An Evidence-based Rationale for Successful CTO Recanalization

Overview of Indications, Technique and Clinical Outcomes for CTO Revascularization – a US-based Perspective

David E. Kandzari, MD, FACC, FSCAI
John B. Simpson Asst Professor of Interventional Cardiology and Genomic Sciences
Duke Clinical Research Institute
Duke University Medical Center
Durham, North Carolina
david.kandzari@duke.edu

DUKE UNIVERSITY MEDICAL CENTER

CRI Duke Clinical Research Institute

An Evidence-based Rationale for Successful CTO Recanalization

Relevant Disclosure

Research/grant support:	Boston Scientific Corporation, Cordis Corporation, Medtronic Vascular
Advisory board/consultant:	Boston Scientific Corporation, Medtronic Vascular

DUKE UNIVERSITY MEDICAL CENTER

CRI Duke Clinical Research Institute

CTOs in Perspective

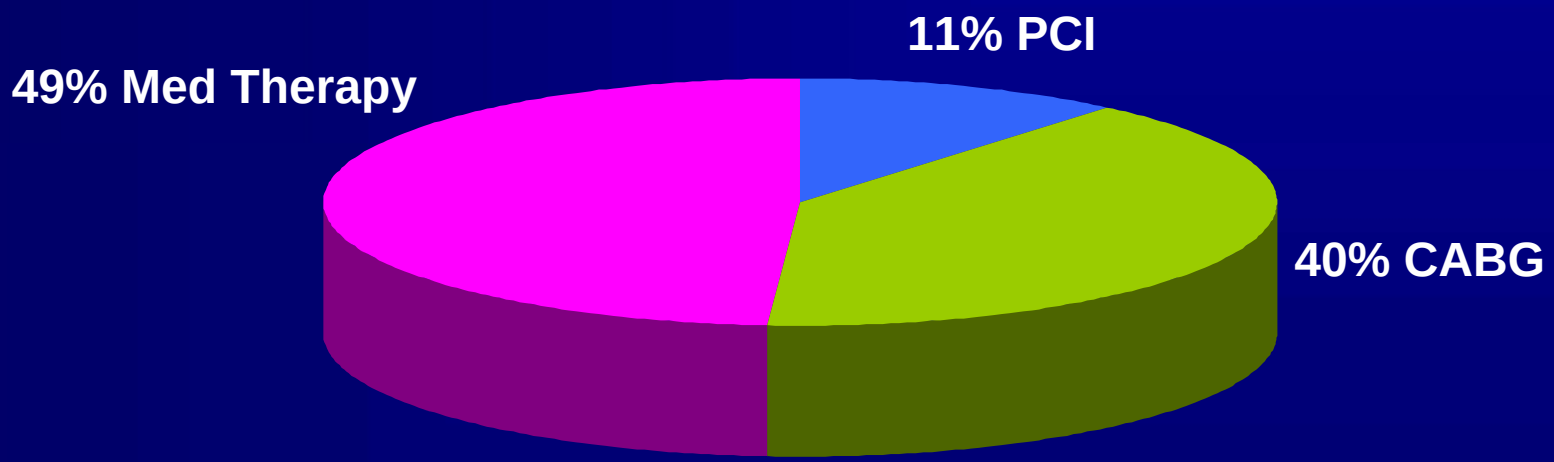
Despite novel technologies/DES, frequency of attempted CTOs has not changed over the past decade

- Technical/procedural challenges
- Uncertainty regarding which patients may benefit balanced by
- Concern for complications in patients who may not derive clinical benefit
- Misperceptions regarding viability, collateral flow

Srinivas et al. *Circulation* 2002
Christofferson et al. *Am J Cardiol* 2005

CTOs in a US Perspective

CTO present in 52% of patients with significant CAD (≥70% stenosis)
1990-2000, N=3,087



Christofferson et al. *Am J Cardiol* 2005

CTO Representation in DES Trials

Trial	N	% CTO
ARRIVE 1	2,586	1.8
ARRIVE 2	4,933	2.0
DIABETES	221	13.1
e-Cypher	14,316	2.9
WISDOM	903	7.0

BMS in CTOs: Procedural and Angiographic Outcomes

		Reocclusion			Restenosis			Target Vessel Revasc		
Trial	**N**	**PTCA**	**Stent**	***P***	**PTCA**	**Stent**	***P***	**PTCA**	**Stent**	***P***
Stenting in Chronic Coronary Occlusion (SICCO)	114	26%	16%	0.058	74%	32%	<0.01	42%	22%	0.025
Gruppo Italiano di Studi sulla Stent nelle Occlusioni coronariche (GISSOC)	110	34%	8%	0.004	68%	32%	0.0008	22%	5%	0.04
Mori et al. 1996	96	11%	7%	0.04	57%	28%	0.005	49%	28%	<0.05
Stent vs Percutaneous Angioplasty in Chronic Total Occlusion (SPACTO)	85	24%	3%	0.01	64%	32%	0.01	40%	25%	NS
Total Occlusion Study of Canada (TOSCA)	410	20%	11%	0.02	70%	55%	<0.01	15%	8%	0.03
Primary Stenting of Occluded Native Coronary Arteries (PRISON)	200	7.3%	8.2%	NS	33.3	21.9	0.14	10%	2.5%	0.002
Stents in Total Occlusion for Restenosis Prevention (STOP)	96	17%	8%	NS	71%	42%	0.032	42%	25%	NS

DES in CTO Revascularization

SES and PES Registries

Trial	N	ABR	TVR	MACE	TVR	MACE
		6 months			1 year	
SICTO, EuroPCR 2004	25	0	8.0	0		
E-Cypher, TCT2004	360		1.4*	3.1		
RESEARCH, JACC 2004	56	9.1	3.6	3.6		
Werner, JACC 2004	48	8.3			6.3	12.5
Nakamura, AJC 2005	60	2.0	3.0		3.0	
TRUE Registry, TCT2005	183	17.0†	16.9†	17.1†		
Ge, EHJ 2005	122	9.2	9.0	16.4		

Data expressed as percentages. *Denotes TLR, †7-month outcomes

Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

DES in CTO Revascularization

SES and PES Comparative Studies

Trial	N		ABR (%)		TVR (%)		MACE (%)	
	SES	PES	SES	PES	SES	PES	SES	PES
RESEARCH/ T-SEARCH, ACC 2004*	76	57			2.6	3.6		
Asian Registry, TCT2005*	396	526	4.0	6.7	3.6	6.7	3.6	6.7
Suarez de Lezo, AHA 2005†,‡	60	58	7.4	19.0	3.3	7.0	3.0	7.0

P=NS for all comparisons.

*1-year outcomes, †8 month outcomes, ‡Angiographic f/u in only 48% of patients

PRISON II

200 CTO* Patients

- 2 centers
- Single Blinded Randomization
- Successful recanalization

Bx Velocity Stent	Cypher SES
N=100	N=100

Primary Endpoint: In-segment angiographic binary restenosis at 6 months

Antiplatelet Therapy: ASA/ Clopidogrel 6 months

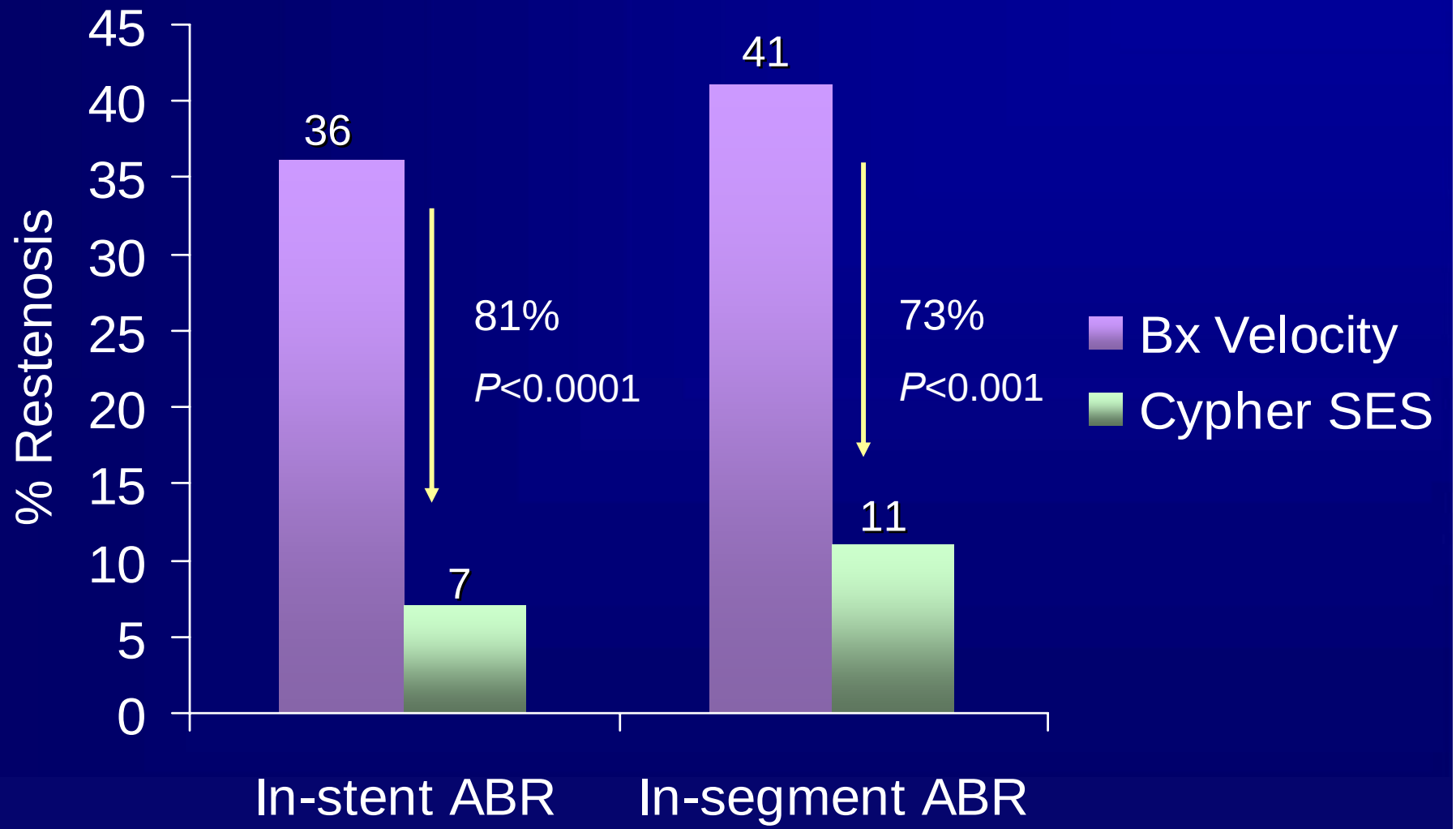
Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

Suttorp et al. TCT2005

PRISON II

	Bx Velocity N=100	Cypher SES N=100
Diabetes mellitus (%)	16	10
LVEF>50% (%)	82	76
CTO> 3 mos (%)	44	46
TIMI 0 (%)	64	69
Lesion length (mm)	16.3	16.0
Stent length (mm)	28.9	31.9
Stent/patient	1.4	1.4

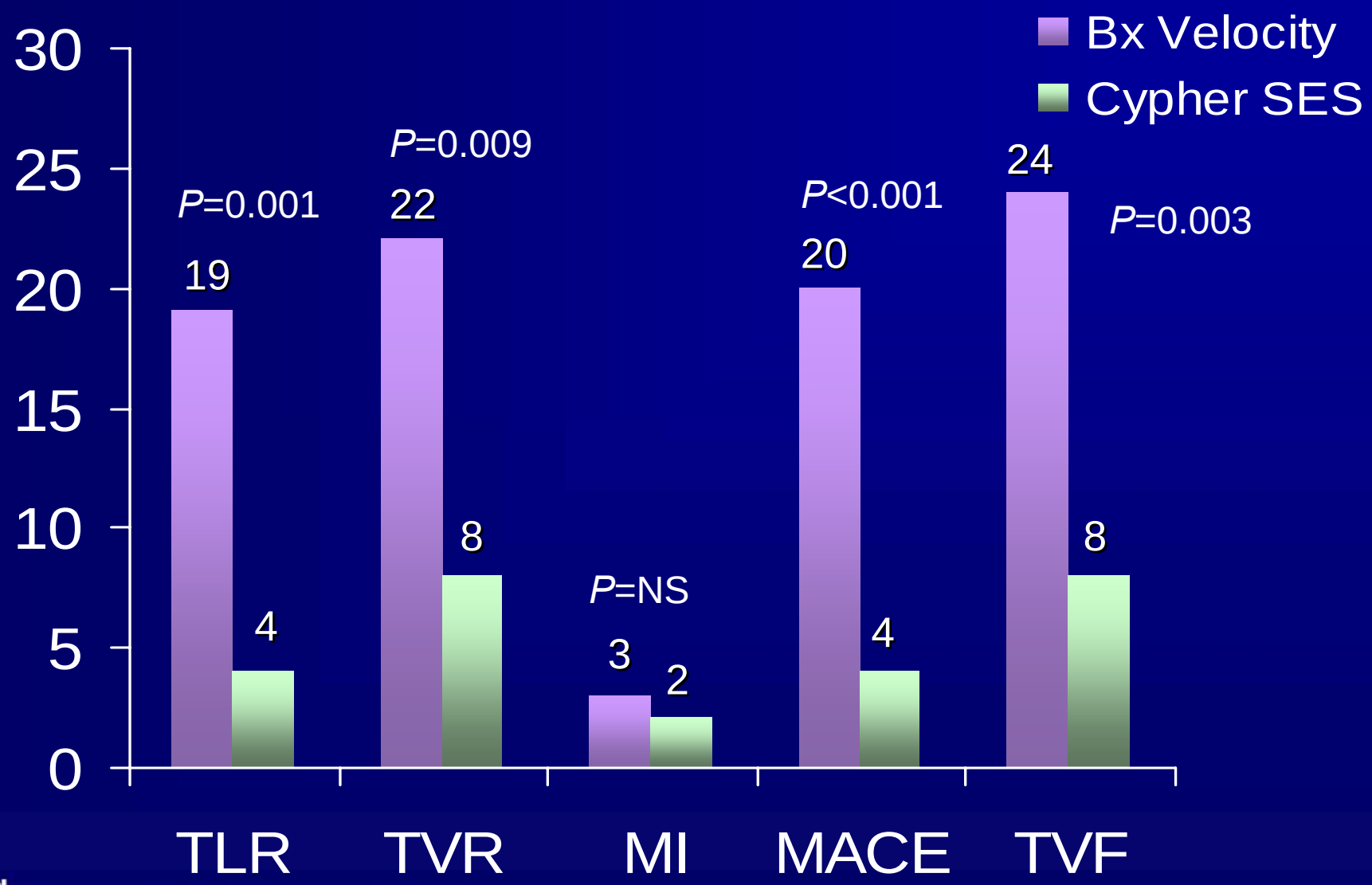
PRISON II



Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

Kandzari.AsiaPacific

PRISON II



Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

Kandzari.AsiaPacific

Procedural and Angiographic Outcomes

DES in CTO Revascularization

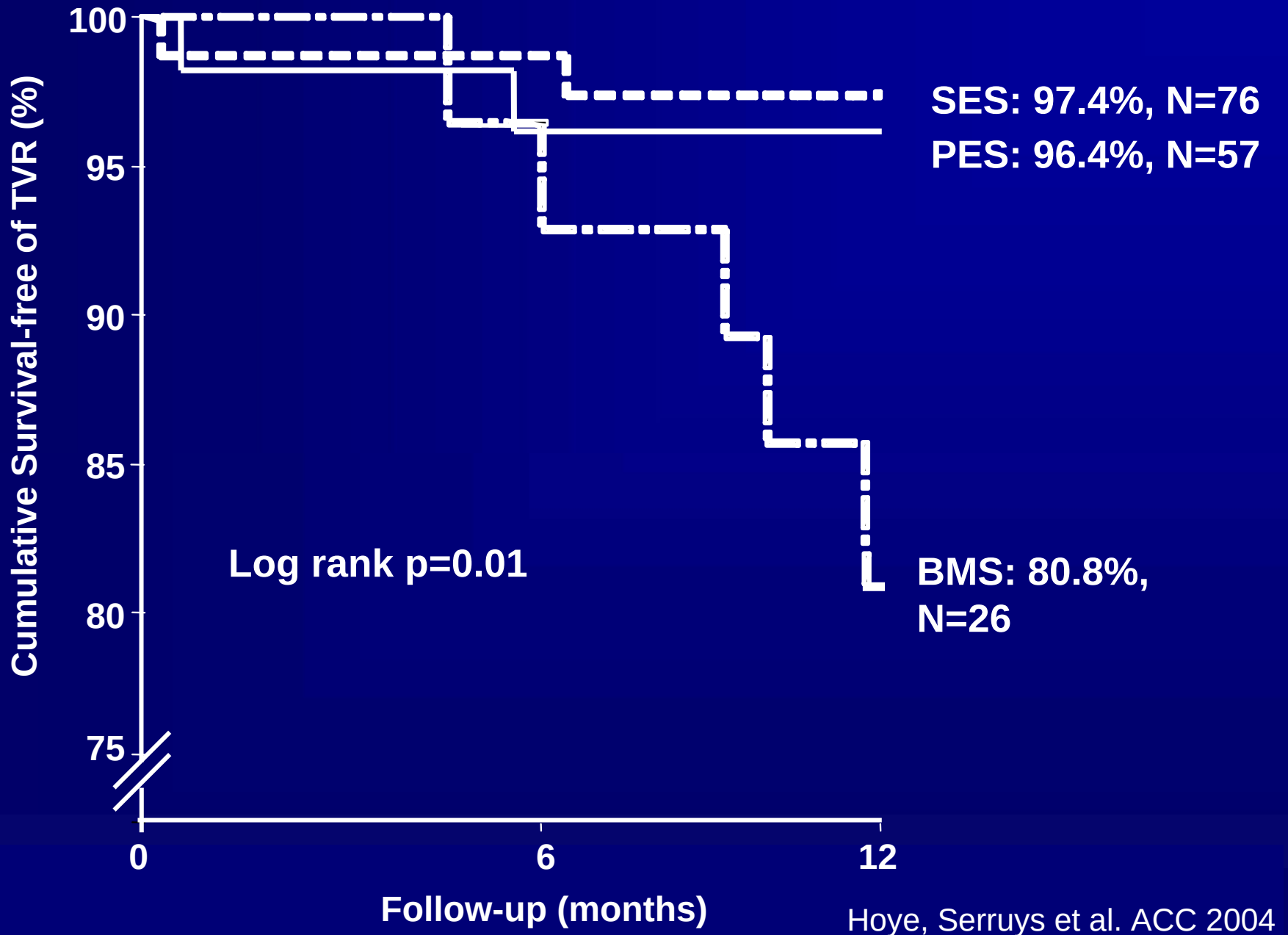
RESEARCH and T-SEARCH Registries

	Bare Metal	Sirolimus	Paclitaxel
	N=26	N=76	N=58
Occlusion length	13.0 ± 7.2	10.3 ± 5.9	11.2 ± 6.6
Reference diameter*	2.34 ± 0.43	2.35 ± 0.51	2.60 ± 0.49
Number of stents*	1.8 ± 0.8	2.2 ± 1.2	2.6 ± 1.3
Total stent length*	41.5 ± 23.3	48.8 ± 27.4	58.0 ± 32.8

Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

*P<0.05; Hoye, Serruys et al. ACC 2004

RESEARCH and T-SEARCH Registries



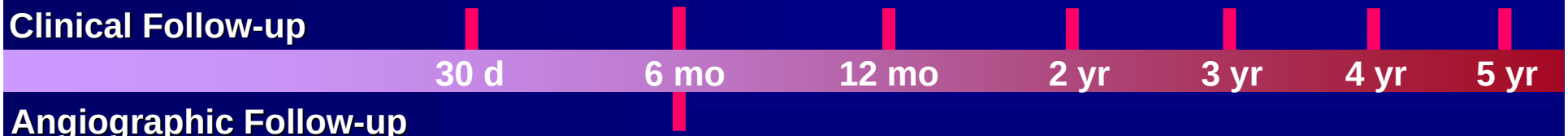
Hoye, Serruys et al. ACC 2004

Approaches to ChRonic Occlusions With Sirolimus Stents

ACROSS-Cypher™/Total Occlusion Study of Coronary Arteries (TOSCA 4)

ACROSS CYPHER®

250 patients with *de novo* total coronary occlusions
17 sites within North America
Single-arm trial design



Primary Endpoints: Angiographic restenosis at 6 months compared with TOSCA-1

Secondary Endpoints: Angiographic in-segment restenosis at 6 months; TVF, MACE and TLR at 6 and 12 months; late loss at 6 months

Stent Sizes: Cordis Cypher™ 2.5-3.5 mm x 8-33 mm

Pre- and post-dilatation specified with balloon length < stent length

Antiplatelet therapy for ≥ 3 months

Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

Kandzari.AsiaPacific

Innovation in CTO Revascularization

An Evolution in Technology and Strategy

Guidewire	**Tapered tip: CROSS IT, Confianza, Miracle** **Steerable guidewire (Steer-It)/ catheter (Venture)** **Optical coherence reflectometry (ILT)** **Penetration (Tornus)** **Vibrational angioplasty** **Magnetic Navigation (Stereotaxis)**
Ablative	**Excimer laser (Spectranetics)** **Ultrasound (Flowcardia)** **Radiofrequency ablation (ILT)**
Mechanical	**Blunt microdissection (Lumend)** **Fibrinolysis** **Demineralization, collagenase**
Re-Entry	**Percutaneous bypass** **Subintimal angioplasty**
Post-Crossing	**Drug eluting stents** **Distal protection**

ACROSS Pilot

Predictors of Procedural Outcome, n=103

Characteristic	Failed	Successful	*P* value
Multiple wires*			
>1 wire	36% vs.	5%	<0.001
>2 wires	53% vs.	12%	<0.001
Fluoro time, min	28 vs.	21	0.04
TIMI 0	24% vs.	7%	0.054
Support catheter	29% vs.	14%	0.07
Collaterals	23% vs.	10%	0.12
Female	29% vs.	16%	0.17
Length >15mm	19% vs.	10%	0.24
Ref <3mm	29% vs.	17%	0.23
Multivessel dz	23% vs.	15%	0.30

*p<0.05 in multivariable analysis

Kandzari, Menown et al. TCT2003

Theoretical Rationale for CTO Revascularization

- Increase long-term survival
- Improve left ventricular function
- Electrical stability of myocardium and reduced predisposition to arrhythmic events
- Increased tolerance of future coronary occlusion events

Long-term Survival with Successful CTO Revascularization

Support for the Late Open Artery Hypothesis

Trial	Success (N)	Failure (N)	Follow-up Duration (years)	Mortality (%)		
				Success	Failure	*P* value
British Columbia Cardiac Registry[1]	1118	340	6	10.0	19.0	<0.001
Suero et al.[2]	1491	514	10	26.0	35.0	0.001
TOAST-GISE[3]	286	83	1	1.1	3.6	0.13
Aziz et al.[4]	377	166	2.4	2.5	7.3	0.049
Hoye et al.[5]	568	306	5	6.5	12.0	0.02

[1]Ramanathan. TCT2003; [2]Suero. JACC 2001; [3]Olivari. JACC 2003; [4]Aziz. TCT2005; [5]Hoye Eur Heart J 2005

Long-term Outcome after Intended Recanalization of Non-acute Coronary Occlusions

Multivariate Mortality Model

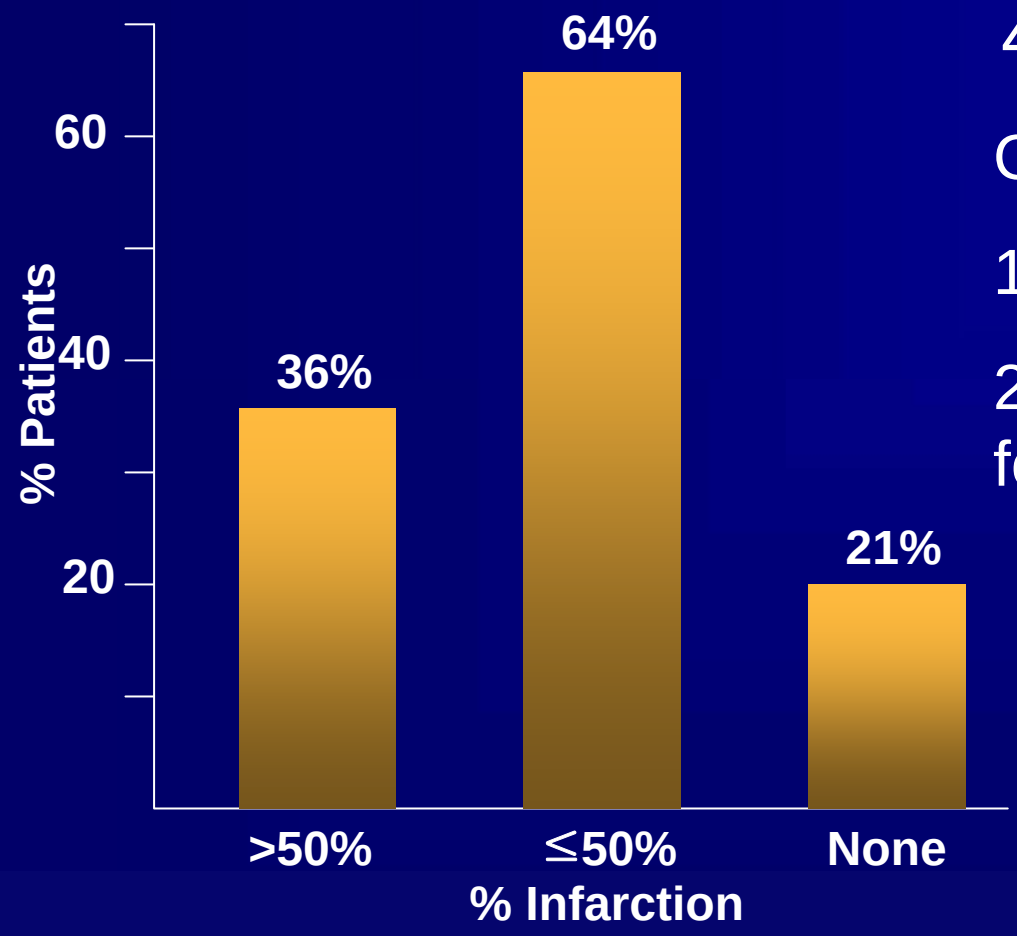
	Hazard Ratio	95% Confidence	*P* value
Failure	2.27	1.56 – 3.30	<0.0001
Age (per decade)	1.33	1.12 – 1.58	0.001
EF <50	2.33	1.58 – 3.43	<0.0001
Multivessel CAD	1.62	1.09 – 2.40	0.02
Prior CHF	1.73	1.10 – 2.76	0.02
ESRD	2.77	1.36 – 5.66	0.005
CVD	1.92	1.04 – 3.55	0.04
COPD	1.64	1.01 – 2.67	0.05
Diabetes	1.50	0.99 – 2.27	0.055

Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

Ramanathan and Buller *TCT2003*

Myocardial Viability, Collateral Flow, and Regional Wall Motion

Cardiac MR Imaging



44 pts, 58 CTO segments

Collateral flow *did not* predict:

1. Myocardial viability

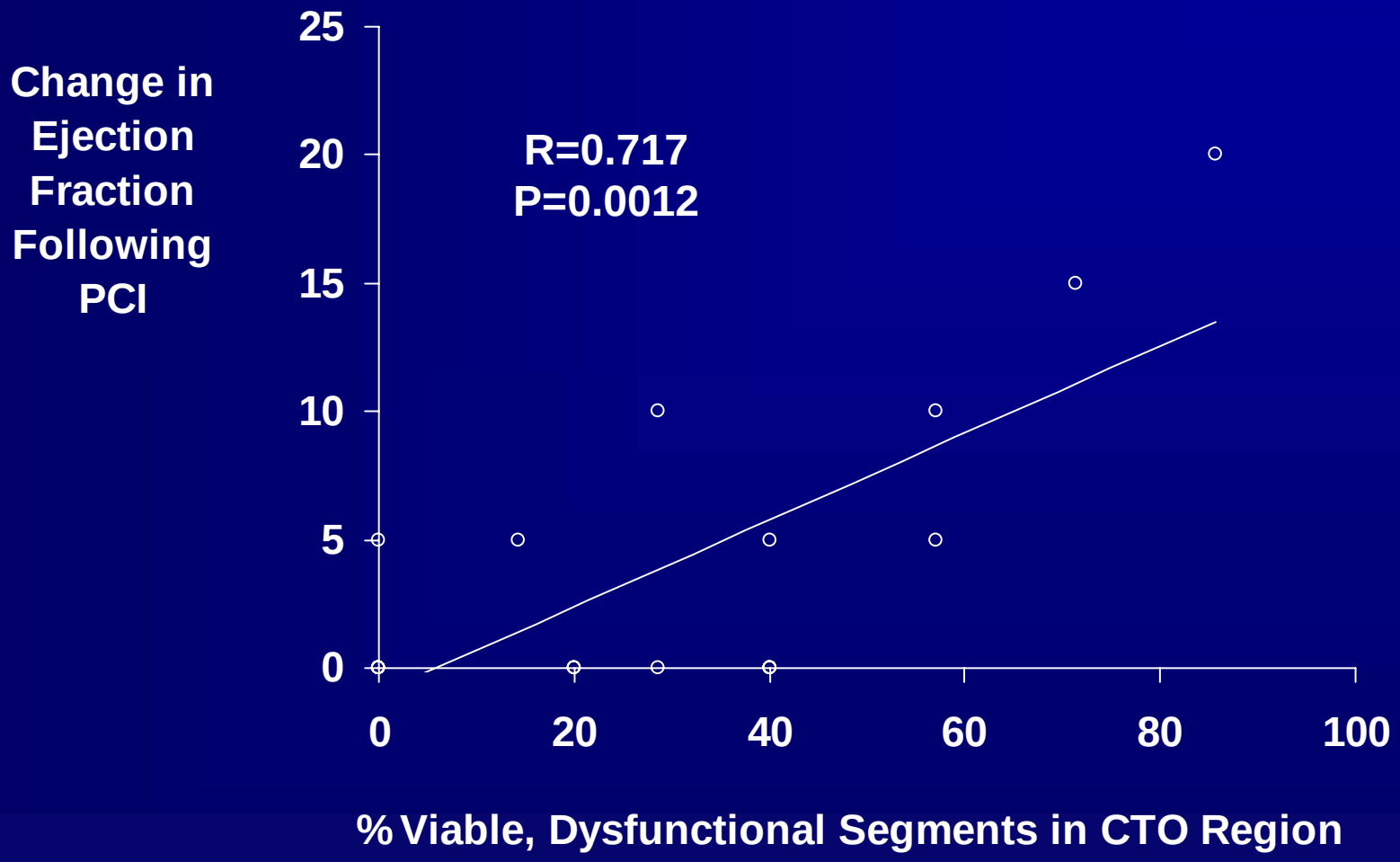
2. Regional improvement following revascularization

Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

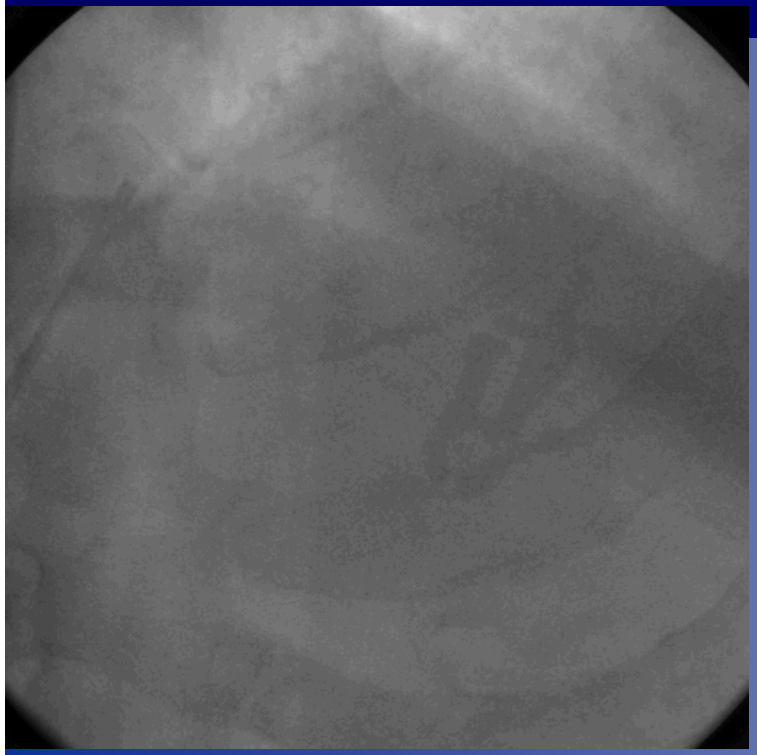
Kim, Shah, Kandzari et al AHA 2003

Cardiac MR Imaging in CTO Revascularization

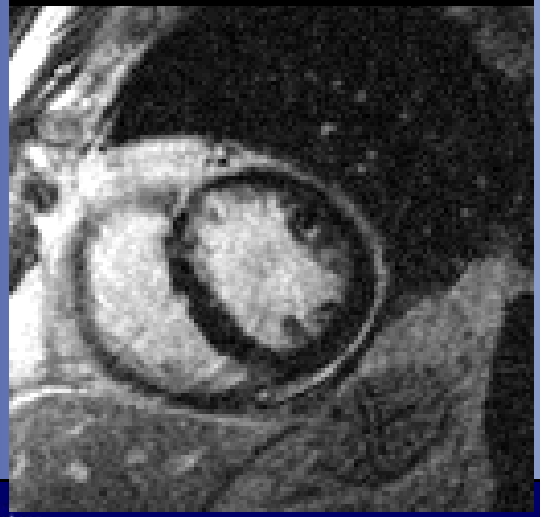
Influence of Revascularization on Wall Motion and LVEF

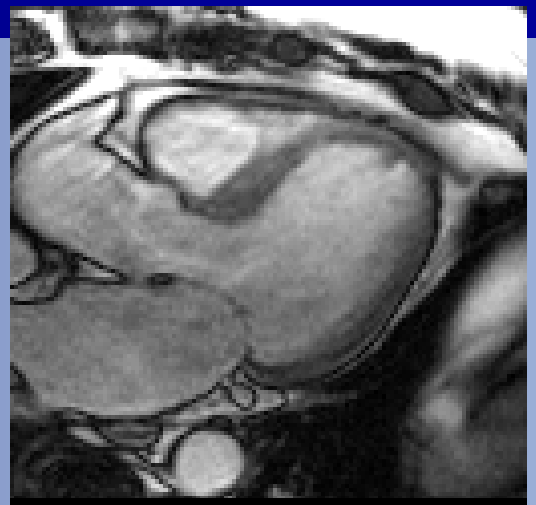


MR Imaging of Myocardial Viability and Performance in CTO Revascularization



<50% infarction

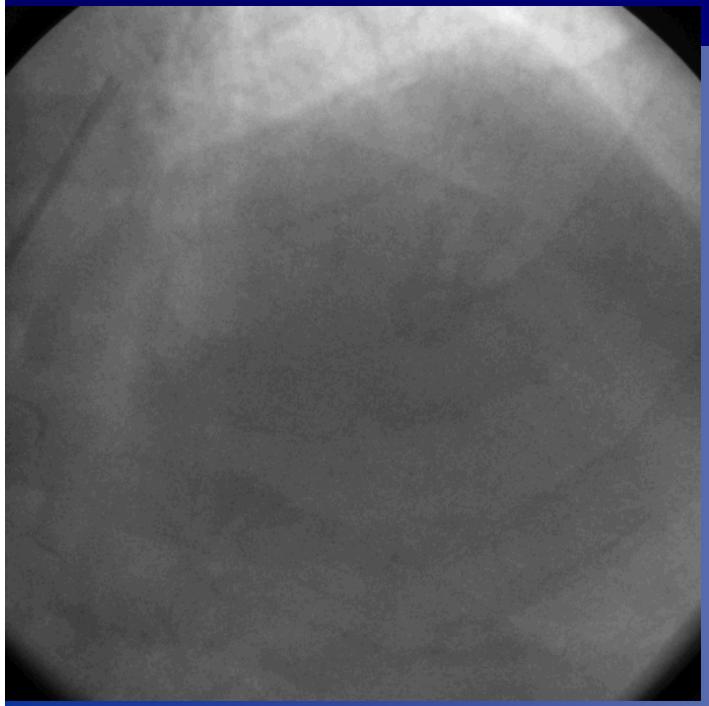




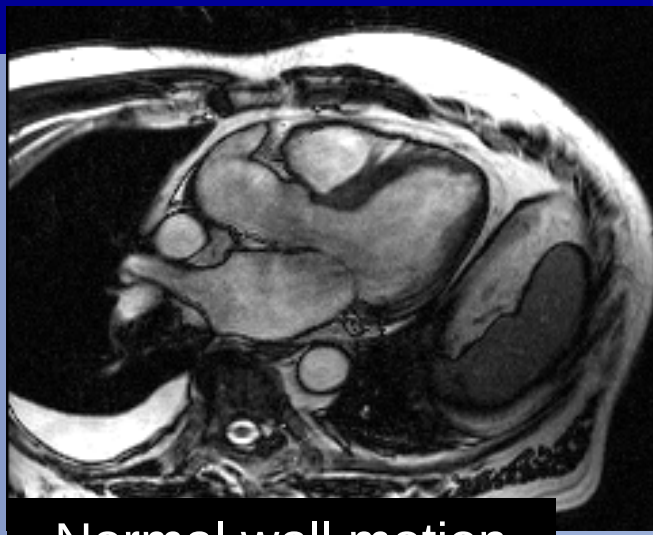
LV dysfunction

CTO Revascularization: Myocardial Performance

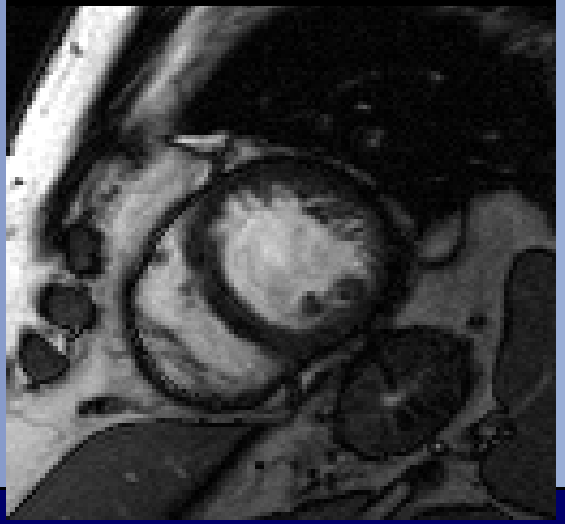
MR Imaging to Identify Revascularization Candidates



1 year post PCI

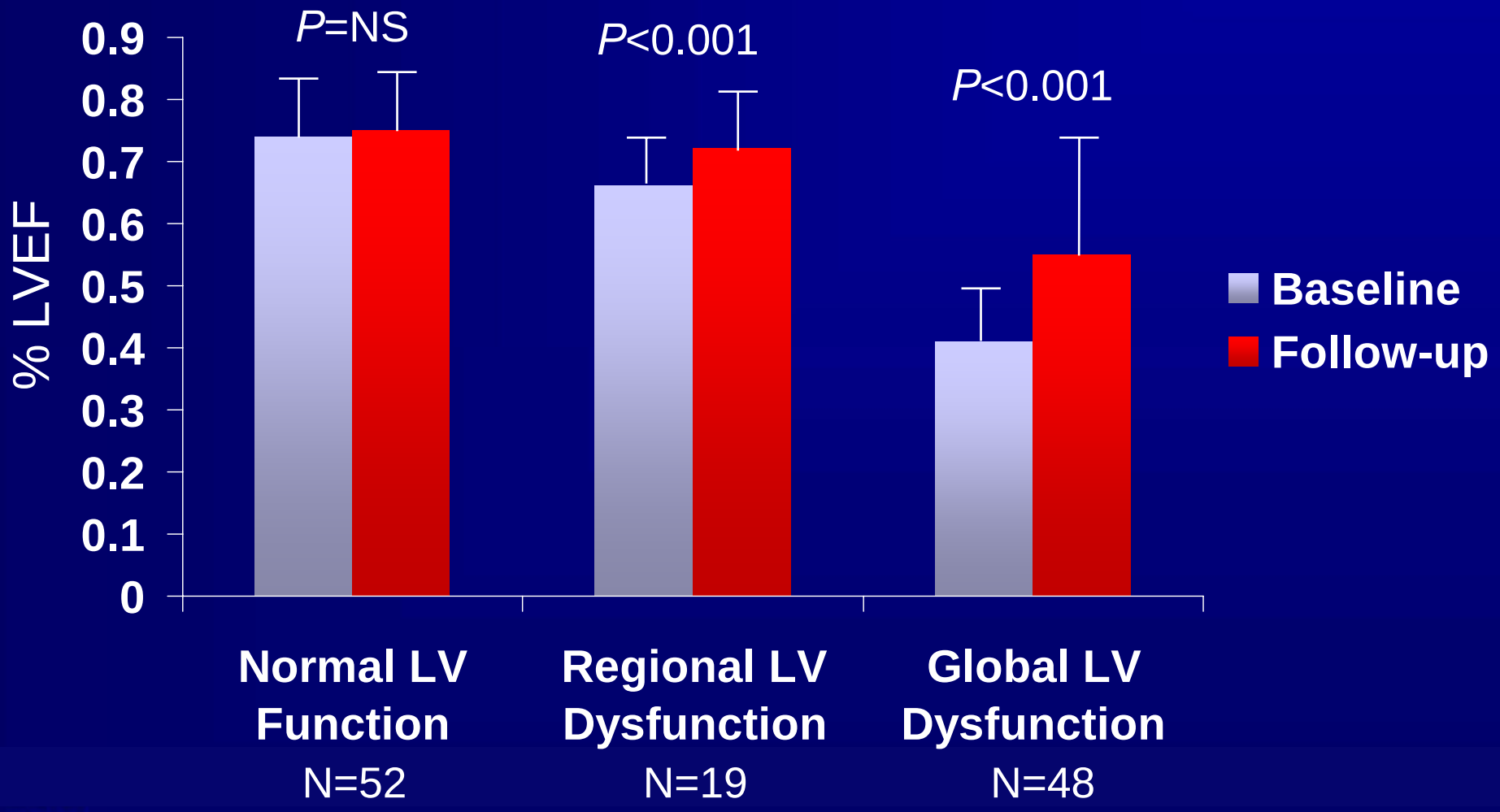


Normal wall motion



Recovery of LV Function After CTO Recanalization

Most Improvement with Baseline LV Dysfunction



Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

Werner et al. Am Heart J 2005

Recovery of LV Function After CTO Recanalization
Predictors of Improvement in LV Function

Positive

- **Baseline LV dysfunction**
- **Preserved microvasculature**

No Effect

- **Collateral development**
- **Prior MI**
- **Duration of occlusion**
- **Nonocclusive restenosis**

Negative

- **Reocclusion**

Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

Werner GS, Am Heart J, 2005

Evidence-based Rationale for CTO Revascularization Summary

- The ‘Last Great Barrier to PCI Success’— most frequently encountered yet least treated lesion subset
- Development of novel technologies and technique implies higher success, reappraisal of predictors of failure, but still sparse evidence to support efficacy and indications
- Pathophysiologic rationale to support late open artery hypothesis

Evidence-based Rationale for CTO Revascularization Summary (Continued)

- Several trials with DES in CTO revascularization have demonstrated significant reductions in ABR and TLR
  - Several indirect comparisons with BMS historical controls
  - 1 RCT of DES vs. BMS

  …..'Class Ib' recommendation
- Aside from ↓ABR, long term patency with DES may be associated with preservation of improved LV function
- Duration of dual antiplatelet therapy uncertain
  - Restenotic occlusions offset by thrombotic reocclusions with extensive stenting?

Evidence-based Rationale for CTO Revascularization Summary (Continued)

- Several trials with DES in CTO revascularization have demonstrated significant reductions in ABR and TLR
- Aside from ↓ABR, long term patency with DES may be associated with preservation of improved LV function
- Duration of dual antiplatelet therapy uncertain
- Ongoing study to clarify role of novel technologies and technique, identify those who derive greatest clinical benefit