CTO-PCI
Success or Failure Does not Matter ?
## ASAN/SoonCheonHyang CTO registry

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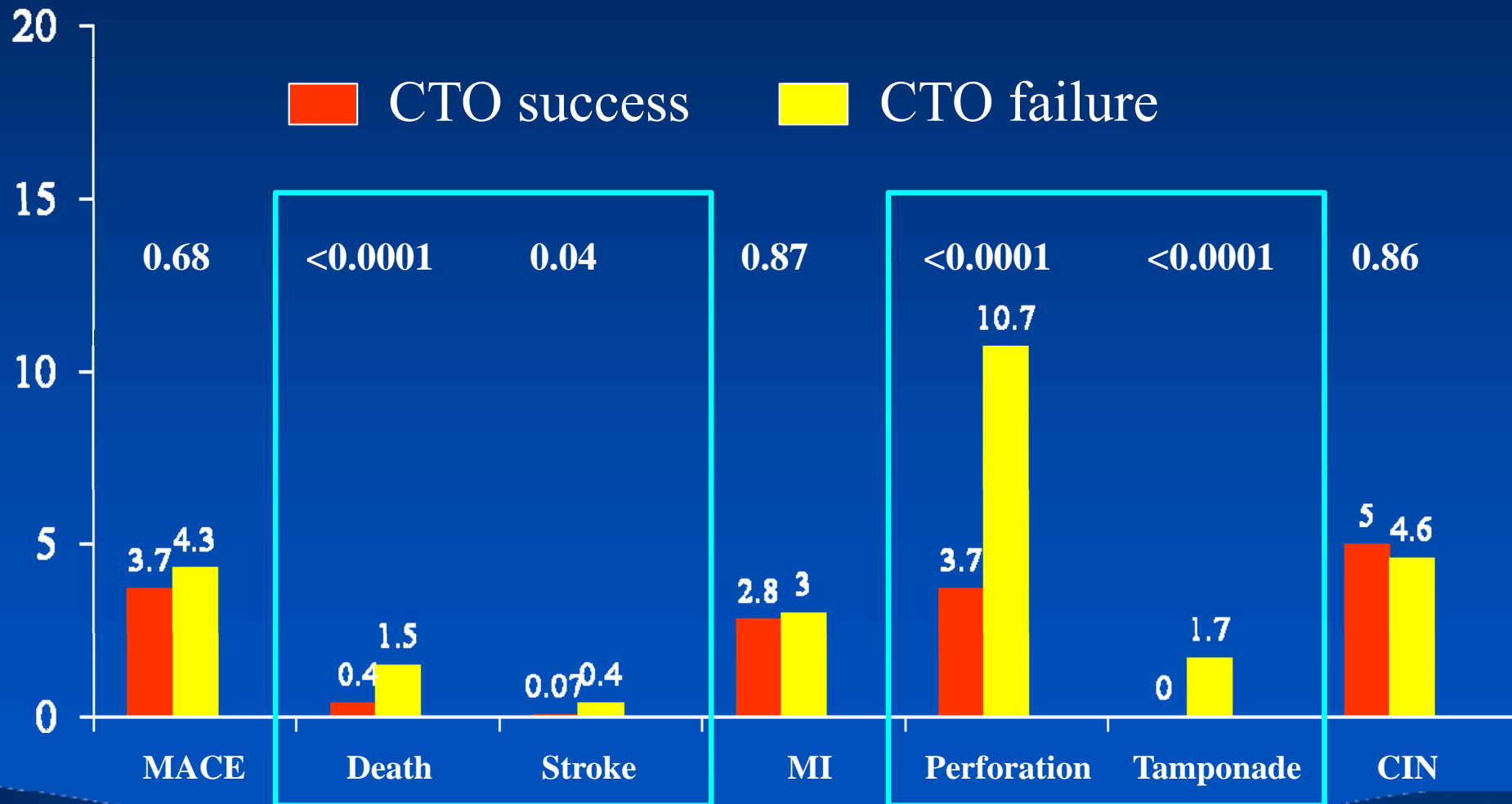
Rationale and Dilemmas of CTO-PCI

- Reduction in ischemic burden
- Enable completeness of revascularization
- Improvement of symptoms
- Improvement in LV function
- Reduced predisposition to arrhythmic events and ischemic events
- Avoidance of procedures and reduced medications
- Survival benefit

- Technical and procedural challenges
- Misperceptions regarding viability, collateral flow
- Uncertainty regarding which patients may benefit balanced by concern for complications in patients who may not derive clinical benefit
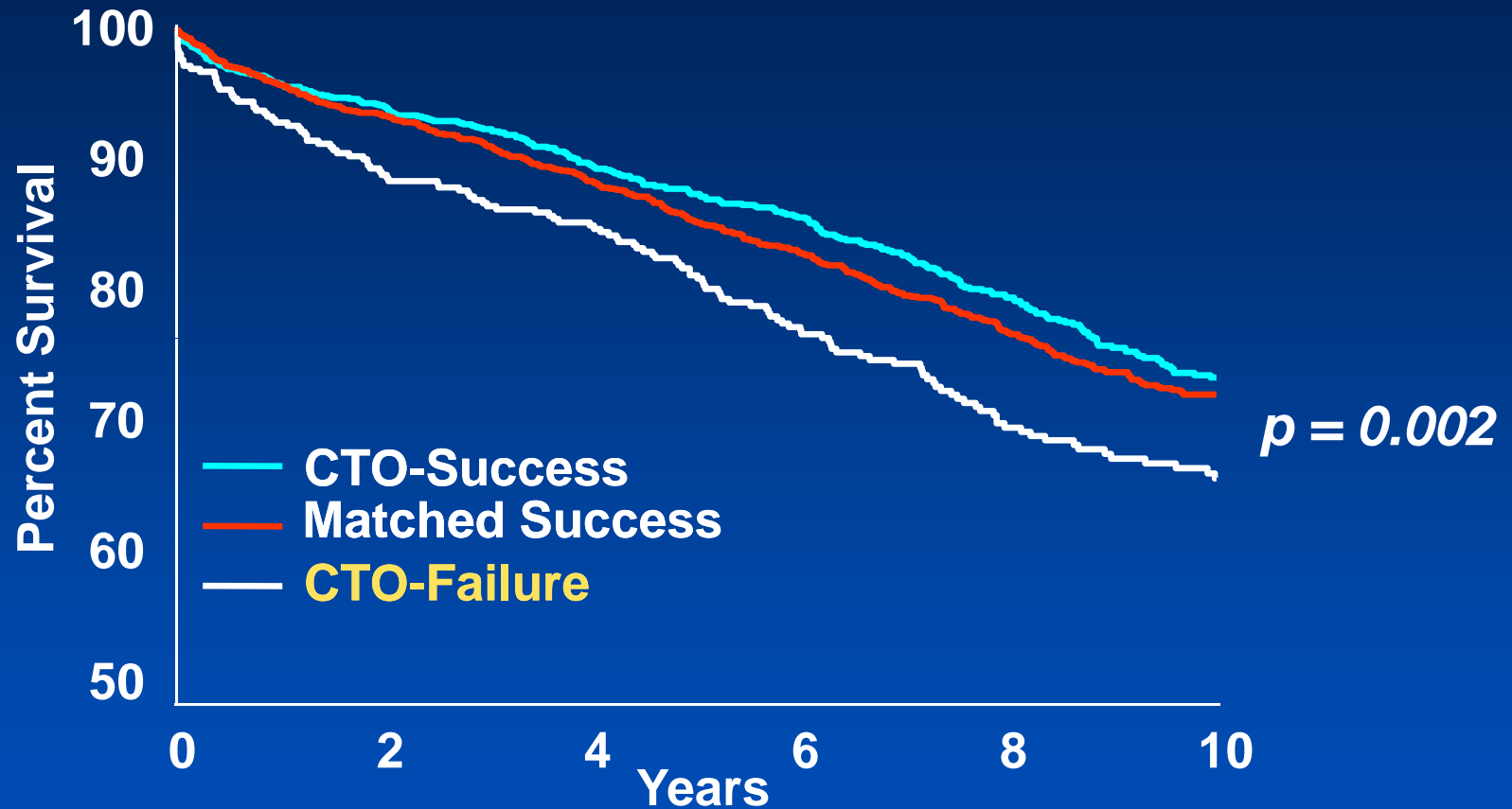
Temporal trend of success & Cx

Patel VG et al. J Am Coll Cardiol Intv 2013;6:128–36
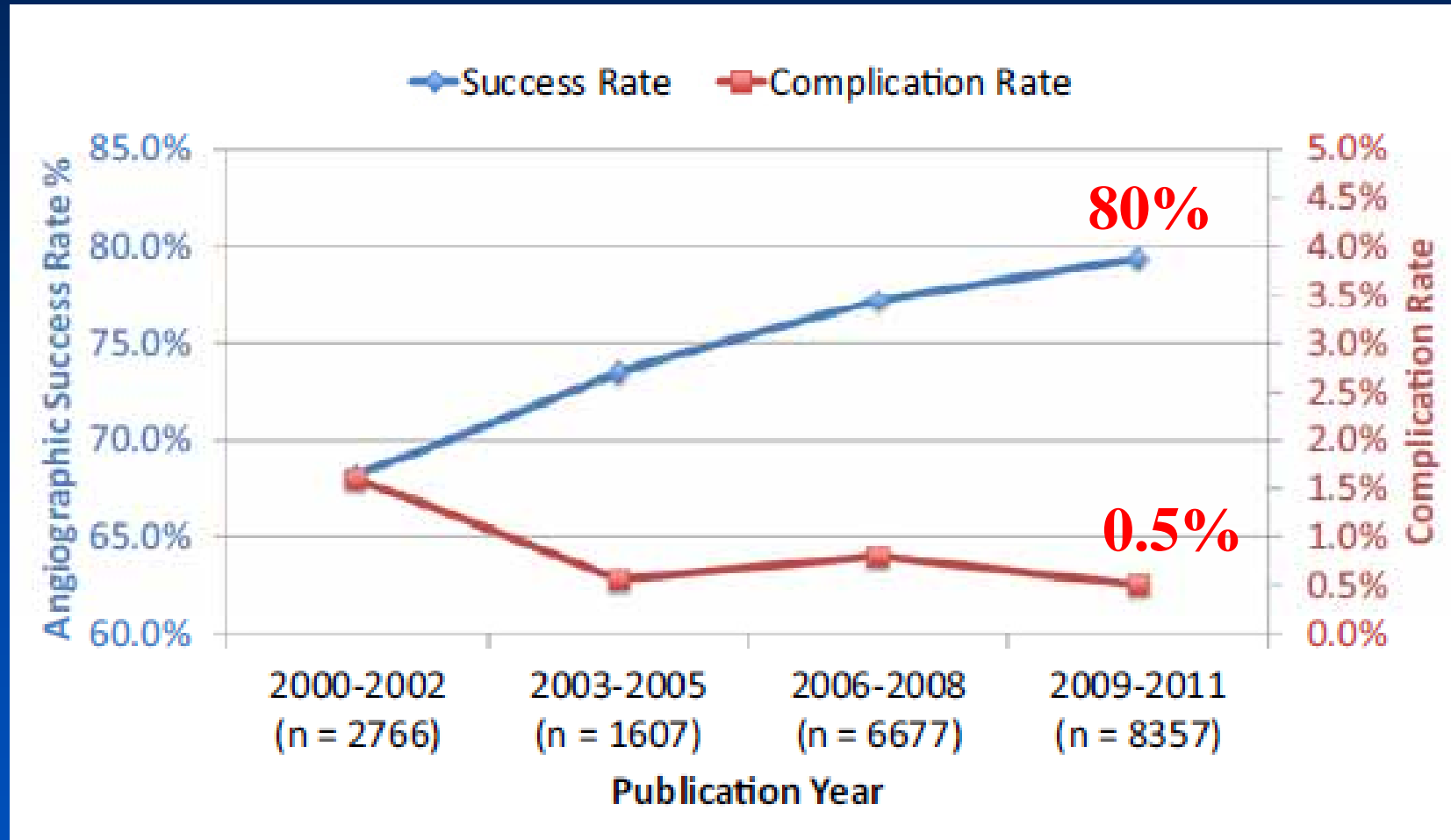
CTO-PCI: Complication rate

65 studies with 18,061 patients and
18,941 target CTO vessels

Patel VG et al. J Am Coll Cardiol Intv 2013;6:128–36

Procedural Outcomes and Long-term Survival for PCI of CTO

CTO-Success %	93.9	89.4	85.5	79.3	73.5
CTO-Failure %	88.7	84.8	76.8	69.4	65.1
Matched-Success %	93.2	88.2	82.7	76.6	71.9

p = 0.002

Suero J et al. JACC 2001;38:409.

CTO-PCI: Mortality Benefit

| Study	PCI successful n/N	PCI failed n/N	RR(95%CI)	%Weight	RR (Random effects model)
Aziz	9/377	12/166	0.33(0.14-0.77)	7.63	
Borgia	19/237	9/65	0.58(0.28-1.22)	8.68	
de Labriolle	7/127	2/40	1.10(0.24-5.01)	3.41	
Lee	8/251	4/82	0.65(0.20-2.11)	5.07	
Mehran	74/1226	49/565	0.70(0.49-0.98)	13.88	
Noguchi	7/134	15/92	0.32(0.14-0.76)	7.51	
Prasad	220/914	101/348	0.83(0.68-1.01)	15.60	
Chen	2/132	3/20	0.10(0.02-0.57)	2.80	
Valenti	17/344	17/142	0.41(0.22-0.78)	9.88	
Yi	135/1202	24/130	0.61(0.41-0.90)	13.23	
Jones	26/582	44/254	0.26(0.16-0.41)	12.30	
D+L pooled RR	654/5526	280/1904	0.50(0.36-0.68)	100	
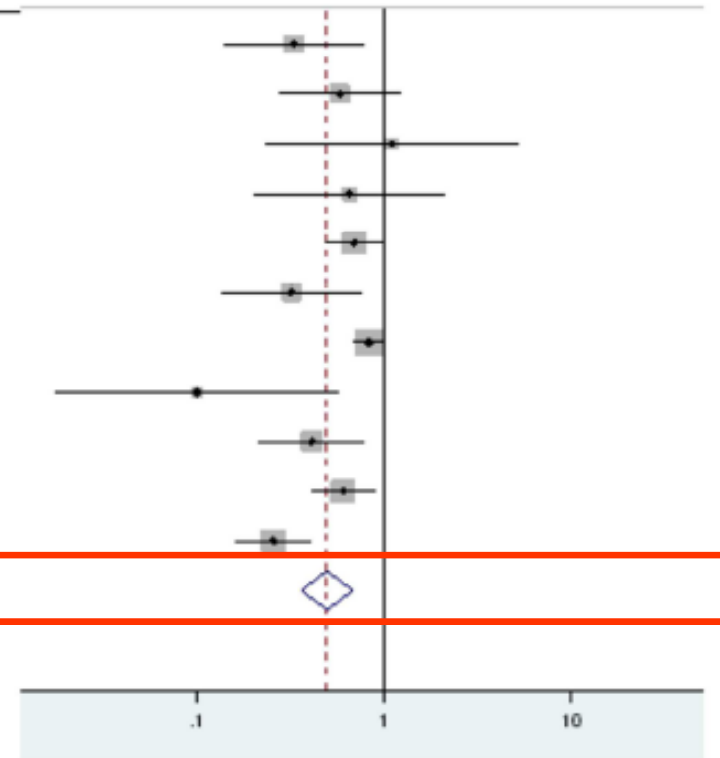
Heterogeneity chi-squared = 33.11 (d.f. = 10) p = 0.000
I-squared (variation in RR attributable to heterogeneity) = 69.8%
Estimate of between-study variance Tau-squared = 0.1572

Favors successful PCI   Favors failed PCI

Khan MF et al. Catheter Cardiovasc Interv (in press)

CTO-PCI: CABG benefit

Study	PCI successful n/N	PCI failed n/N	RR(95% CI)	% Weight
Angioi	8/93	22/108	0.42 (0.20-0.90)	3.64
Aziz	12/377	36/166	0.15 (0.08-0.28)	5.29
Borgia	4/237	10/65	0.11 (0.04-0.34)	1.68
Drozd	10/280	12/149	0.44 (0.20-1.00)	3.18
Jolicoeur	8/213	19/133	0.26 (0.12-0.58)	3.32
Finci	7/100	37/100	0.19 (0.09-0.40)	3.65
Hoye	71/567	117/304	0.32 (0.25-0.42)	26.22
Ivanhoe	41/317	59/158	0.35 (0.24-0.49)	15.73
Mehran	39/1226	75/565	0.24 (0.16-0.35)	13.96
Noguchi	9/134	26/92	0.24 (0.12-0.48)	4.16
Olivari	7/286	13/83	0.16 (0.06-0.38)	2.70
Sathe, S	8/116	15/62	0.28 (0.13-0.63)	3.29
Valenti	7/344	13/142	0.22 (0.09-0.55)	2.63
Warren	3/26	7/18	0.29 (0.09-0.99)	1.46
Yang	2/87	4/49	0.28 (0.05-1.48)	0.78
Yi	51/1202	19/130	0.29 (0.18-0.48)	8.32
Jones	18/582	56/254	0.14 (0.08-0.23)	8.01
D+L pooled RR	305/6187	540/2578	0.25 (0.21-0.30)	100.00

RR (Random effects model)
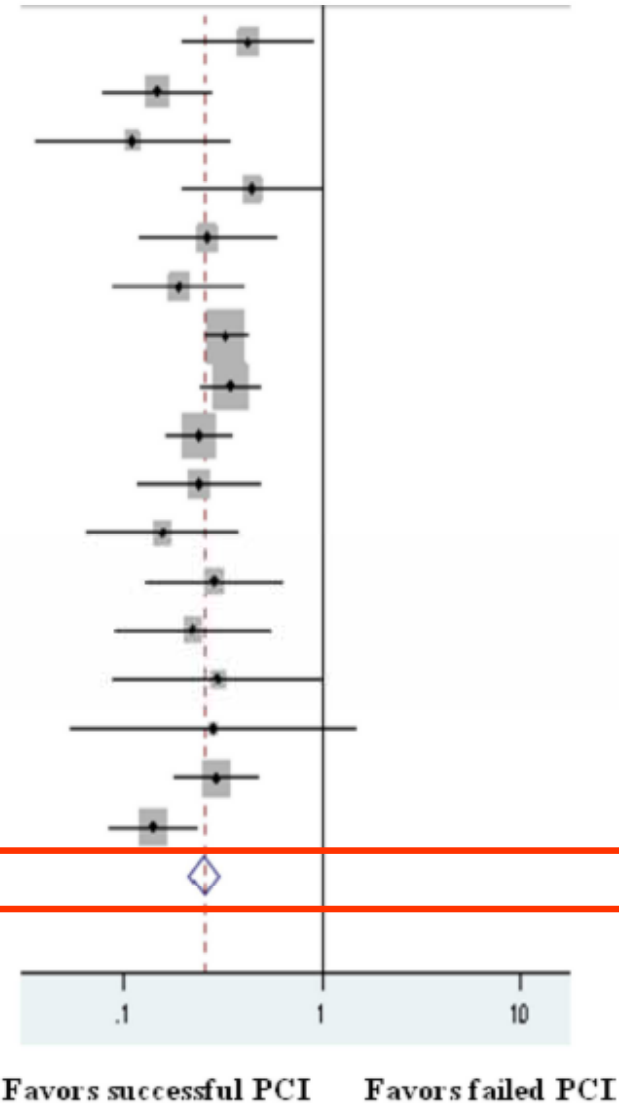
Heterogeneity chi-squared = 22.19 (d.f. = 16) p = 0.137
I-squared (variation in RR attributable to heterogeneity) = 27.9%
Estimate of between-study variance Tau-squared = 0.0337

Favors successful PCI   Favors failed PCI

Khan MF et al. Catheter Cardiovasc Interv (in press)

CTO-PCI: MACE Benefit

Study	PCI successful n/N	PCI failed n/N	RR(95% CI)	% Weight	RR (Random effects model)
Angioi	38/93	44/108	1.00(0.72-1.40)	6.65	
Arslan	55/117	60/115	0.90(0.70-1.17)	6.65	
Borgia	35/237	28/62	0.34(0.23-0.52)	5.34	
de Labriolle	30/127	2/40	4.72(1.18-18.90)	1.24	
Drozd	71/280	43/149	0.88(0.64-1.21)	6.13	
Jolicoeur	75/213	69/133	0.68(0.53-0.87)	6.77	
Finci	33/100	4/100	0.80(0.56-1.16)	5.76	
Hoye	206/567	177/304	0.62(0.54-0.72)	7.47	
Ivanhoe	63/317	76/158	0.41(0.31-0.54)	6.53	
Lee	24/251	6/82	1.30(0.55-3.09)	2.58	
Mehran	147/1226	137/565	0.49(0.40-0.61)	7.04	
Noguchi	67/134	46/92	1.00(0.77-1.30)	6.61	
Olivari	35/286	21/83	0.48(0.30-0.78)	4.79	
Sathe	52/116	22/62	1.26(0.85-1.87)	5.53	
Chen	19/132	7/20	0.41(0.20-0.85)	3.18	
Valenti	70/344	30/142	0.96(0.66-1.40)	5.63	
Warren	3/26	7/18	0.30(0.09-0.99)	1.55	
Yang	19/87	19/49	0.56(0.33-0.96)	4.42	
Yi	293/1202	48/130	0.66(0.52-0.84)	6.76	
D+L pooled RR	1335/5855	883/2415	0.70(0.59-0.83)	100.00	

Heterogeneity chi-squared = 83.05 (d.f. = 18) p = 0.000
I-squared (variation in RR attributable to heterogeneity) = 78.3%
Estimate of between-study variance Tau-squared = 0.0929

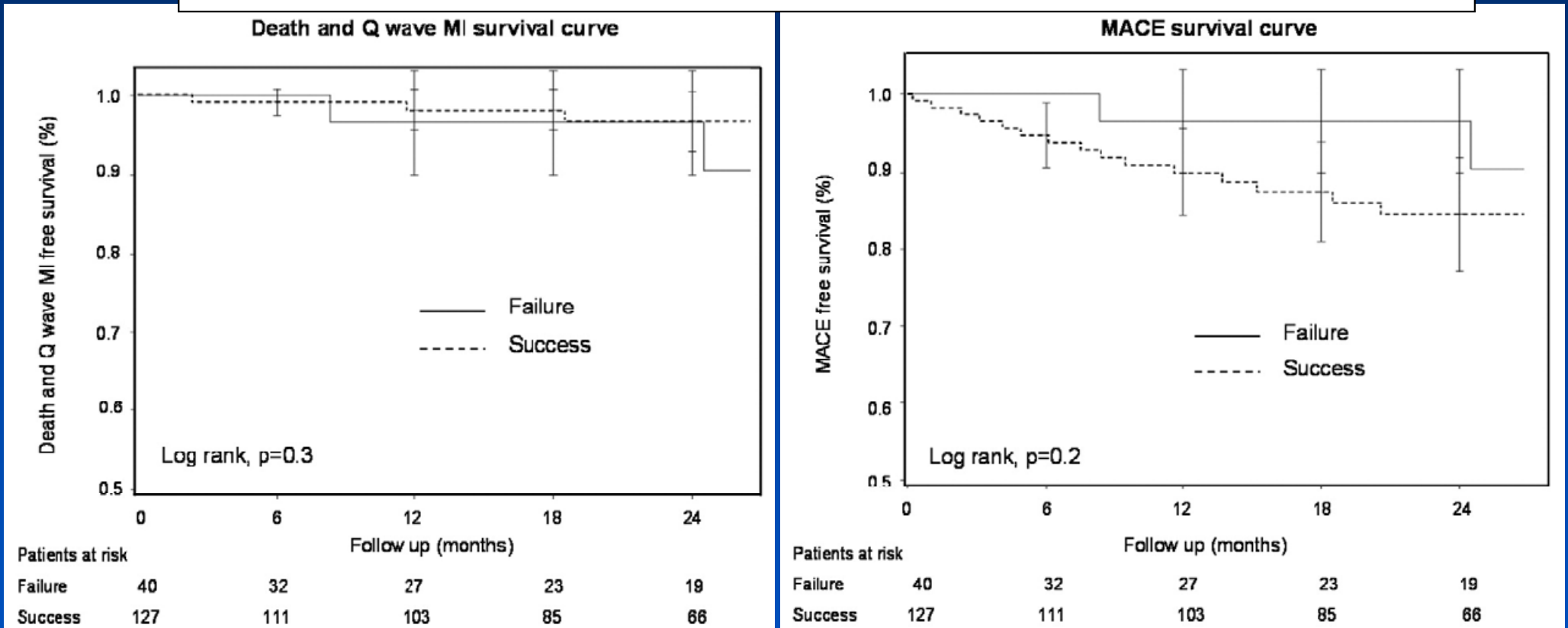Favors successful PCI   Favors failed PCI

Khan MF et al. Catheter Cardiovasc Interv (in press)

Long-term (2-year) Outcomes for CTO Revascularization

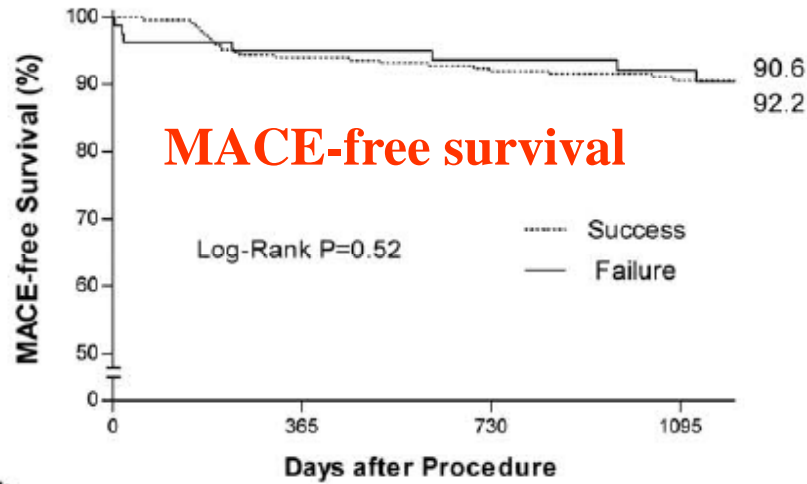## CTO Success (n=127) vs. Failure (n=45)

No benefit of CTO success

Labriolle A et al, Am J Cardiol 2008;102:1175-1181
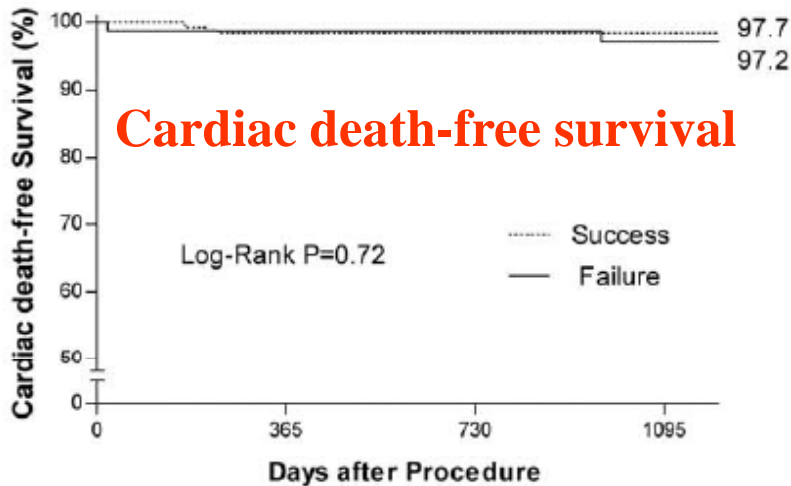
Success (n=251) vs. failed PCI (n=81)
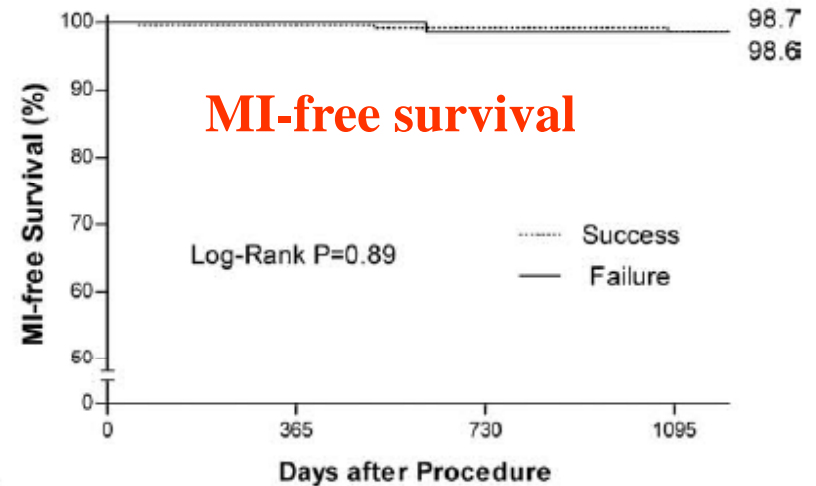
NCDR 2005-2008:
BMS vs. DES in CTOs

92069 patients, of these 10766 with a CTO PCI and stent
BMS: 2043   DES: 8218

Mortality

BMS

DES

Any MI

BMS

DES

Patel MR et al. JACC Interv 2012; 5: 1054-61
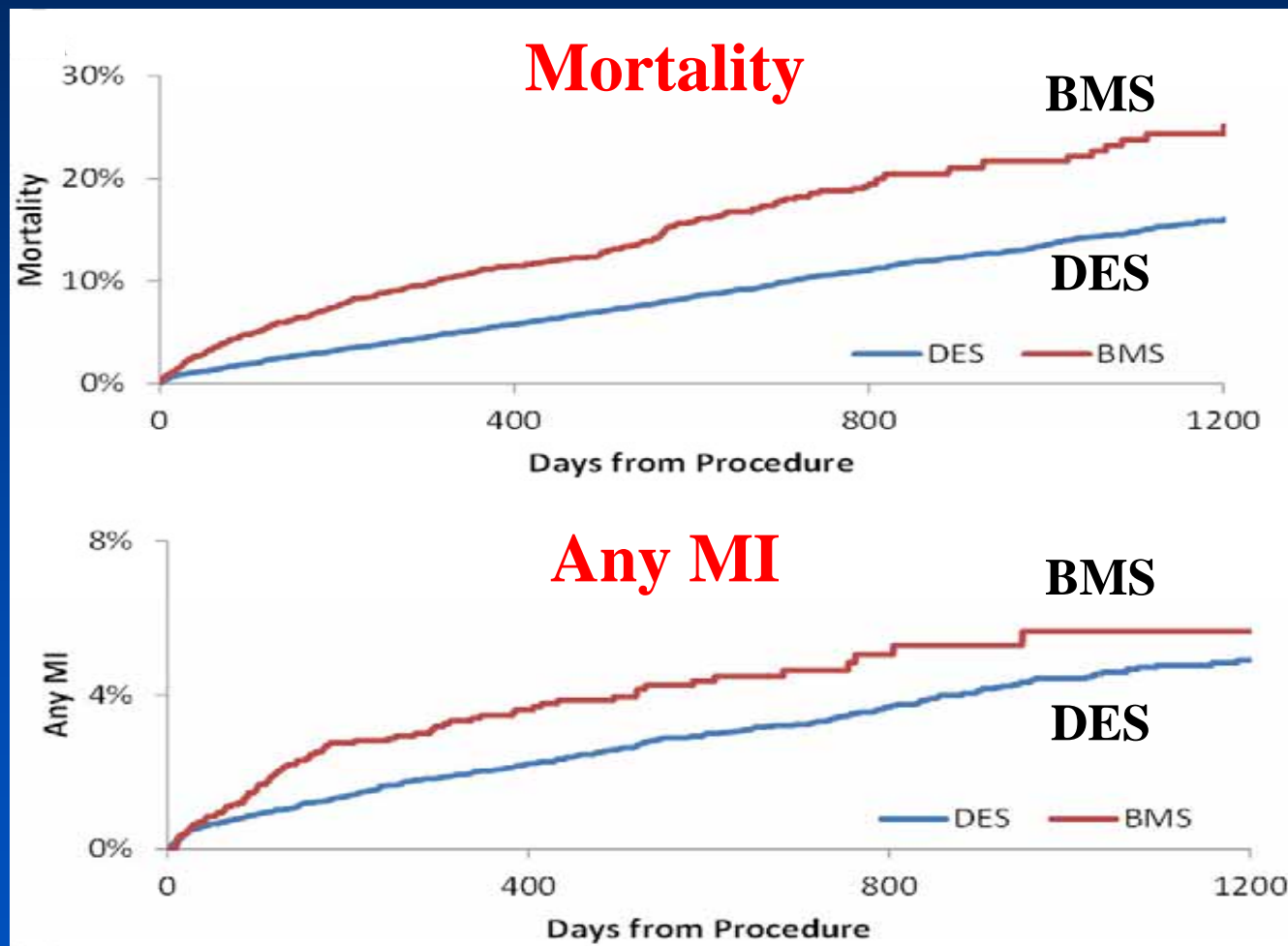
Debates of Outcomes after CTO PCI

- There remains controversy of benefit of CTO revascularization compared to CTO failure (medical treatment) because reported benefits were based on the retrospective registries.

- Furthermore, recent small registries of CTO did not show any benefit of CTO revacularization with DES compared to CTO failure

- Evolving medical treatment

- Benefits of CTO PCI with DES should be re-evaluated in the DES era in a randomized manner.

Methods

- Center : Asan Medical Center
  SoonCheonHyang University Bucheon Hospital

- Enrollment period : February 2003 ~ March 2006

- Patient numbers : consecutive 333 patients
  PCI success (n = 251)
  PCI failure (n = 82)

- Follow-up duration : median 1317 days
  (inter-quartile range : 1059 – 1590)

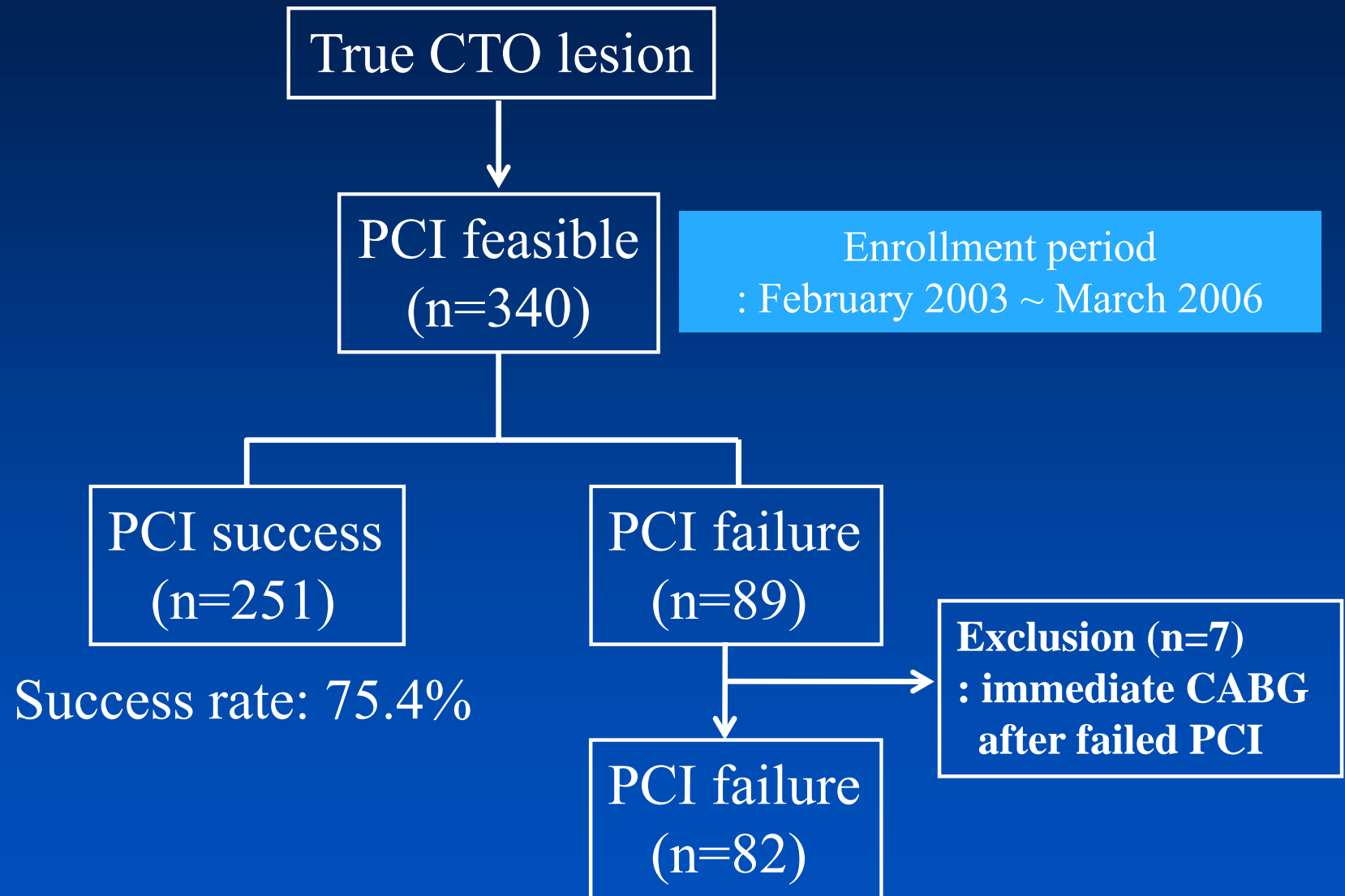# Methods

- Inclusion criteria

    "True" CTO lesions

    defined as Thrombolysis In Myocardial Infarction (TIMI) flow grade 0 on angiography and estimated duration ≥3 months

    Stone GW et al. Circulation 2005;112:2364-2372
    Hoye A et al. Circulation 2005;112:2530-2537

- Exclusion criteria

    - STEMI undergoing primary PCI

    - NSTEMI on admission

    - Receive CABG after PCI failure during in-hospital period

Study Design

True CTO lesion

↓

PCI feasible
(n=340)

Enrollment period
: February 2003 ~ March 2006

PCI success
(n=251)

PCI failure
(n=89)

Success rate: 75.4%

Exclusion (n=7)
: immediate CABG
after failed PCI

PCI failure
(n=82)

Objective

- The aim of this study was

  1. To compare the long-term outcome of successful revascularization versus failed revascularization.

  2. To investigate the safety and efficacy of PCI with DES for "true" CTO.

CardioVascular Research Foundation

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ASAN

Study Endpoints

- ## Primary end-point
  - Composite of all cause death/MI/TVR

- ## Secondary end-point
  - Death (all-cause)
  - Myocardial Infarction
  - Target Vessel Revascularization
  - Stent thrombosis of PCI success group
    (definite/probable by ARC definition)

Results
Baseline Clinical and Angiographic Characteristics

Variables	PCI Success (n=251)	PCI failure (n=82)	P-value
Age (years)	59.2 ± 10.5	63.8 ± 9.2	<0.001
Sex, Male	193 (76.9)	58 (23.1)	0.060
Hypertension	125 (49.8)	40 (48.8)	0.873
Hypercholesterolemia	54 (21.5)	23 (28.0)	0.223
Current Smoking	84 (33.5)	26 (31.7)	0.769
Diabetes mellitus	77 (30.7)	25 (30.5)	0.974
Chronic renal failure	7 (2.8)	13 (15.9)	<0.001
Previous myocardial infarction	19 (17.6)	24 (29.3)	<0.001
Previous PCI	40 (15.9)	27 (33.3)	0.003
Previous heart failure	12 (4.8)	12 (14.6)	0.003

* Date are expressed as mean ± SD for quantitative variables and as number (%) for qualitative variables.

Results

Baseline Clinical and Angiographic Characteristics

Variables	PCI Success (n=251)	PCI failure (n=82)	P-value
Acute coronary syndrome	104 (41.4)	25 (30.9)	0.090
LV ejection fraction (%)	56.2 ± 9.9	55.0 ± 11.2	0.233
Multi-vessel disease	129 (51.4)	45 (54.9)	0.583
Multiple CTOs (≥ 2 CTO)	18 (7.2)	10 (12.2)	0.155
CTO vessel			<0.001
LAD	130 (51.8)	17 (20.7)	
LCX	34 (13.5)	20 (24.4)	
RCA	84 (33.5)	45 (54.9)	
LM	3 (1.2)	0 (0)	

Results
Procedural Characteristics

Variables	PCI Success (n=251)	PCI failure (n=82)	P-value
CTO lesion length (mm)	20.3 ± 9.1	23.7 ± 11.2	0.012
Stent implanted			
Sirolimus-eluting stents	190 (75.7)		
Paclitaxel-eluting stents	61 (24.3)		
Number of stents per lesion	1.8 ± 0.8		
Length of stent per lesion (mm)	51.8 ± 24.0		
Non-CTO lesion intervention	106 (42.2)	32 (39.0)	0.609
Complete revascularization	228 (90.8)	0 (0)	<0.001
Complete revascularization (except CTO lesion)	228 (90.8)	69 (84.1)	0.090

* Date are expressed as mean ± SD for quantitative variables and as number (%) for qualitative variables.

Results
3-year Outcomes

Outcome	Outcome rates (%)		Crude		Multivariable adjusted		Adjusted for propensity	
	Success	Failure	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value
Death	3.8	7.1	0.491 (0.174-1.380)	0.168	1.003 (0.145-6.938)	0.998	1.070 (0.231-4.963)	0.931
MI	1.6	4.4	0.428 (0.096-1.913)	0.252	0.605 (0.076-4.827)	0.636	0.471 (0.045-5.032)	0.533
TVR	6.8	0	1.384 (0.502-3.812)	0.530	1.694 (0.481-5.964)	0.412	1.422 (0.313-6.457)	0.648
Death, or MI	5.4	12.5	0.426 (0.130-0.951)	0.039	0.810 (0.194-3.389)	0.773	0.843 (0.239-2.971)	0.791
Death, MI, or TVR	9.4	12.5	0.657 (0.348-1.239)	0.123	1.168 (0.473-2.886)	0.528	1.028 (0.349-3.028)	0.940

*Adjusted for age, sex, DM. HTN, smoking, hypercholesterolemia, previous PCI, previous MI, renal failure, ACS, multi-vessel disease, multiple CTOs, CTO vessel, CTO length, complete revascularization, EF
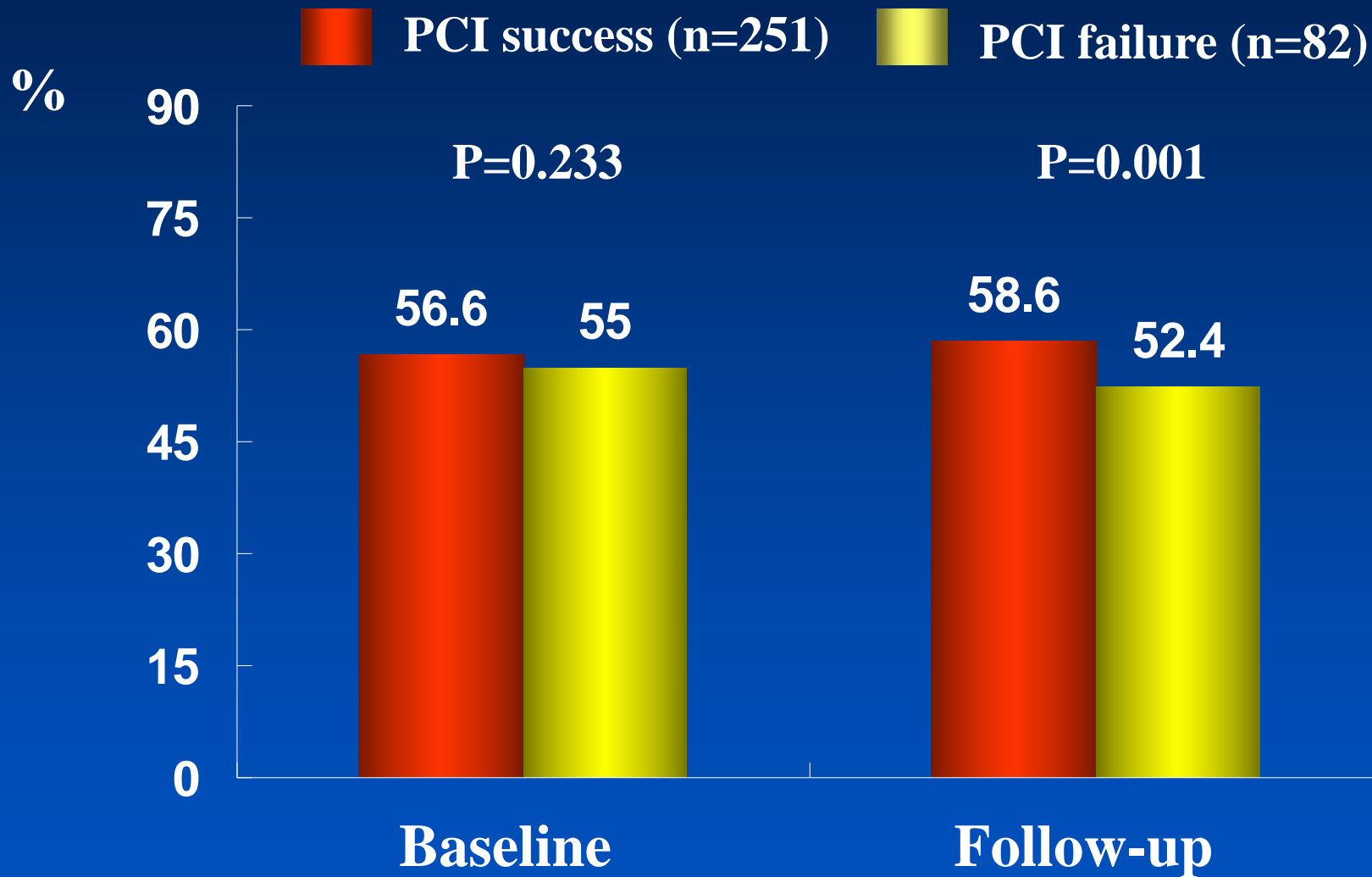
Composite of Death/MI/TVR for 3-year
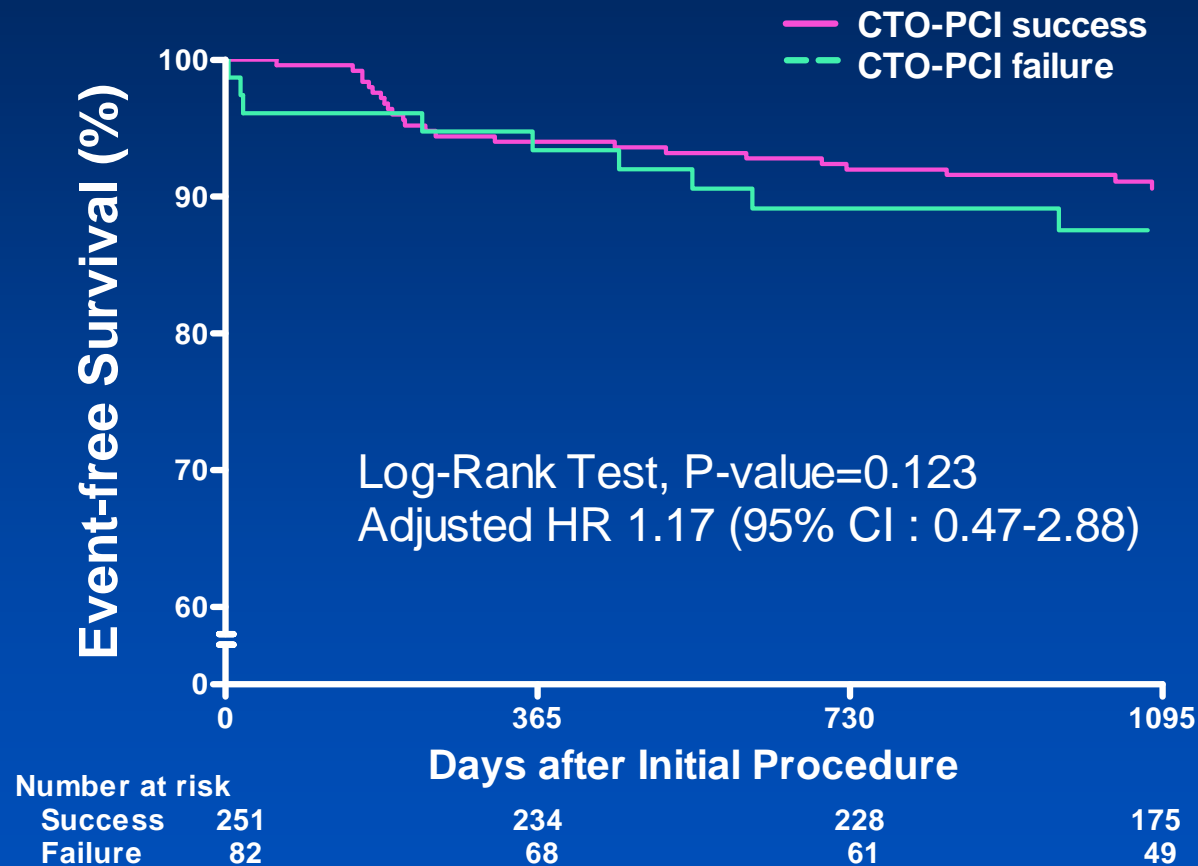
Stent thrombosis of success group (definite/probable)

3-year cumulative incidence by Kaplan-Meier Curve : 1.8%

	Early	Late	Very Late
Definite	0	1	3
Probable	0	0	0
Possible	0	3	0

• **By ARC definition**
: Early (0 to 30 days), late (31 to 360 days), very late (>360 days)
Definite/ Possible/Probable

Independent predictors of MACE

PCI success group

Variables	Hazard Ratio	95% CI	P-value
Previous heart failure	4.658	1.596-13.593	0.004

Entire population

Variables	Hazard Ratio	95% CI	P-value
Previous heart failure	3.142	1.392-7.090	0.005
Multiple CTOs (≥2)	2.383	0.993-5.721	0.050

MACE: Death/MI/TVR

7-year Outcomes
Median f/u duration: 2674 days (1632 ~ 3057)

Outcome	Outcome rates (%)		Crude		Multivariable adjusted	
	Success	Failure	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value
Death	10.8	22.1	1.94 (0.99-3.77)	0.05	1.13 (0.39-3.29)	0.18
Cardiac death	8.7	11.7	1.40 (0.58-3.41)	0.45	0.24 (0.04-1.57)	0.13
MI	3.3	4.2	1.65 (0.35-5.28)	0.65	ns	0.45
Death/MI	14.4	24.5	1.74 (0.95-3.21)	0.075	1.21 (0.48-3.08)	0.67
Cardiac death/MI	10.7	14.1	1.44 (0.68-3.05)	0.37	0.68 (0.17-2.68)	0.58
TVR	13.1	11.8	0.68 (0.28-1.64)	0.69	0.69 (0.23-2.03)	0.50
Cardiac death/MI/TVR	20.9	27.0	1.12 (0.63-1.98)	0.71	0.50 (0.21-1.17)	0.11
Death/MI/TVR	24.2	34.2	1.38 (0.85-2.27)	0.19	0.89 (0.43-1.88)	0.77

*Adjusted for age, sex, DM. HTN, smoking, hypercholesterolemia, previous PCI, previous MI, renal failure, ACS, multi-vessel disease, multiple CTOs, CTO vessel, CTO length, complete revascularization, EF

Composite of Death/MI/TVR for 7-year
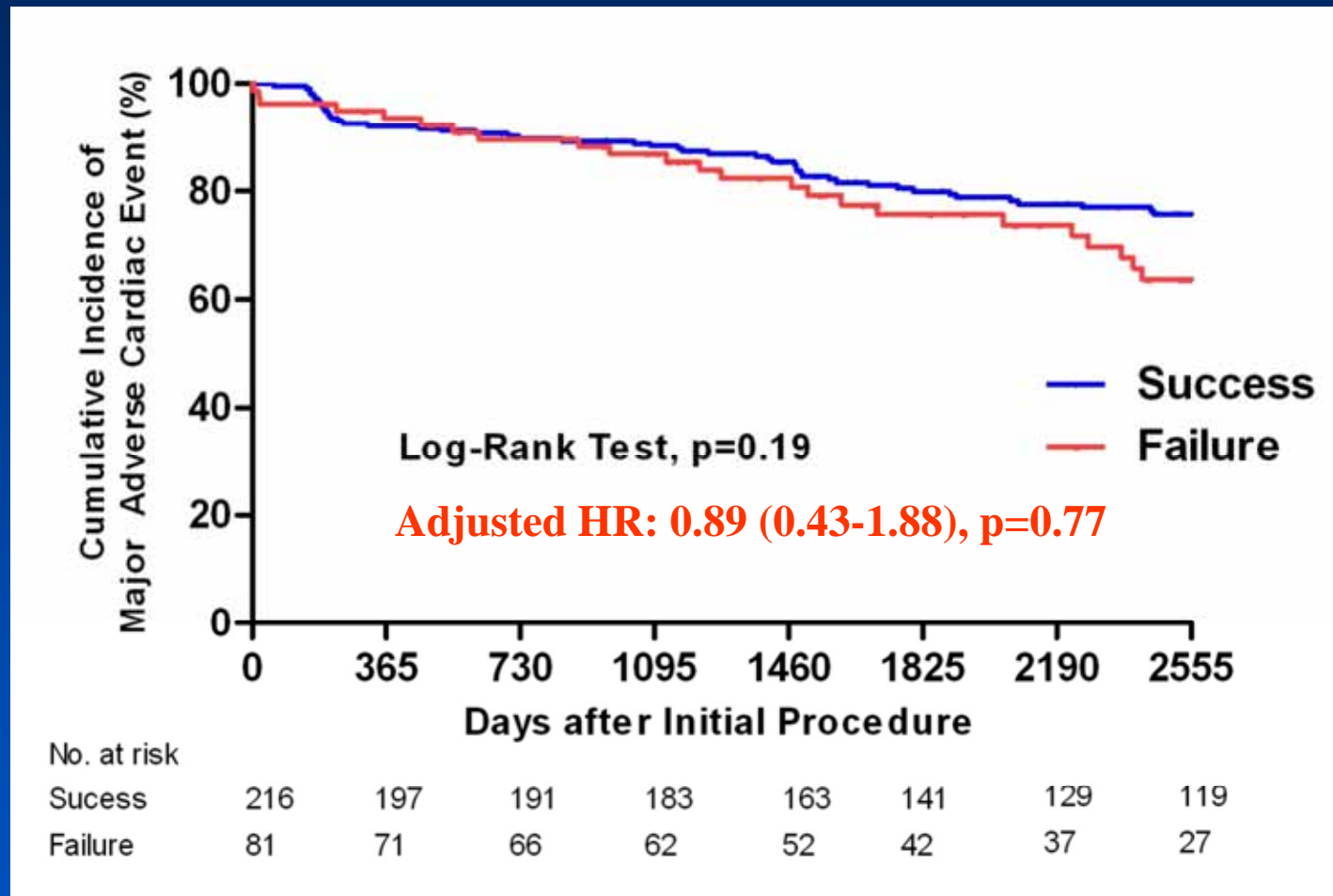
CTO-PCI: To do or not

- Technical success of CTO revascularization has significantly improved given remarkable advances in interventional cardiology over the past 3 decades.

- However, the decision to perform CTO revascularization remains a dilemma, given the lack of robust clinical evidence to support it.

DECISION - CTO

_D_rug-**_E_**luting stent Implantation _versus_ optimal Medical Treatment in patients with **_C_**hron**_I_**c Total Occlu**_SION_**

Objective

To compare the long-term (3-year) efficacy of drug-eluting stent implantation with optimal medical treatment for <u>chronic total occlusion</u>

* CTO: TIMI 0 flow and estimated duration $\geq$ 3 months

DECISION-CTO

CTO lesions - eligible for DES implantation
(Single CTO or MVD with 1 or 2 CTOs)

1:1 randomization
Randomization is stratified by CTO location (LAD vs. Non-LAD), DM and Involving center

DES (n=642)

Medical Treatment (n=642)

DES in non-CTO lesions,
Treat CTO lesions

DES in non-CTO lesions,
Not treat CTO lesions

Optimal Medical Treatment

Clinical outcomes at 3 years
(Composite of Death, MI, Stroke and any Revascularization)

Primary end-point: Composite of death, MI, stroke, and any revascularization
Secondary end-point: any revascularization, hospitalization due to acute coronary syndrome. death, MI, LVEF, and angina class, clinical outcomes at 5yr, 10yrs

Conclusion

- *'The best intervention is prevention and the best prevention is noninvasive'……..*

- Until robust data favoring CTO-PCI are available, we should do PCI in patients with favorable lesion morphology for success or recruited in randomized study.

- Every efforts should be taken to reduce periprocedural complications such as perforation, tamponade, renal dysfunction, and radiation skin injury….