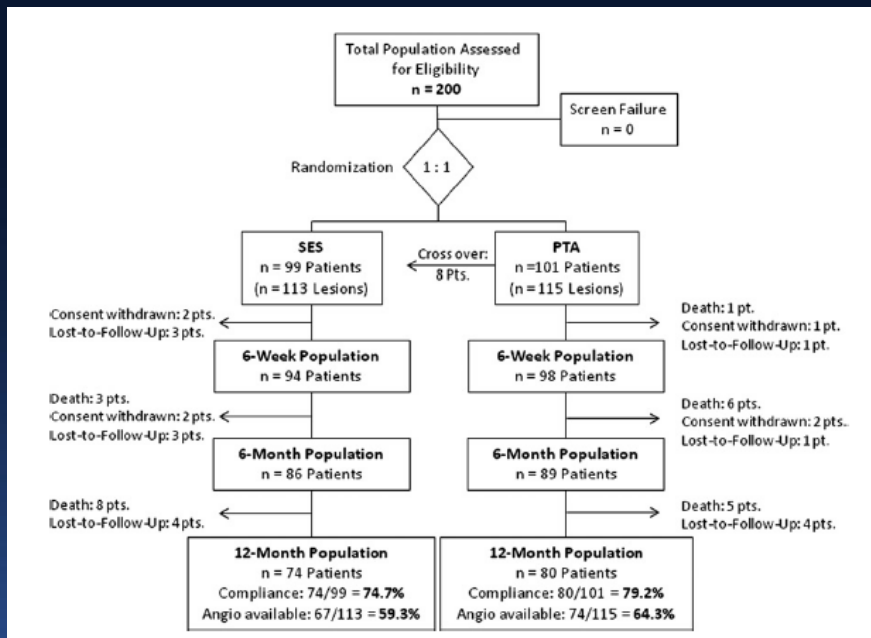


Table 2 Baseline Lesion Characteristics and Procedural Parameters

	SES (n = 113 Lesions)	PTA (n = 115 Lesions)	p Value
Total lesion length, mm	26.9 ± 20.9	26.8 ± 21.3	0.913
Reference vessel diameter, mm	2.6 ± 0.5	2.6 ± 0.6	0.894
CTO, %	81.3	75.4	0.334
Total length of CTO,* mm	6.7 ± 19.3	11.0 ± 22.4	0.114
Restenotic lesions, %	5.3	1.8	0.171
Calcification (moderate/severe), %	15.1	15.2	1.000
Pre-procedure stenosis, %	68.8 ± 19.3	74.0 ± 19.0	0.039
Post-procedure stenosis, %	13.3 ± 14.3	25.9 ± 15.2	<0.001
Device success,† %	95.5	58.2	<0.001
Lesion success,‡ %	100	96.9	0.103
Procedure success,§ %	94.8	92.9	0.758

ACHILLES TRIAL

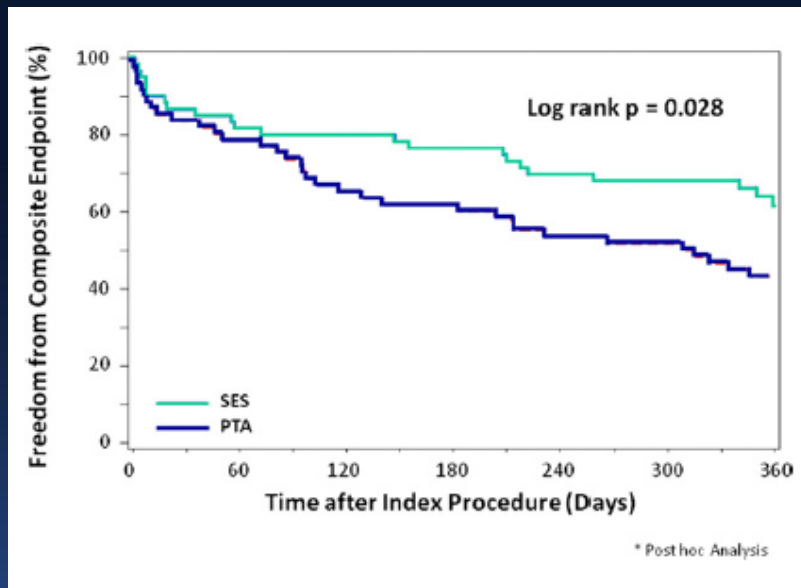
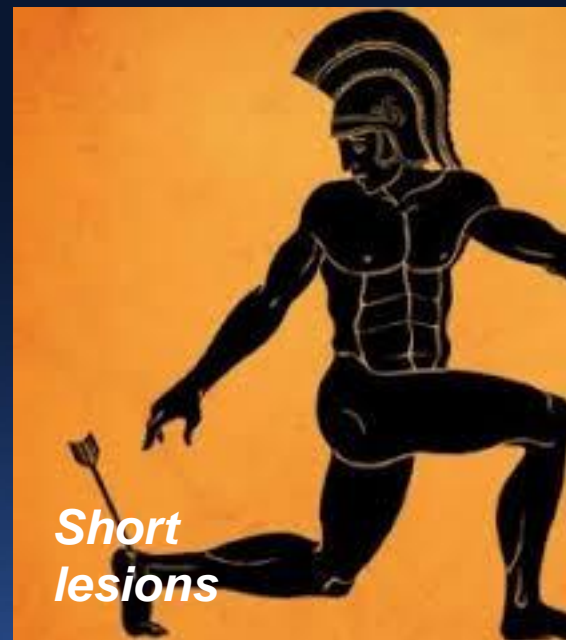
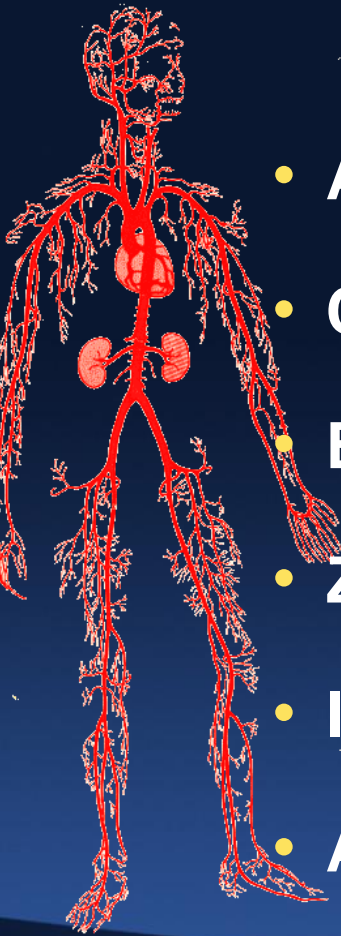


Figure 3

Freedom From Death, Target Lesion Revascularization, Bypass, Amputation, and Rutherford Class ≥ 4



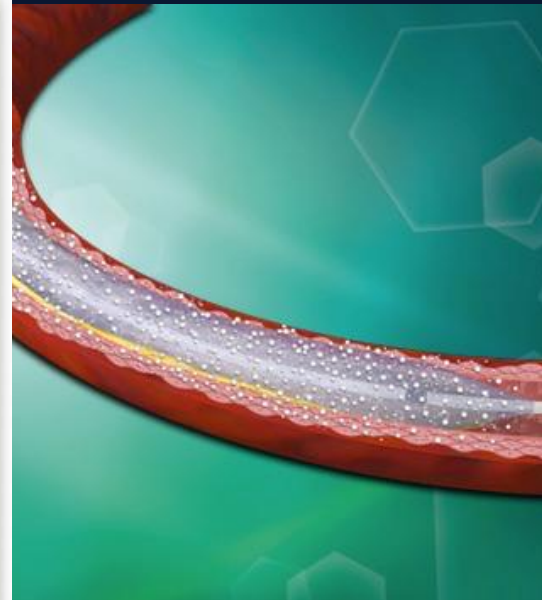
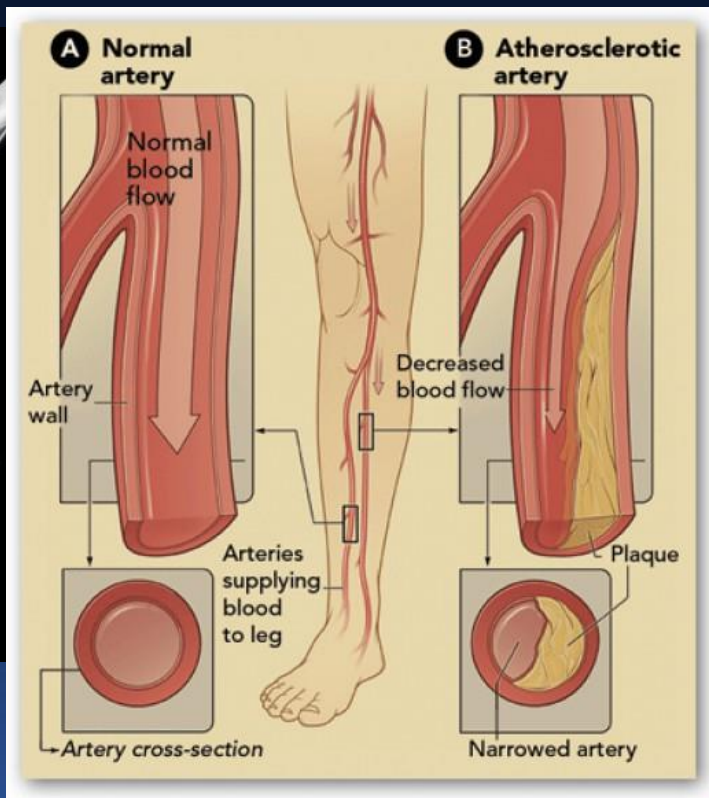
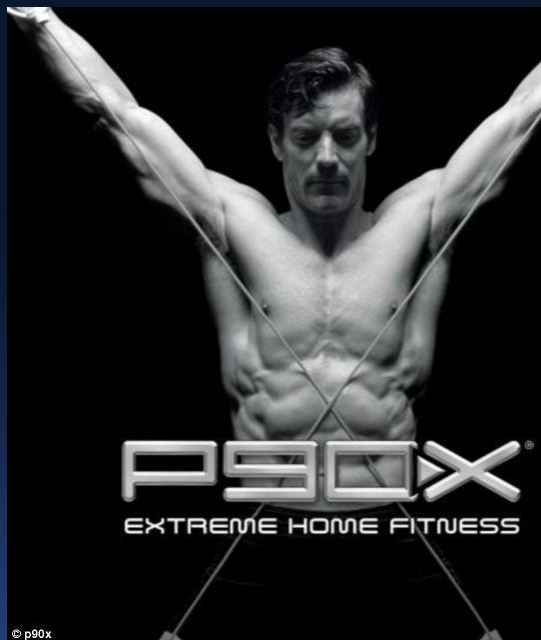
Conclusion Slide



- **ACT**
 - CAS=CEA
- **CLEVER**
 - SET and EVT>OMT
- **ERASE**
 - EVT+ OMT best
- **ZILVER-PTX**
 - DES >BMS or PTA
- **INPACT**
 - DCB>PTA
- **ACHILLES**
 - DES>PTA



CONCLUSION



THE END

**THANK
YOU**