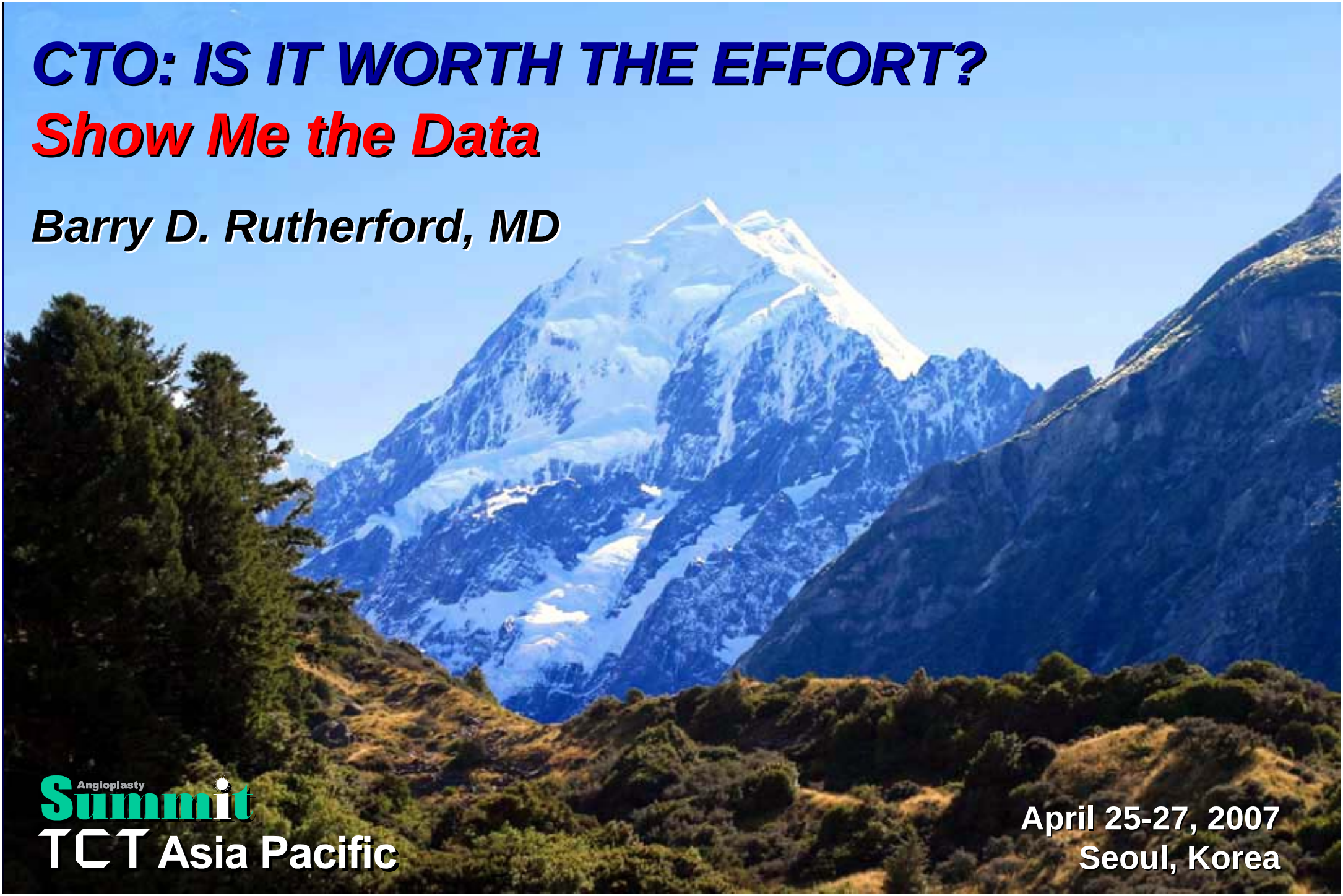
CTO: IS IT WORTH THE EFFORT?

Show Me the Data

Barry D. Rutherford, MD

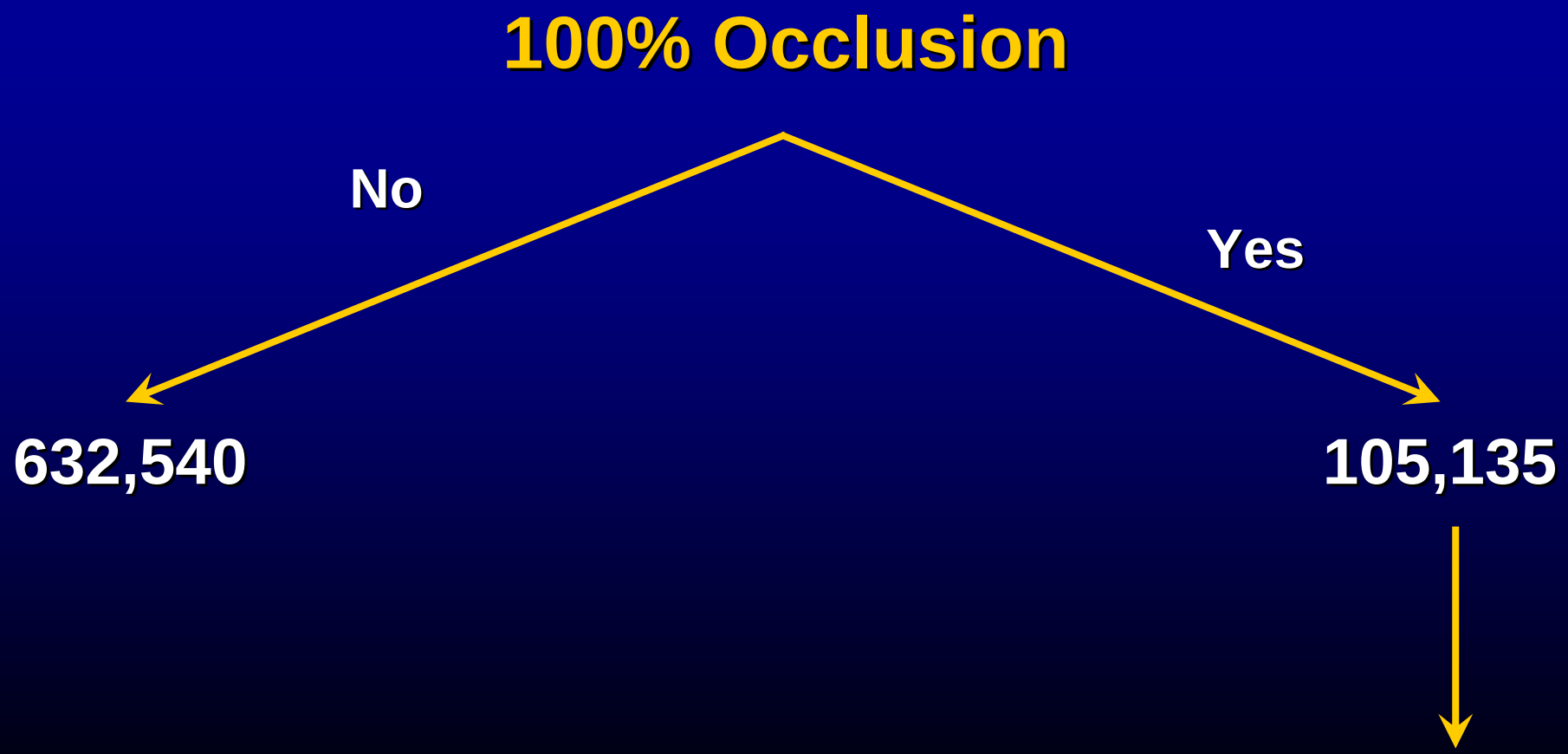


Angioplasty Summit
TCT Asia Pacific

April 25-27, 2007
Seoul, Korea

The Influence of Operator Volume on Attempt Rate of Percutaneous Coronary Intervention for CTO

440 Institutions Reported 737,675 Cases to ACC/NCDR V3.04



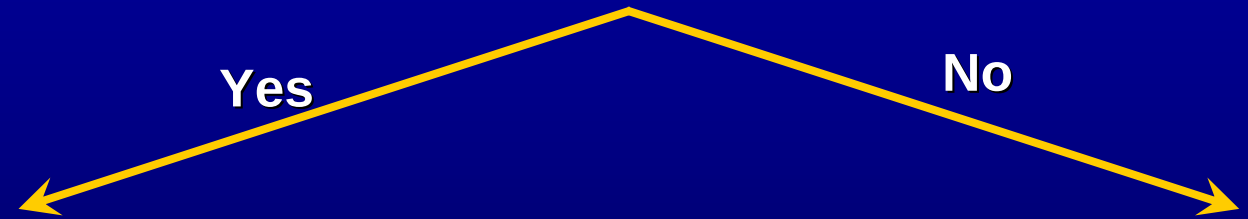
Courtesy of J. Aaron Grantham, MD

The Influence of Operator Volume on Attempt Rate of Percutaneous Coronary Intervention for CTO

440 Institutions Reported 737,675 Cases to ACC/NCDR V3.04

Exclusion Criteria

105,135



65,633

39,502

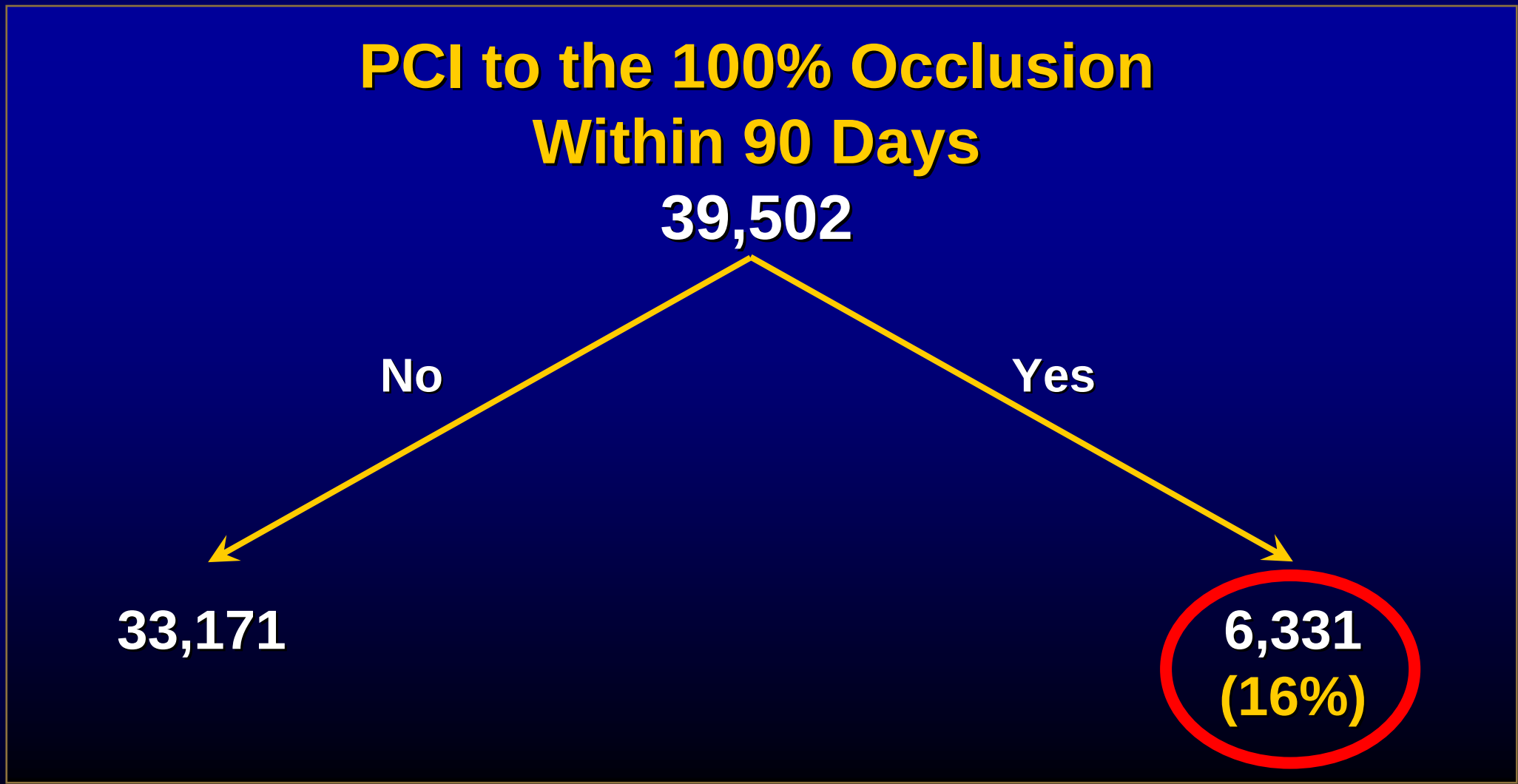
Exclusion Criteria

- STEMI or non STEMI infarct within prior 7 days
- Pts with valvular heart disease, congenital heart disease, transplant evaluation
- Pts with prior CABG
- Pts with emergency or salvage procedures, cardiogenic shock
- Pts that had angiography at a center that did not perform PCI

Courtesy of J. Aaron Grantham, MD

The Influence of Operator Volume on Attempt Rate of Percutaneous Coronary Intervention for CTO

440 Institutions Reported 737,675 Cases to ACC/NCDR V3.04



Courtesy of J. Aaron Grantham, MD

The Influence of Operator Volume on Attempt Rate of Percutaneous Coronary Intervention for CTO

ACC/NCDR 3/04 Registry

MV Analysis: Factors Assoc. with Lower Attempt Rates

	Point Estimate	95% CI
Diabetes	0.79	0.74-0.84
Prior AMI	0.67	0.63-0.71
Creatinine ≥ 2.0	0.53	0.44-0.64
Stress Test Negative vs Positive	0.83	0.75-0.91
Asymptomatic vs. UA	0.58	0.54-0.63
LVEF < 40%	0.77	0.71-0.83
MVD vs SVD	0.29	0.27-0.31
Low vs Intermediate Operator	0.63	0.59-0.69
Low vs High Volume Operator	0.53	0.49-0.58

Courtesy of J. Aaron Grantham, MD

CTO: IS IT WORTH THE TIME? Show Me the Data

Mid America Heart Institute Experience

Last 102 Consecutive CTO Procedures

Average per Case	CTO (n=102)	Non CTO (n=104)
Balloon Catheter	2.47	1.48
Guide Catheter	1.65	1.34
Guide Wires	3.83	1.54
Stents	1.83	1.72
Procedure Time (min) Range	80.9 27-260	44.4 19-139
Fluoro Time (min) Range	39.9 9.3-113	16.9 1.7-67
Contrast Volume (cc) Range	397 200-1200	230 50-560

CTO: IS IT WORTH THE TIME?
Show Me the Data

Opening a CTO is associated with

- **Improvement in symptoms**
- **Improved LV function**
- **Improved longevity**

Quantifying the Health Status Benefits of Successful CTO Recanalization: *Results from FlowCardia's Approach to CTO Recanalization (FACTOR Trial)*

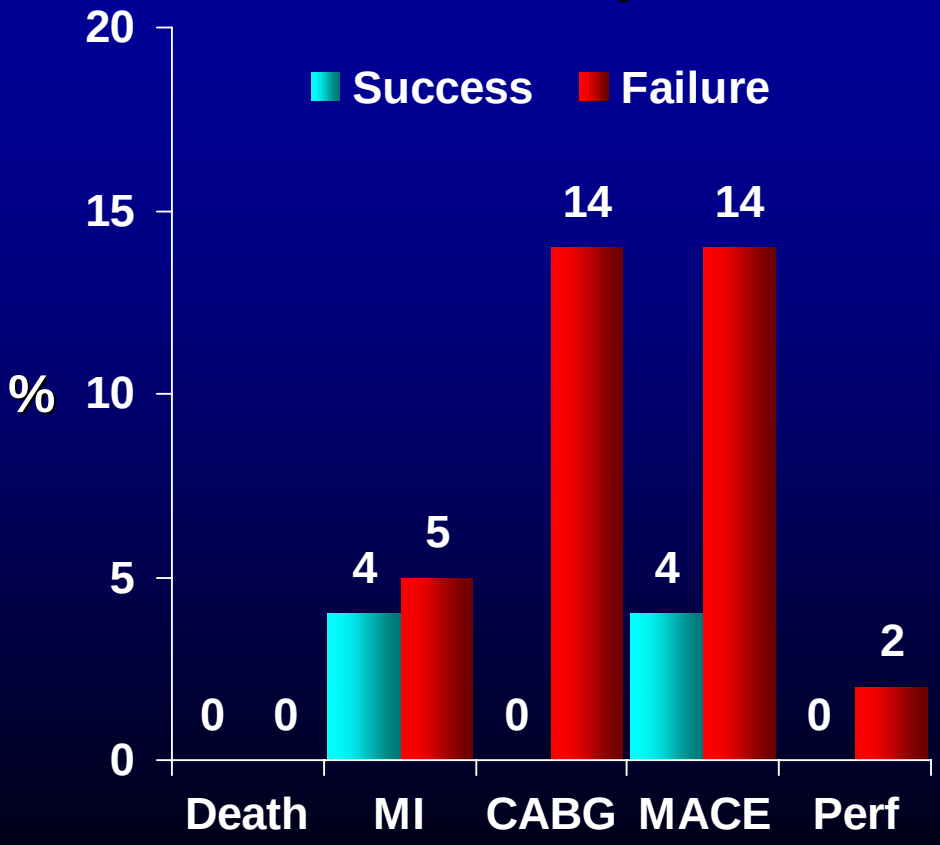
125 pts completed the Seattle Angina Questionnaire (SAQ) before and one month after PCI.
69 procedural success, 56 failures (55%)
Baseline Demographics, Health Score Status

		Successful N = 69	Unsuccessful N = 56	p-value
Age (yrs)		62 ± 11	62 ± 12	0.98
Male (%)		81	88	0.34
Prior MI (%)		40	41	0.88
Diabetes (%)		29	23	0.47
Prior CABG (%)		17	21	0.57
LVEF (%)		54 ± 12	54 ± 9	0.81
SAQ Scores:	AF	74 ± 23	76 ± 27	0.69
	PL	65 ± 27	68 ± 24	0.50
	QoL	50 ± 24	60 ± 26	0.04

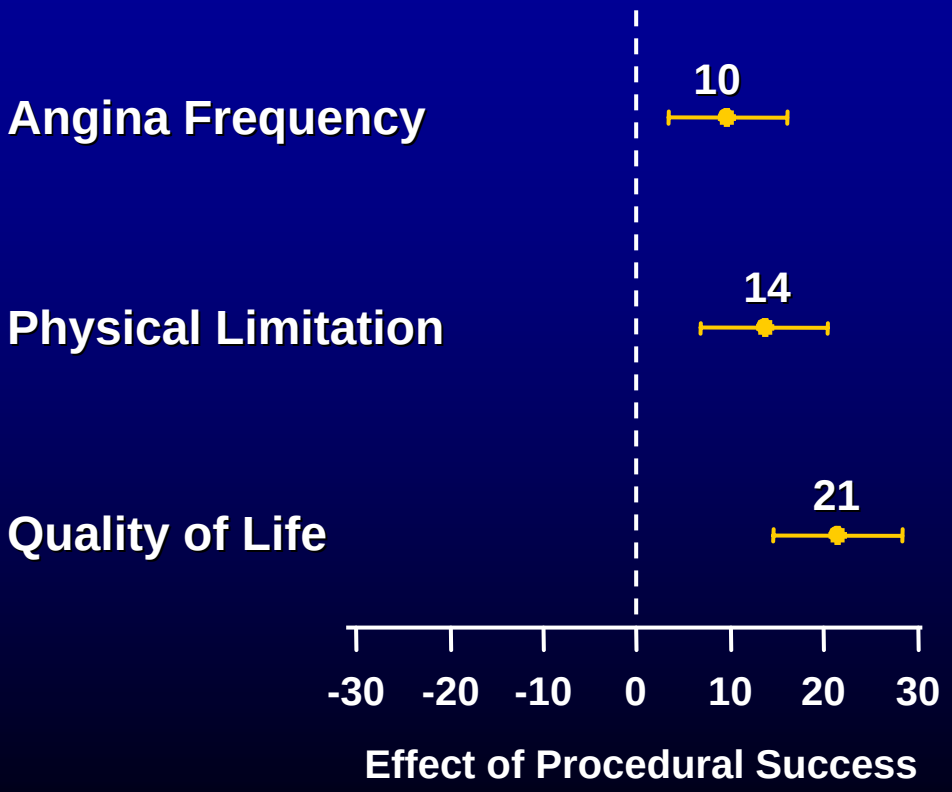
Courtesy of J. Aaron Grantham, MD and John A. Spertus, MD, MPH

Quantifying the Health Status Benefits of Successful CTO Recanalization: *Results from FlowCardia's Approach to CTO Recanalization (FACTOR Trial)*

Clinical Endpoints



SAQ Health Status at 1 Month



Courtesy of J. Aaron Grantham, MD and John A. Spertus, MD, MPH

Early and Late Improvement of LV Function After DES for Chronic Total Occlusion

- 20 patients, MRI before and 5 months and 3 years post PCI

	Before	3 Years	p-value
Mean End-Diastolic Vol. Index (ml/m^2)	87 ± 14	80 ± 14	0.03
Mean End-Systolic Vol. Index (ml/m^2)	36 ± 12	31 ± 13	0.03
Mean LVEF (%)	60 ± 8	61 ± 10	0.11
Segmental wall thickening (%)			
< 25% transmural extent of infarct	20 ± 21	71 ± 51	0.008
25-75% transmural extent of infarct	17 ± 20	50 ± 45	0.005
> 75% transmural extent of infarct	14 ± 21	13 ± 49	0.54

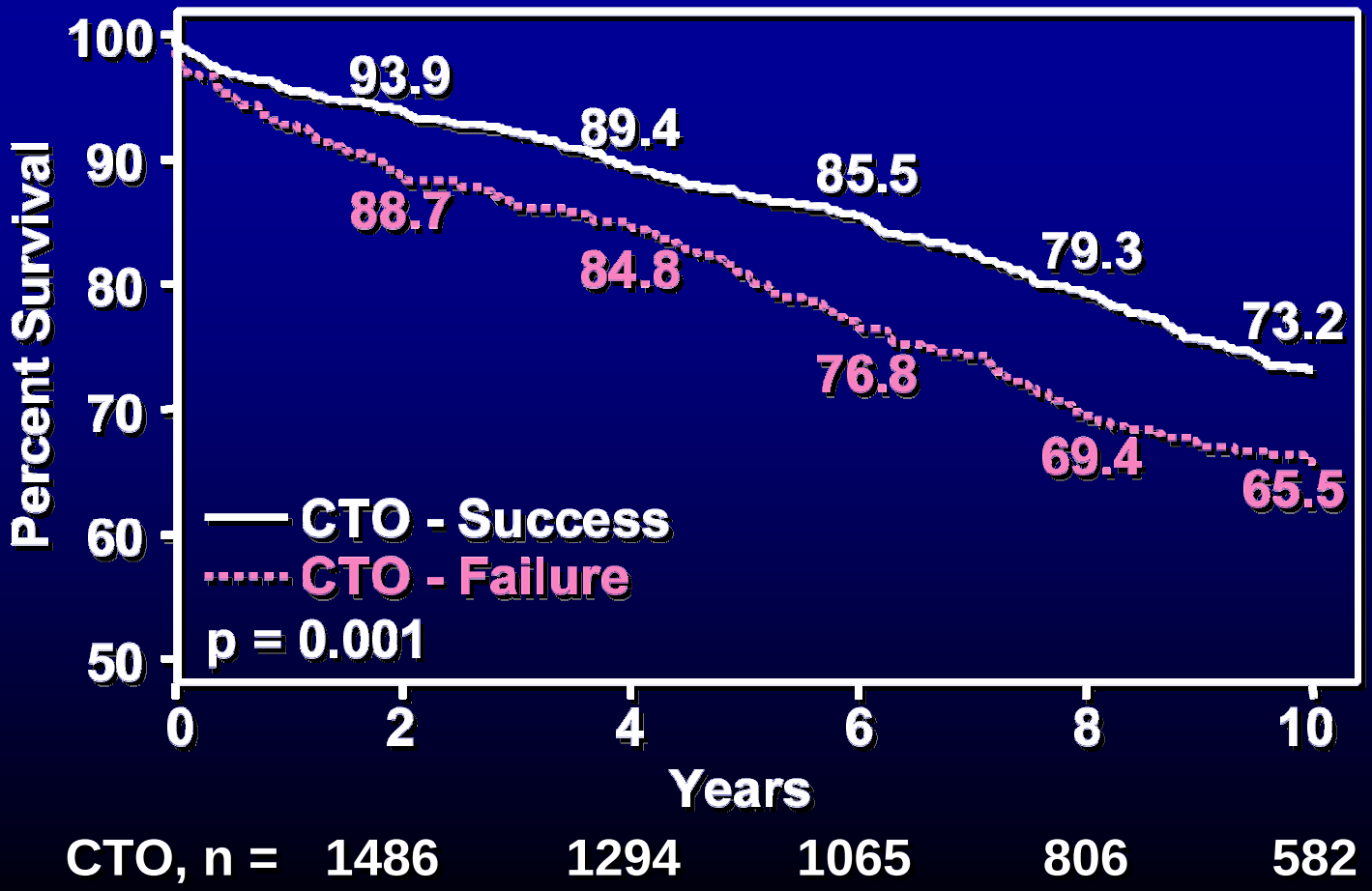
S. Kirschbaum et al. JACC 2007;49:213A

Procedural Outcomes & Long-Term Survival Among Patients Undergoing PCI of a CTO: A 20-Year Experience

- June 1980 – December 1999, 2007 consecutive patients underwent PCI of a CTO
- Utilizing propensity scoring a matched cohort of 2007 patients was identified from the MAHI PTCA database
- Long-term follow-up was available for 93.6%
  Mean follow-up time: 91.4 ± 55.4 months

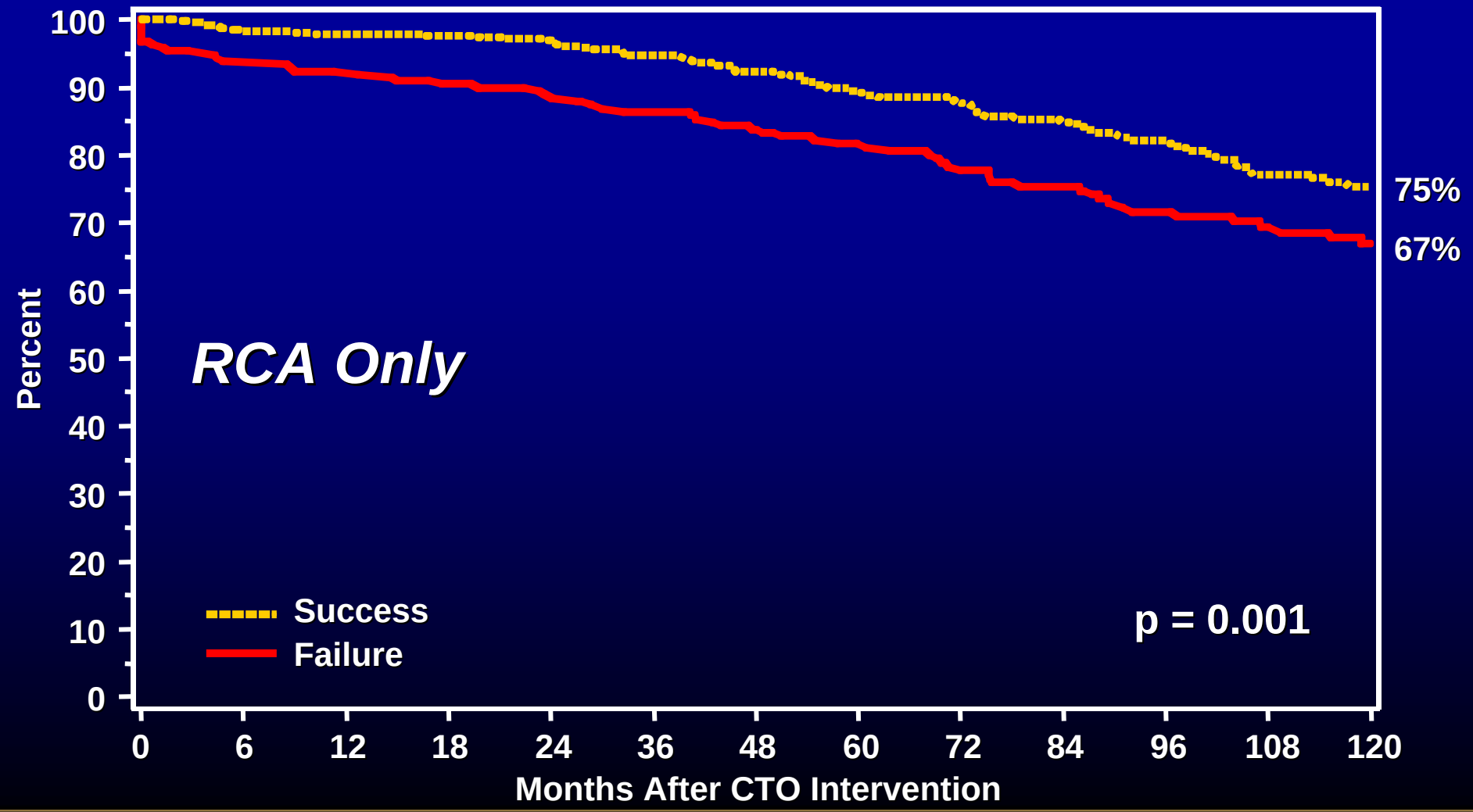
Procedural Outcomes and Long-Term Survival for PCI of Chronic Total Occlusion

2007 Patients, 20-Year Experience

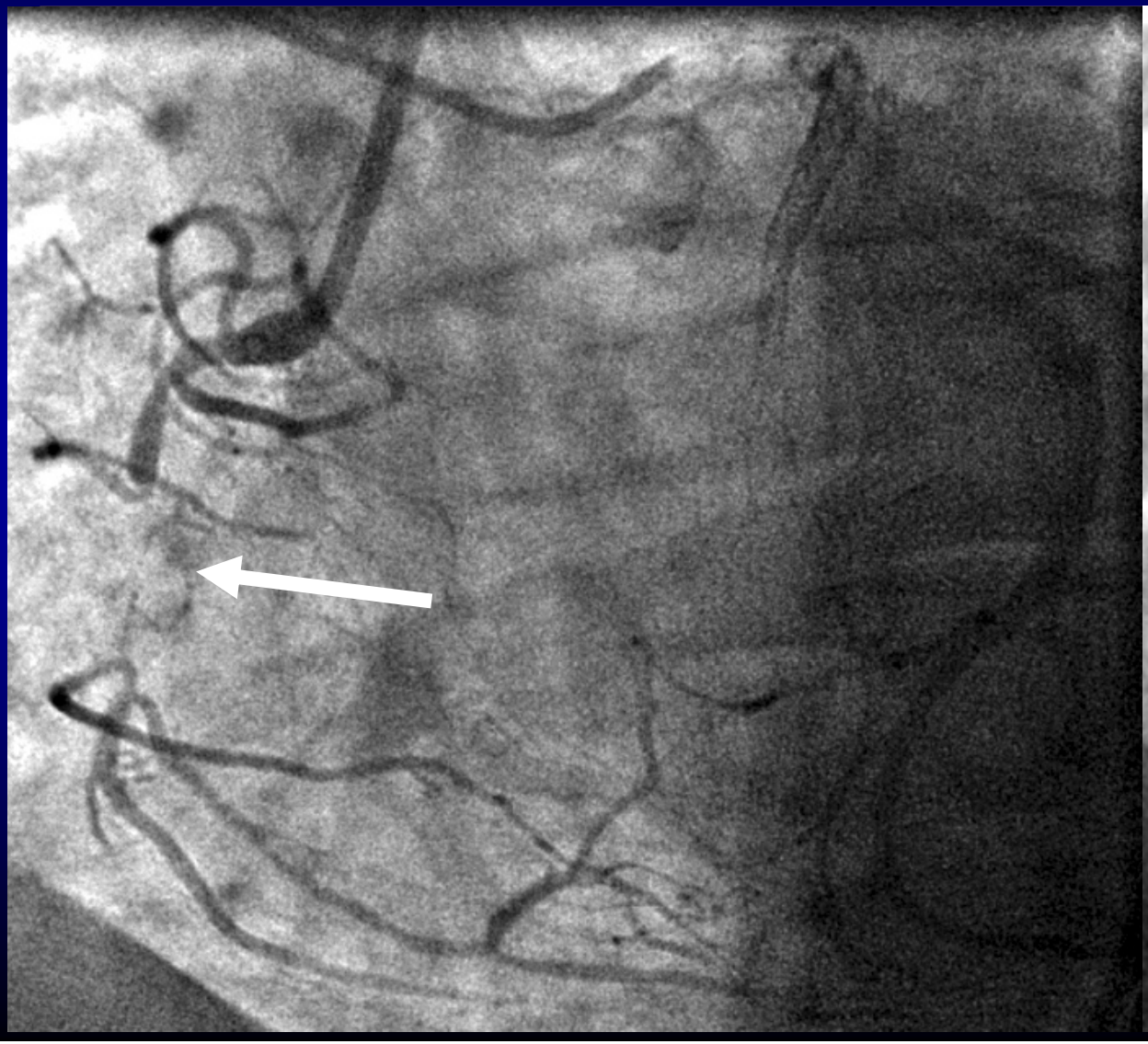


Suero et al. JACC 2001;38:409

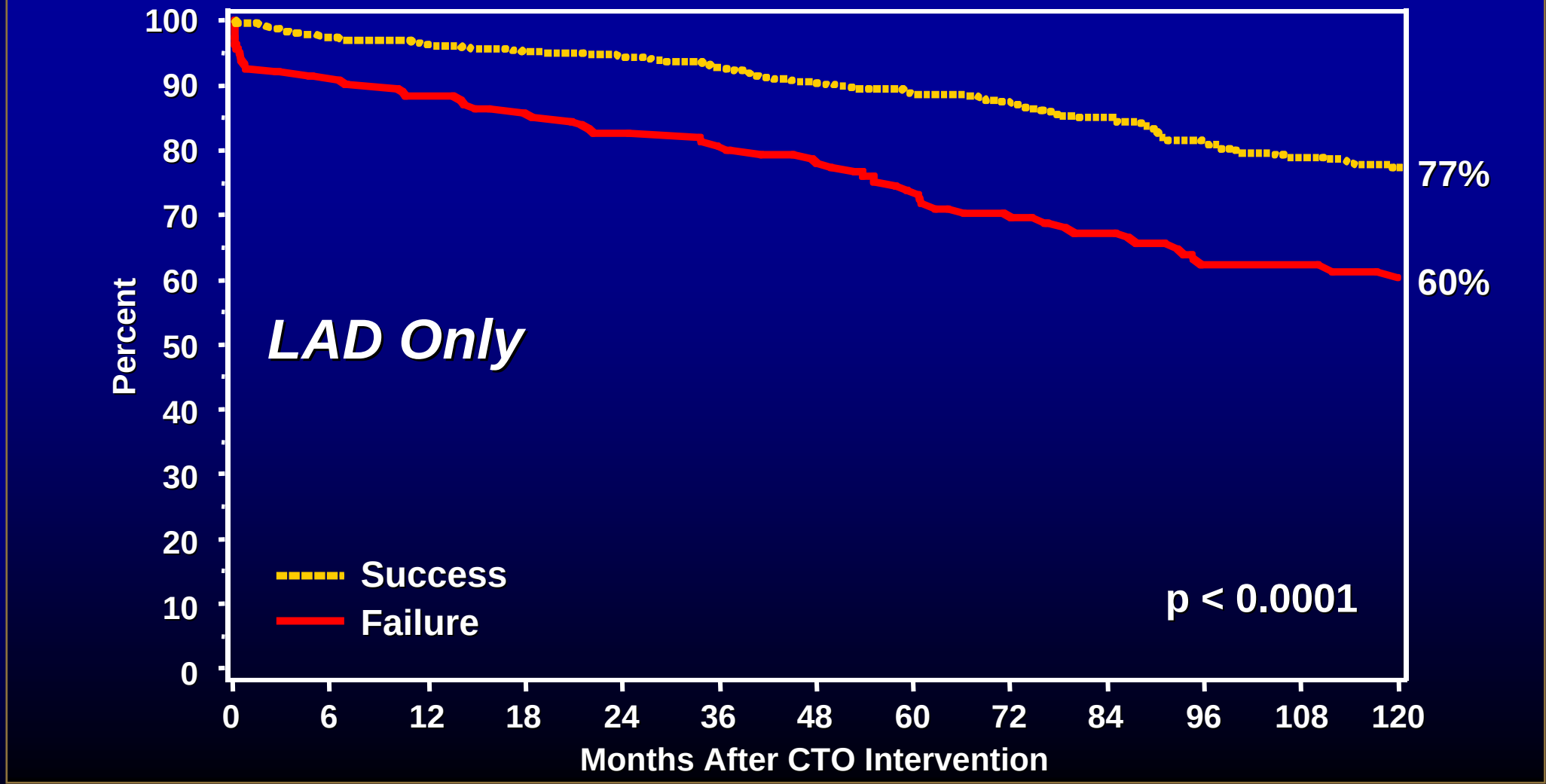
Procedural Outcomes and Long-Term Survival for PCI of Chronic Total Occlusion



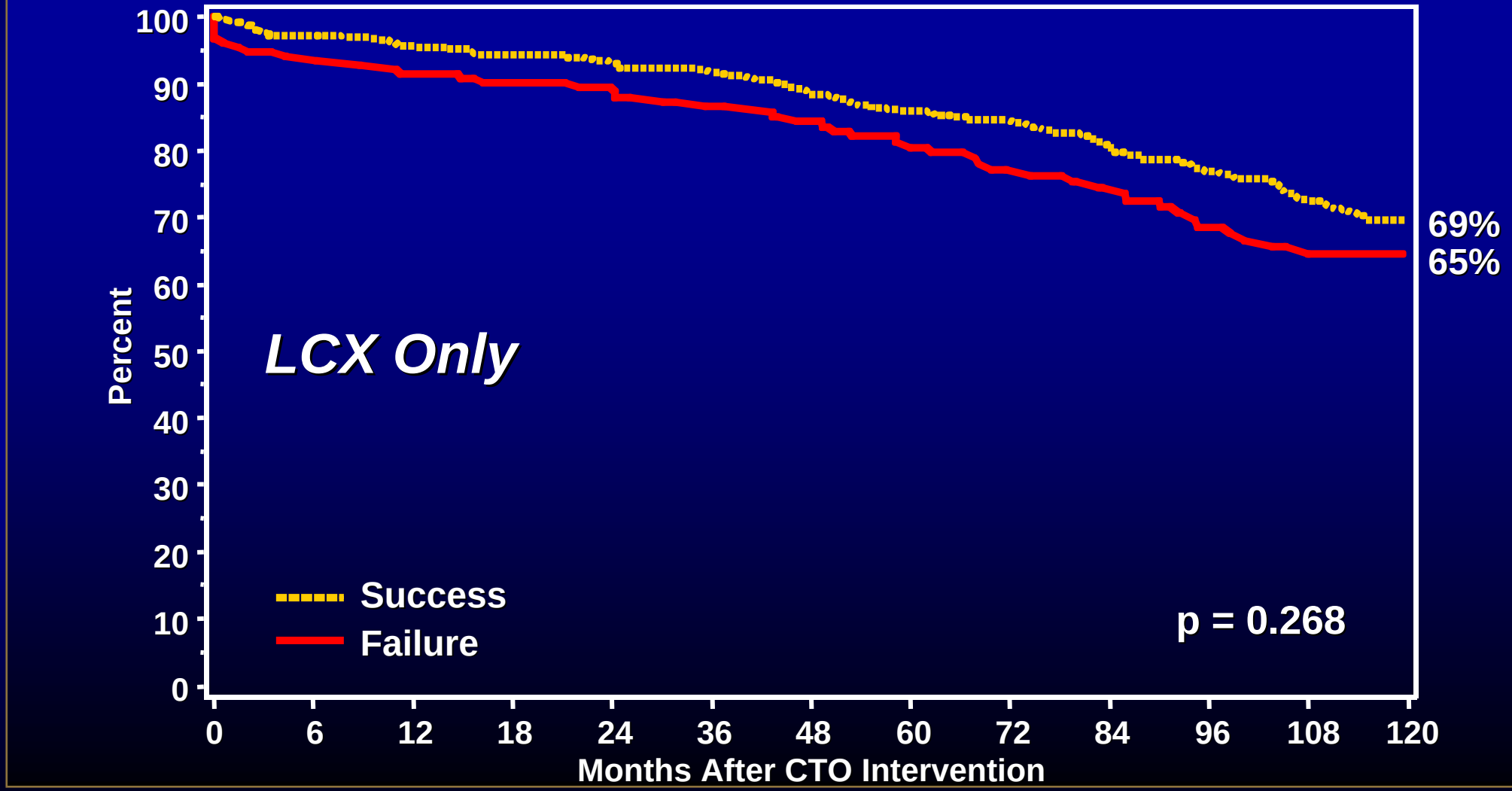
64-Year-Old Male
24-Month CTO of RCA



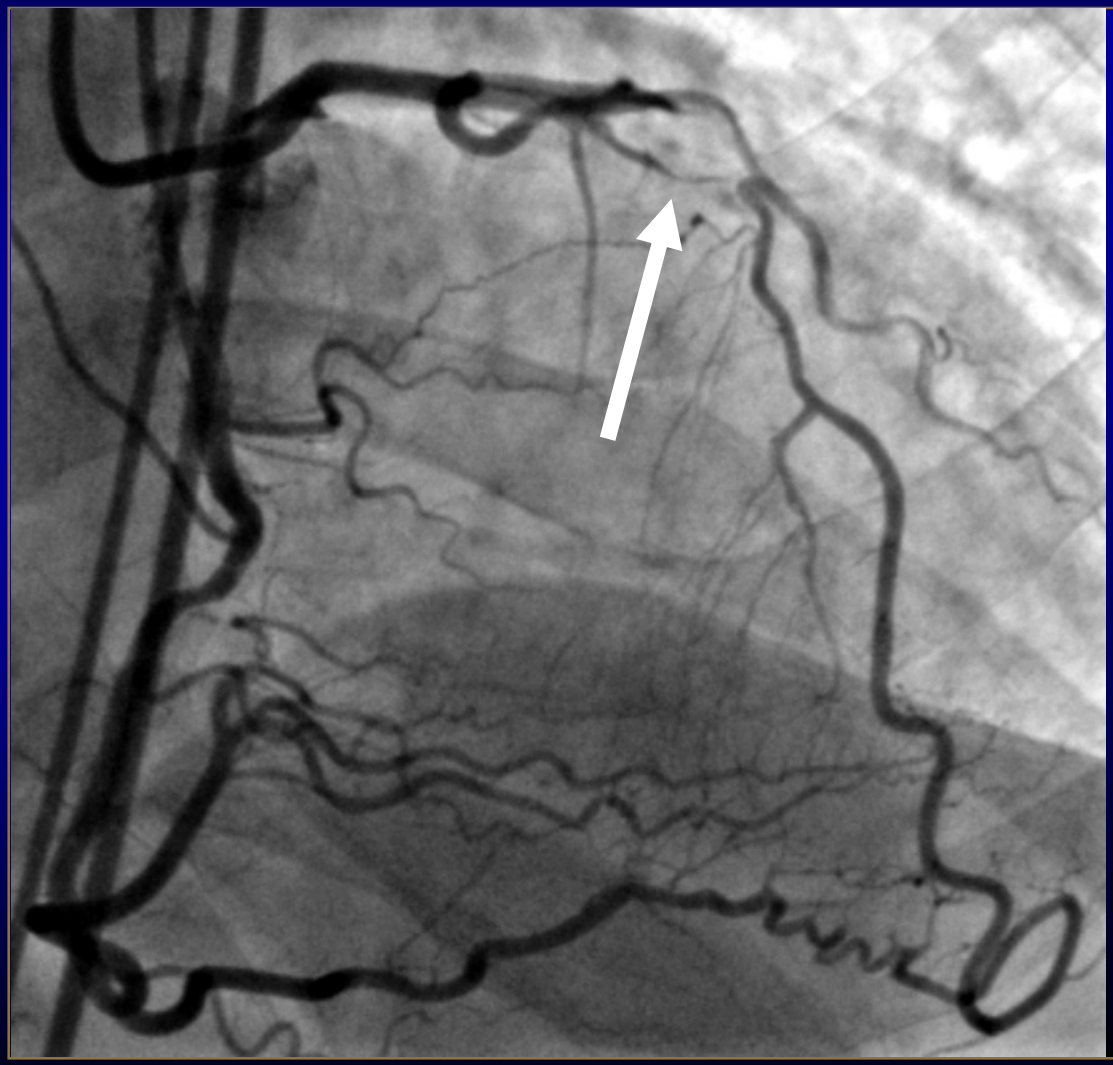
Procedural Outcomes and Long-Term Survival for PCI of Chronic Total Occlusion



Procedural Outcomes and Long-Term Survival for PCI of Chronic Total Occlusion



53-Year-Old Male
6-months CTO LAD



CTO: IS IT WORTH THE TIME?

Show Me the Data

Time-independent benefit on longevity for successful opening of LAD and RCA

Coronary Intervention for Persistent Occlusion After Myocardial Infarction (OAT Trial)

- 2166 patients recruited from 26 countries
- Feb 2000-December 2005
- Total occlusion of infarct artery 3-28 days post AMI
- Proximal occlusion, LVEF < 50%
- Randomized to PCI plus medical therapy vs medical therapy only
- Primary endpoint: composite of death, recurrent MI, or NYHA Class IV heart failure

Hochman et al. NEJM 2006;355

Coronary Intervention for Persistent Occlusion After Myocardial Infarction (OAT)

- Initial goal was 3,200 pts, 90% power to detect 25% reduction in the rate of primary endpoint, assuming a 3-year event rate of 25% in the medical group
- Five years to recruit 2166 pts, from 26 countries, over 200 centers!
- 10.8 pts/center, 2 pts/year/center!!

Coronary Intervention for Persistent Occlusion After Myocardial Infarction (OAT Trial)

Baseline Clinical and Angiographic Characteristics

	PCI Group N = 1082	Medical Therapy N = 1084	p-value
Age (yrs)	58.6 ± 10.8	58.7 ± 11.1	0.78
Male (%)	78	78	-
Previous AMI (%)	12	11	0.49
Previous CABG (%)	0.5	0.4	0.74
Diabetes (%)	18	23	0.02
ST-Seg Elevation (%)	68	66	0.34
ST Elev, Q waves, ↓ R wave (%)	87	86	0.58
Interval between MI and R Median (days)	8	8	
Stress test performed (%)	27	28	0.68
Ischemia in infarct territory (%)			
Severe or moderate	9	11	0.22
Mild or none	91	89	

Hochman et al. NEJM 2006;355

Coronary Intervention for Persistent Occlusion After Myocardial Infarction (OAT Trial)

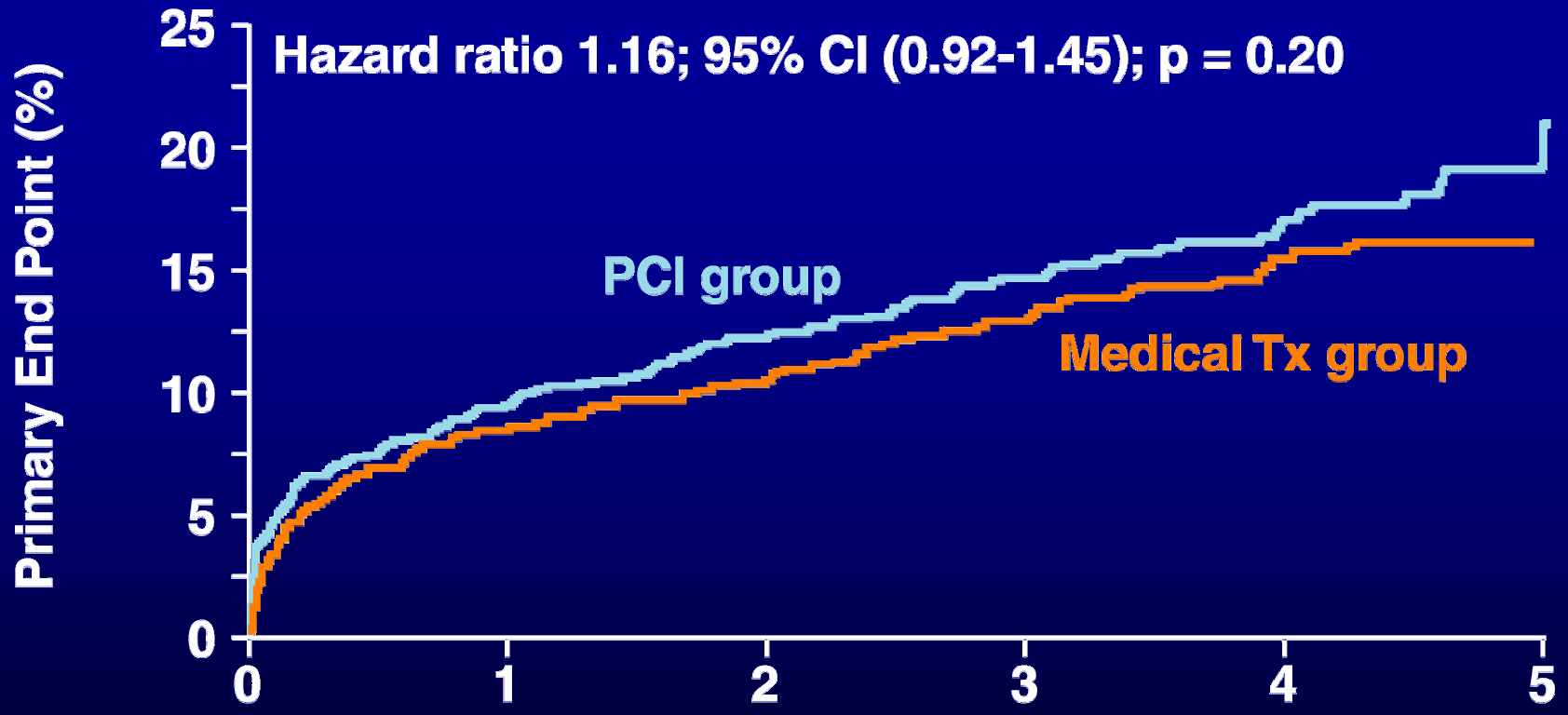
Primary and Secondary Outcomes

Estimated 4-year Cumulative Event Rate

	PCI Group N = 1082	Medical Tx N = 1084	p-value
Primary endpoint (%)	17.2	15.6	0.20
Death (all causes, %)	9.1	9.4	0.83
Fatal and Nonfatal MI (%)	7.0	5.3	0.13
Nonfatal Reinfarction (%)	6.9	5.0	0.08
Class IV Heart Failure (%)	4.4	4.5	0.92
Death or Nonfatal MI (%)	14.9	13.2	0.13

Hochman et al. NEJM 2006;355

Coronary Intervention for Persistent Occlusion After Myocardial Infarction (OAT Trial)



No. at Risk						
PCI group	1082	895	719	482	265	85
Med Tx group	1084	909	714	474	268	78

66% 44%

Hochman et al. NEJM 2006;355

Coronary Intervention for Persistent Occlusion After Myocardial Infarction (OAT Trial)

Substudy of Patients with Angiographic Follow-Up at 1 Year

PCI group (173 pts)

Infarct artery patent: 154 (89%)

Medical Group (159 pts)

Infarct artery patent: 40 (25%)

$p < 0.001$

Meta-Analysis of 1,193 Pts Shows that Late PCI for the Occluded Infarct-Related Artery Improves Survival

- Comparison of late PCI vs medical therapy in hemodynamically stable patients > 12 hours following onset of symptoms.
- Enrolled 1193 patients from 8 studies. Median time from AMI to randomization: 8 days (1-42).

12-Month F/U	PCI N = 601	Medical Therapy N = 592	p-value
Death (%)	3.7	7.3	0.005

D. Appleton et al. JACC 2007;49:248A

CTO: IS IT WORTH THE TIME?

Show Me the Data

Clear indication for CTO Attempt:
Recent AMI or not

- **Symptomatic patient:**
  Angina, dyspnea, fatigue
- **Moderate to severe ischemia in the distribution of the CTO**
- **Adequate distal vessel**
  - **> 2.5 mm in diameter**
  - **> 30-40 mm visible length**

Any two of the above

EXTRA SLIDES

OAT IN PERSPECTIVE:
When is CTO Angioplasty Clinically Indicated and What Are the Benefits

Long-Term Survival Following PCI for CTO

	1-yr	5-yr	10-yr	p-value
Mid America Heart Inst.				**0.001**
Success	95%	89%	73%	
Failure	88%	78%	65%	
Thoraxcenter				**0.02**
Success	94%	93.5%	-	
Failure	89%	88%	-	
TOAST-GISE				**0.03**
Success	99%	-	-	
Failure	96%	-	-	

Suero, et al. JACC 2001;38:409 *Olivari, et al. JACC 2003;41:1672* *Hoye, et al. Eur Heart J. 2005;26:2630*

"We opened those patients that we thought should be opened and any patient left went to OAT"

Anonymous Investigator Quote

Immediate Results and One-Year Clinical Outcome After PCI in Chronic Total Occlusions

Data from Multicenter, Prospective Study (TOAST-GISE)

12-Month Clinical Outcome

	CTO Success N = 286	CTO Failure N = 83	p-value
All deaths	3 (1.05%)	3 (3.6%)	0.13
Cardiac death	1 (0.3%)	3 (3.6%)	0.03
Non fatal Q MI	1 (0.3%)	-	
Non fatal Non Q MI	1 (0.3%)	3 (3.6%)	0.3
Cardiac death/MI	3 (1.0%)	6 (7.2%)	0.005
CABG	7 (2.4%)	13 (15.7%)	< 0.0001
Any TLR	33 (11.5%)	19 (22.9%)	0.01
Any MACE	35 (12.2%)	21 (25.3%)	0.005

Only MV predictor of MACE free survival was successful opening of CTO

Olivari et al. JACC 2003;41:1672

Percutaneous Coronary Intervention for CTO: *Thoraxcenter Experience 1992-2002*

874 pts, 885 CTO's, Follow-up mean 4.1 years
Success Rate 65.1%, Stents in 81%

	CTO Success N = 567	CTO Failure N = 3.4	p-value
MACE at 30 days (%)	5.5	14.8	< 0.0001
Death or AMI (%)	1.2	2.3	0.2
Death or CABG (%)	1.8	9.9	< 0.0001
5-Year Survival (%)	93.5	88.0	0.02
5-Year MACE-Free Survival (%)	63.7	41.7	0.0001

A. Hoye et al. Eur Heart J. 2005;26:2630

Percutaneous Coronary Intervention for CTO: *Thoraxcenter Experience 1992-2002*

Independent Predictors of Death and MACE After Attempted PCI of CTO

	Hazard Ratio	p-value
Death		
Successful Revascul.	0.58	0.04
Age	1.04	0.002
Diabetes mellitus	2.49	0.005
MVD	4.29	< 0.001
MACE		
Successful Revascul.	0.55	< 0.001
MVD	1.43	0.002
Use of Stent	0.69	0.002

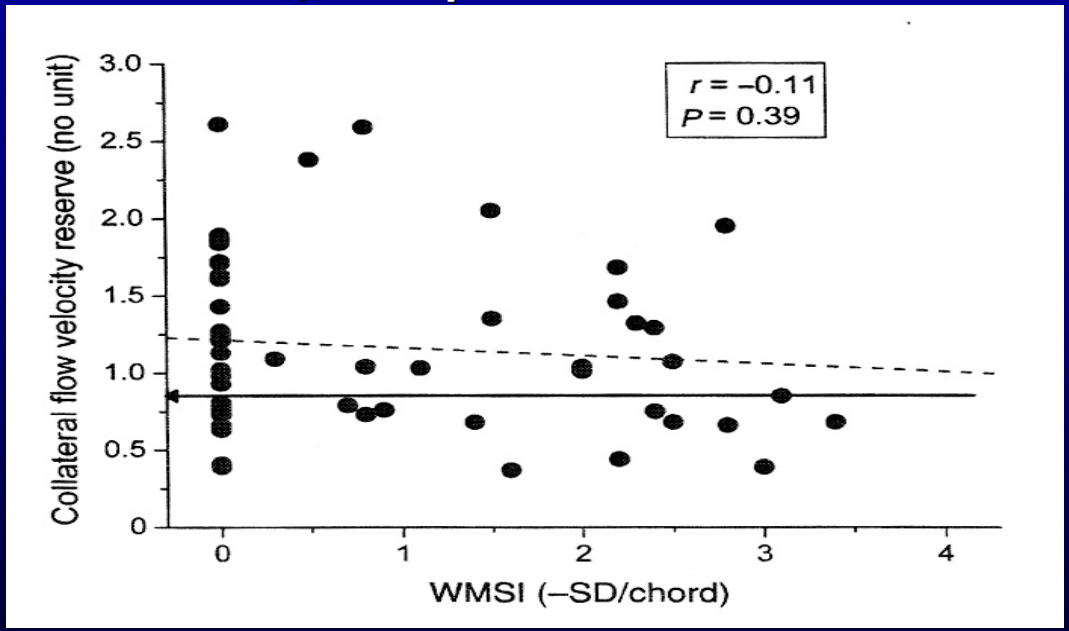
A. Hoye et al. Eur Heart J. 2005;26:2630

IF YOU DON'T TRY IT,

YOU WON'T LIKE IT!

The Functional Reserve of Collaterals Supplying Long-Term CTOs in Pts Without Prior AMI

- 107 pts, Doppler and Pressure measurements before initial balloon inflation
- 62 of 107 pts had IV adenosine (140 µg/kg/min)
- 66 pts had normal LV function, 41 impaired LV



- 78% of collaterals provided a pressure index > 0.3
- Only 7% of patients had CFVR > 2.0
- 36% of pts CFVR dropped below 0.85 with adenosine indicating coronary steal

Gerald Werner et al. Eur Heart J. 2006;27:2406

Comparison of PCI and CABG Among Patients with a CTO and MVD in the BMS Era

CREDO – Kyoto, Jan 2000-Dec 2002
1165 pts with MVD + CTO (PCI 623; CABG 542)
CTO attempted in 71%, success 76%
CTO grafted in 89% of CABG group

	PCI N = 623	CABG N = 542	p-value
Overall 3-yr Survival (%)	91.1	94.1	NS
Cardiac Survival (%)	94.2	95.5	NS
Event-Free Survival (%) (Death, AMI, CVA)	86.2	87.0	NS
Revascularization (%)	50.6	8.6	0.0001

S. Shizula et al. JACC 2007;49:229A

Long-Term Follow-up of Pts with ST-Segment Elevation MI, Treated with SES

559 pts, Mar 2006-Jun 2006. Hartford Hospital, CT

	Death	Recurrent MI	TLR	ST
In-Hospital (%)	2.0	-	-	0.9
9-months	2.0	1.3	1.8	
18-months	0	0	0	
24-months	1.8	0	0	

S. Shizula et al. JACC 2007;49:229A

CTO: Is It Worth the Effort?
Show Me the Data

- PCI for CTO in 1263 pts: Shenyang General Hospital, China
- Univariate Variables related to failure
  - Duration of CTO > 12 months
  - Length of CTO > 15 mm
  - Abrupt stump
  - Bridging collaterals
  - Moderate to severe Ca++
  - Ostial or distal location

Han et al. China Med J. 2006;119(14):1165

CTO: Is It Worth the Effort?
Show Me the Data

- PCI for CTO in 1263 pts: Shenyang General Hospital, China
- 1625 CTO lesions, mean occlusion time 48.9 mths

Patient Success	1147/1263	90.8%
Lesion Success	1445/1625	88.9%
Target Vessel:		
LMCA	0.4%	
LAD	35.7%	
LCX	19.1%	
RCA	34.0%	
Other major brs	10.8%	
Mean Lesion Length (mm)	21.7 ± 12.2	
Bridging Collaterals	19.3%	
Retrograde collaterals	80.7%	
Antegrade Approach	98%	

Han et al. China Med J. 2006;119(14):1165


Dumb bunny.
ANIMAL FARM
Smart ass.
Larson

Impact of Age on Procedural and 1-Yr Outcome in PTCA: *Report from NHLBI Dynamic Registry*

	Age			
	< 65 yrs N = 2537	65-79 yrs N = 1776	≥ 80 yrs N = 307	p-value
Total Occlusion				
RCA (%)	18.2	21.3	22.8	<0.05
LAD (%)	13.8	19.1	21.5	<0.001
LCX (%)	11.0	13.2	12.7	<0.01
Any CTO (%)	36.5	39.1	40.7	<0.01
Calcified (%)	22.0	31.7	40.8	<0.001
Attempted PCI (%)	15.5	10.5	10.4	<0.001

Howard A. Cohen et al. Am H J 2003;146:513

Radiation Exposure to Pts Skin During PCI for Various Lesions Including CTO

	Single Lesion N = 487	Multiple Lesions SVD N = 22	MVD N = 14	CTO N = 13	Overall N = 97
Total Fluoro Time (min)	14.6 ± 8.0	20.8±10.4	25.1±8.0	42.6±17	21.3±13.6
Total Number of Cine Frames	1851 ± 594	2512±1137	3050±804	4763±558	2564±1518
Max Entrance Skin Dose (Gy)	1.4 ± 0.9	1.8±1.0	2.3±0.7	4.5±2.8	2.0±1.6

CTO vs. Single Lesion $p < 0.001$
CTO vs. Multiple Lesions $p < 0.05$
Max ESD exceeded 5 Gy in 46% of CTO Procedures

S. Suzuki et al. Circ 2006;70:44

Does Revascularization Using the New Wiring Technique of CTO Contribute to Improve the Long Term Prognosis?

CTO Patients with average F/U of 770 ± 560 days

	Successful CTO & Long-Term Patency N = 577		Long-Term Occlusion N = 179		p-value
Age (yrs)	66 ± 11		67 ± 10		
Long-Term Survival	96%		69%		0.01
Pts w/o Viability	**89%**		**60%**		**0.01**

K. Hirano et al. JACC 2005;45:62A

Long-Term Survival is Compromised by the Presence of a Chronic Coronary Total Occlusion

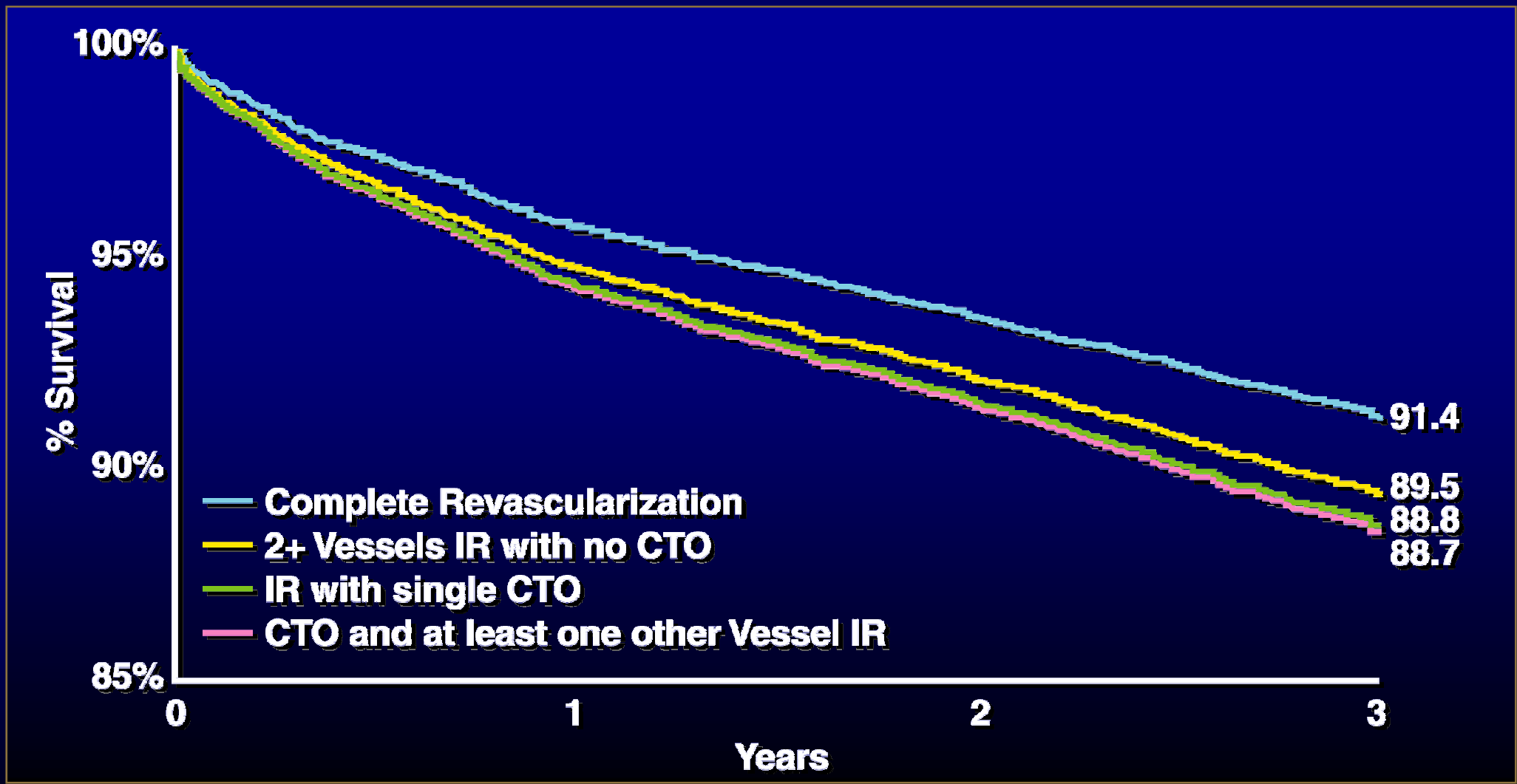
Impact of Completeness of PCI Revascularization on Long-Term Outcomes in the Stent Era

21,945 NY State PC IRS. 01/97-12/00.
CR attempt all lesions ≥ 50% in major epicardial vessels

Hazard Ratios (IR/CR) for Mortality	No. Pts	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
CR	6817		
One IR vessel, no CTO	8518	1.20 (1.04-1.38)	1.00 (0.87-1.15)
≥ 2 IR Vessels, 1 CTO	1321	2.77 (2.29-3.35)	1.36 (1.12-1.66)
One IR is a CTO	3232	1.81 (1.53-2.13)	1.35 (1.14-1.59)
≥ 2 IR vessels, no CTO	2057	1.88 (1.57-2.27)	1.25 (1.03-1.50)

E.L. Hannan et al. Circ 2006;113:2406-12

Impact of Completeness of PCI Revascularization on Long-Term Outcomes in the Stent Era



E.L. Hannan et al. Circ 2006;113:2406-12

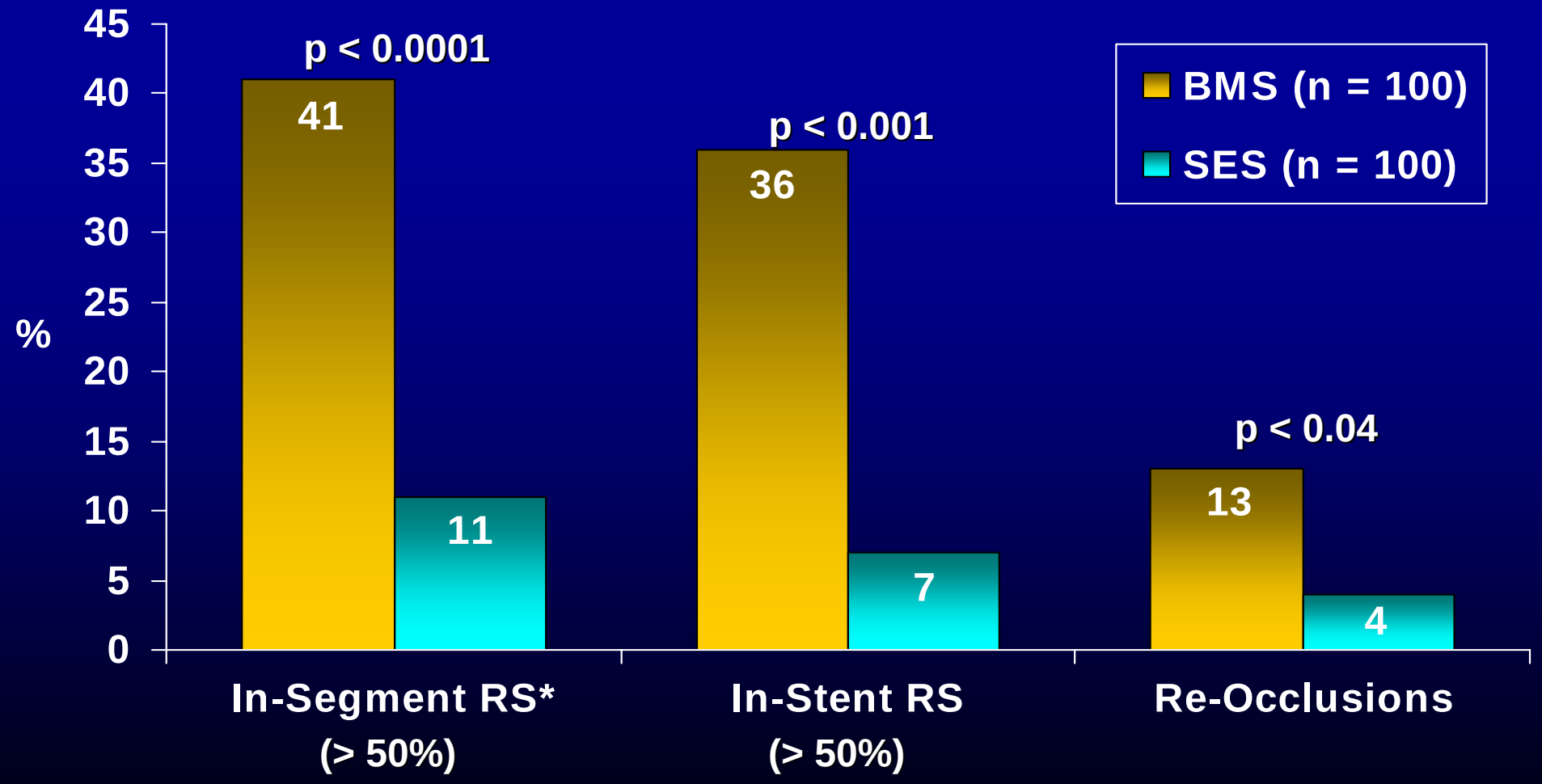
Prognostic Impact of a CTO in a Non-Infarct Vessel in Pts with AMI and MVD

630 patients within 12 hours of STEMI

Freedom From (%)	SVD N=345	MVD N=285	p-value	MVD No CTO N = 201	MVD + CTO N = 84	p-value
Cardiac Death	91	84	0.002	88	77	0.02
Death	88	82	0.003	84	77	0.09
Reinfarction	95	94	0.380	94	93	0.39
TVR	92	88	0.028	90	84	0.09
Total Events	81	71	<0.001	75	63	0.006

R. Moreno et al. J Invas Cardiology

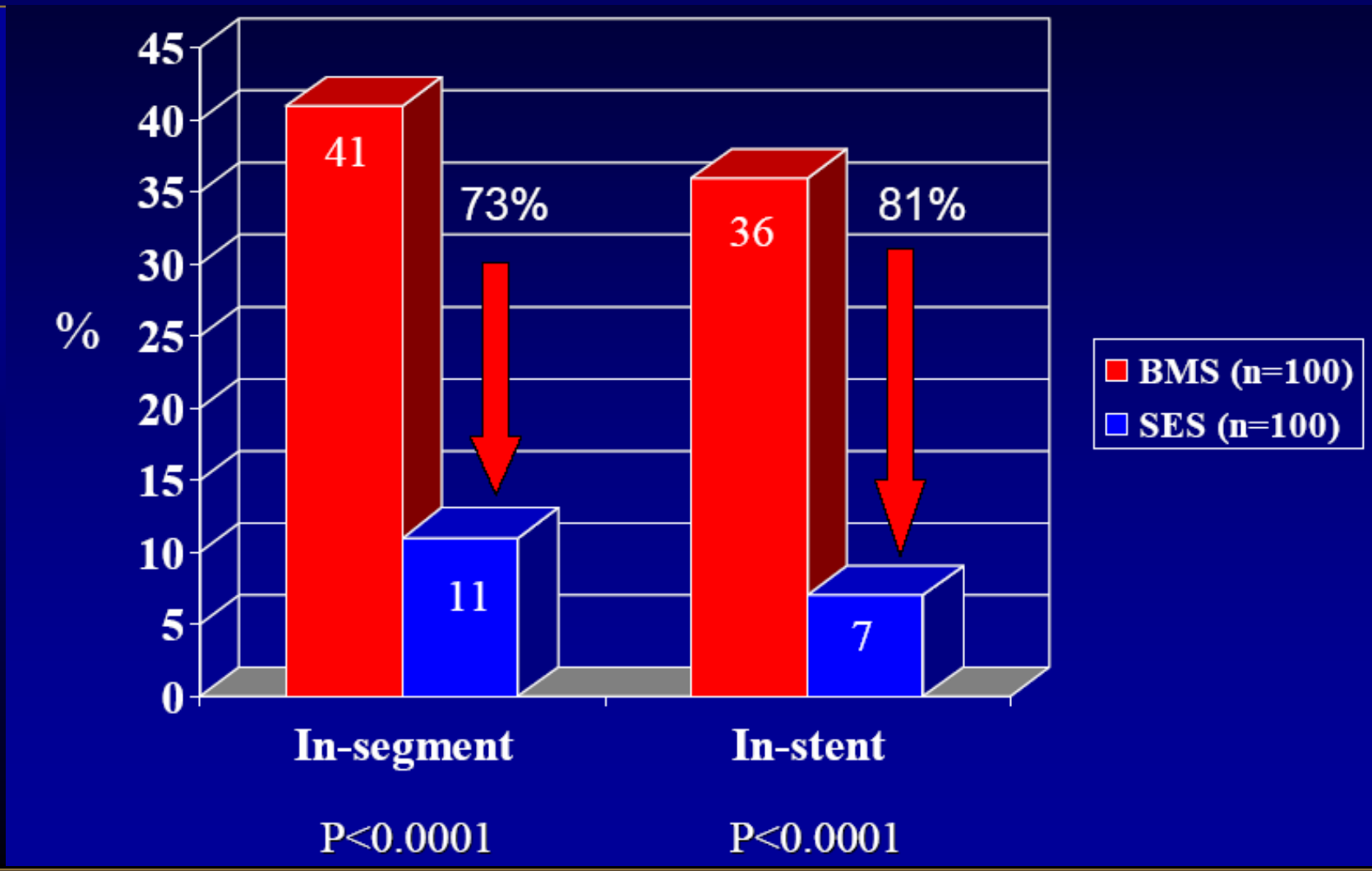
PRISON II: *6-Month Angiographic F/U Binary Restenosis (> 50%)*



*Note: *Stented segment including proximal & distal 5 mm*

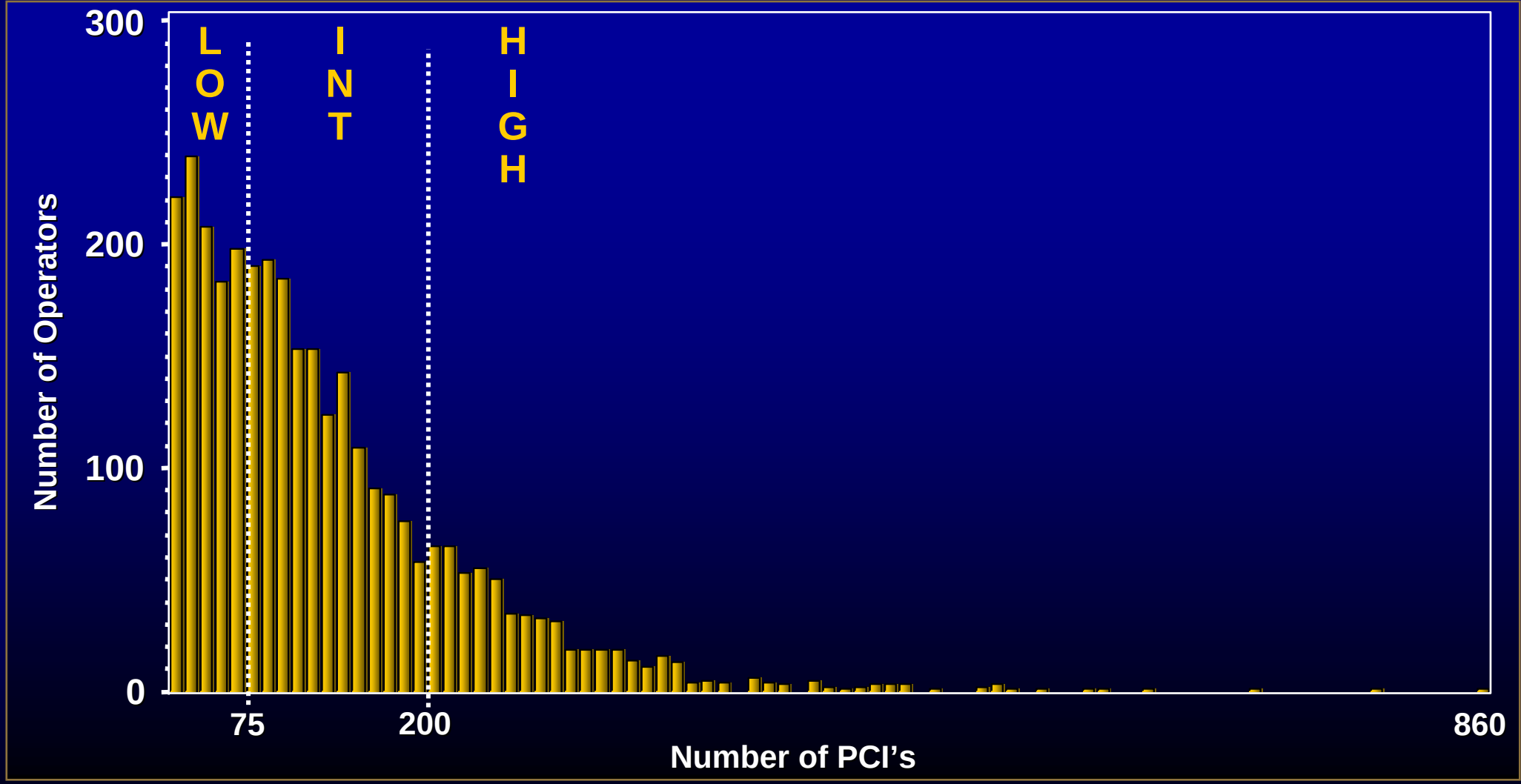
MJ Suttorp & PRISON II Investigators. TCT 2005

PRISON II: *Angiographic Binary Restenosis Relative Risk Reduction*



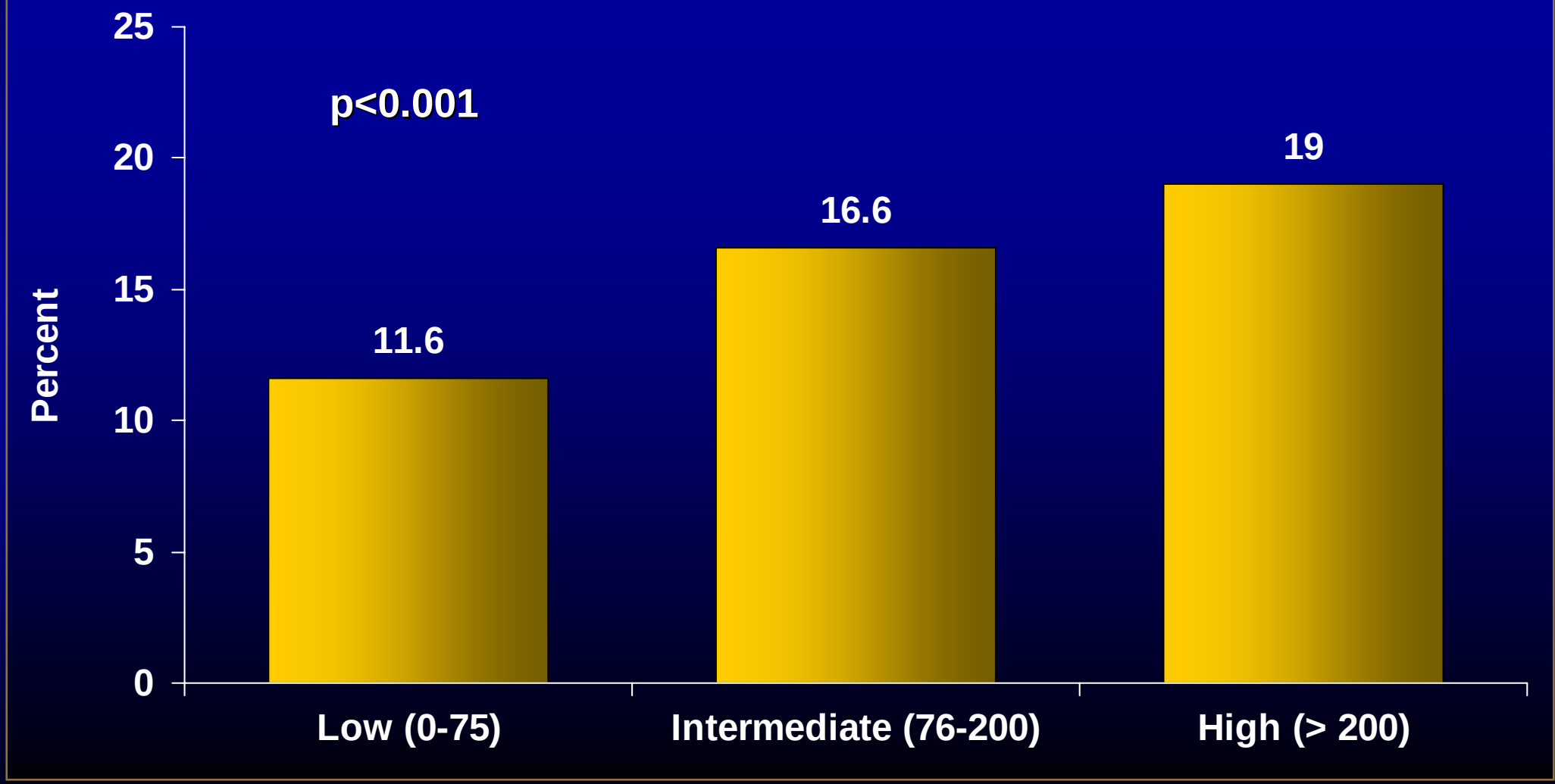
MJ Suttorp & PRISON II Investigators. TCT 2005

Number of Operators by Annual PCI Volume



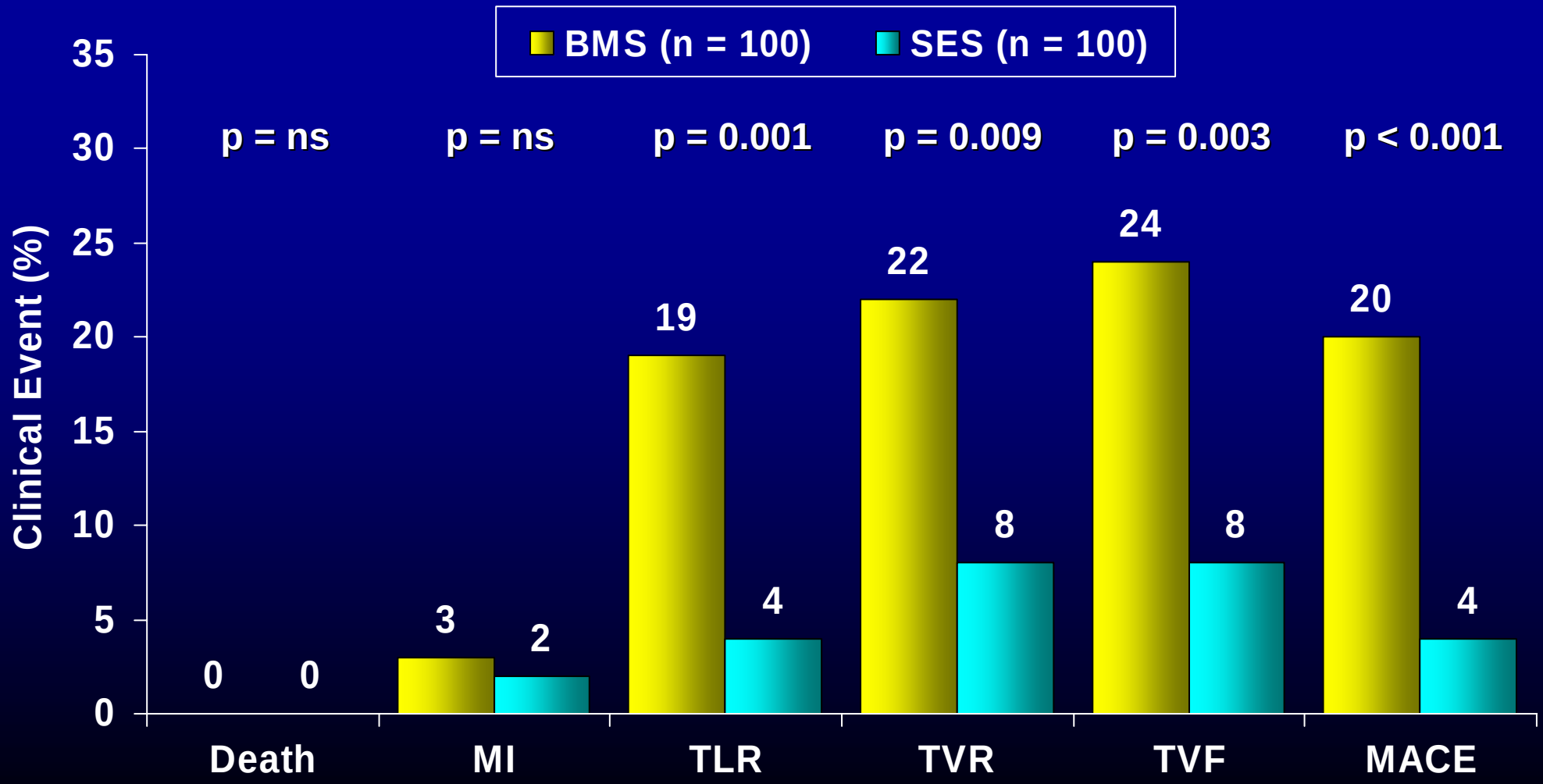
Courtesy of J. Aaron Grantham, MD

Overall Attempt Rate



Courtesy of J. Aaron Grantham, MD

PRISON II:
6-Month Clinical F/U



MJ Suttorp & PRISON II Investigators. TCT 2005

Comparison Between Sirolimus and Paclitaxel Eluting Stents for the Treatment of CTO

- 136 pts, March 2003-Dec 2004
- 6 month angiographic and IVUS evaluation

	SES n=107	PES n=29	p-value
Procedural Success	98.1%	100%	NS
Post Procedural MLD (mm)	2.9 ± 0.3	2.7 ± 0.4	0.007
6-month Restenosis	9.4%	28.6%	0.02
Late Loss (mm)	0.4 ± 0.8	0.8 ± 0.8	0.02
12-month MACE-free Survival	95.8%	85.8%	0.04
TLR	3.7%	6.9%	NS

Jang, SJ Park et al. J Invas Cardiology 2006;18:205

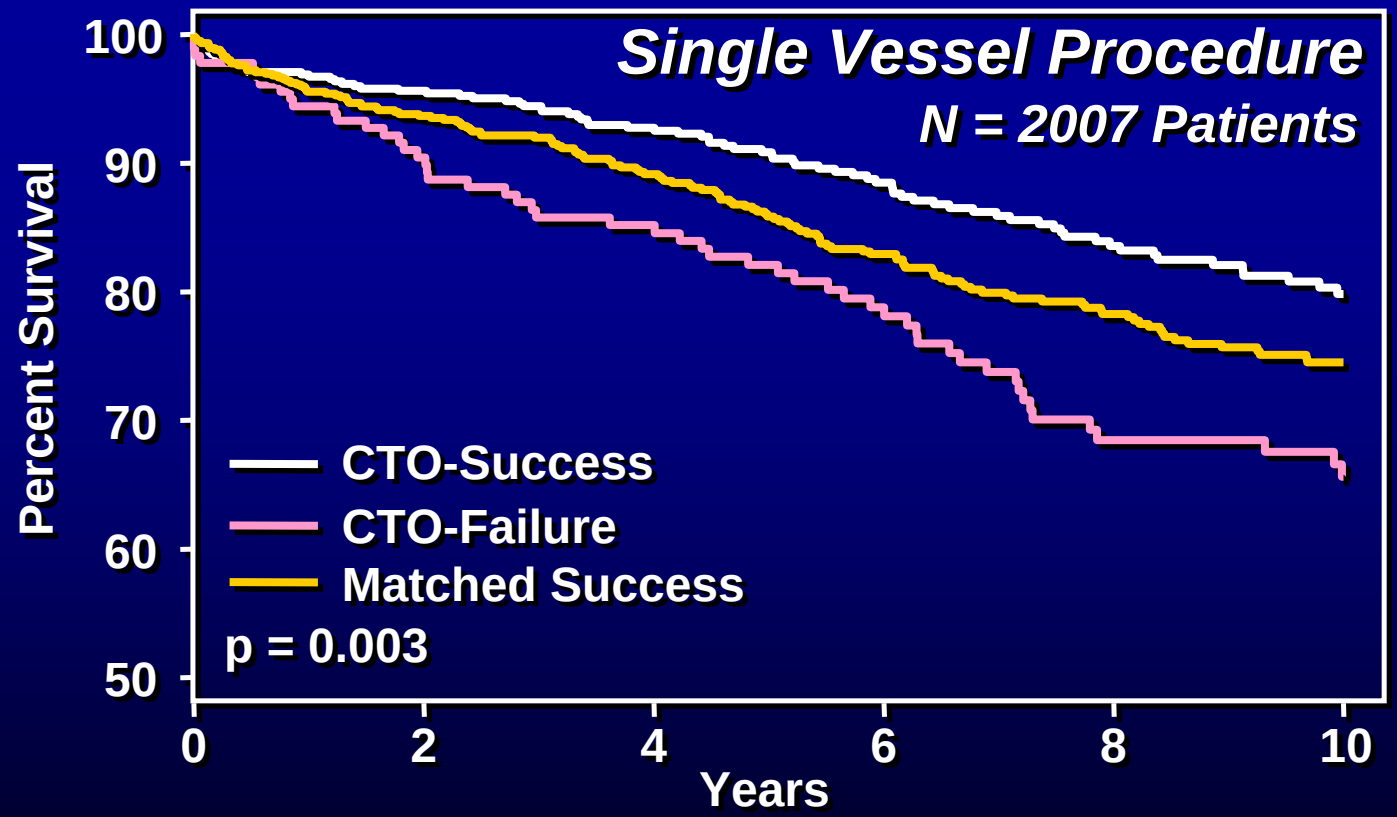
Predictors of Improvement in LV Function After PCI of Occluded Coronary Arteries (TOSCA)

244 pts, baseline & 6-month F/U angios, target vessel patency

	Baseline LVEF	Change	p-value
All patients (%)	59.4 ± 11.9	1.6 ± 7.8	< 0.005
Occlusion Duration			
≤ 6 weeks	56.0 ± 11.6	3.0 ± 8.7	0.014
> 6 weeks	62.0 ± 11.5	0.5 ± 7.0	
Baseline LVEF (%)			
≤ 60 (%)	45.6 ± 8.7	3.8 ± 8.4	< 0.001
> 60 (%)	68.3 ± 6.0	-0.4 ± 6.7	
F/U Vessel Patency			
TIMI 0-2	59.4 ± 11.4	-0.6 ± 6.1	0.06
TIMI 3	59.4 ± 12.0	2.0 ± 8.1	

V. Dzavik et al. AHJ 2001;42:301

Procedural Outcomes and Long-Term Survival for PCI of Chronic Total Occlusion



CTO-Success %	95.6	92.7	88.5	83.6	79.8
CTO-Failure %	90.4	85.2	78.8	68.5	65.6
Matched Success %	93.7	89.1	82.9	78.3	74.5

Suero et al. JACC 2001;38:409

Coronary Intervention for Persistent Occlusion After Myocardial Infarction (OAT Trial)

Exclusion Criteria

- Rest or low-threshold angina after MI
- Severe inducible ischemia on low level exercise or pharmacological stress testing
- LMCA $\geq$ 50% stenosis or triple vessel disease
- S creatinine > 3.0 mg/dL
- Infarct artery < 2.5 mm, > 90° angulation

Hochman et al. NEJM 2006;355

Coronary Intervention for Persistent Occlusion After Myocardial Infarction (OAT Trial)

Critical Review

- Extraordinary amount of time to recruit
- Study underpowered for endpoints
- Represents a very small % of post-MI pts
- Most had no viability in distribution of IRA
- Only 8% had DES
- No statistically significant difference in primary or secondary endpoints
- 89% of stented pts had patent artery at 1 year
- Long term F/U incomplete – only 44% to 3 years
- Data meaningless in treating most post-MI pts