Master's Case Presentation for Changing Concept: CTO

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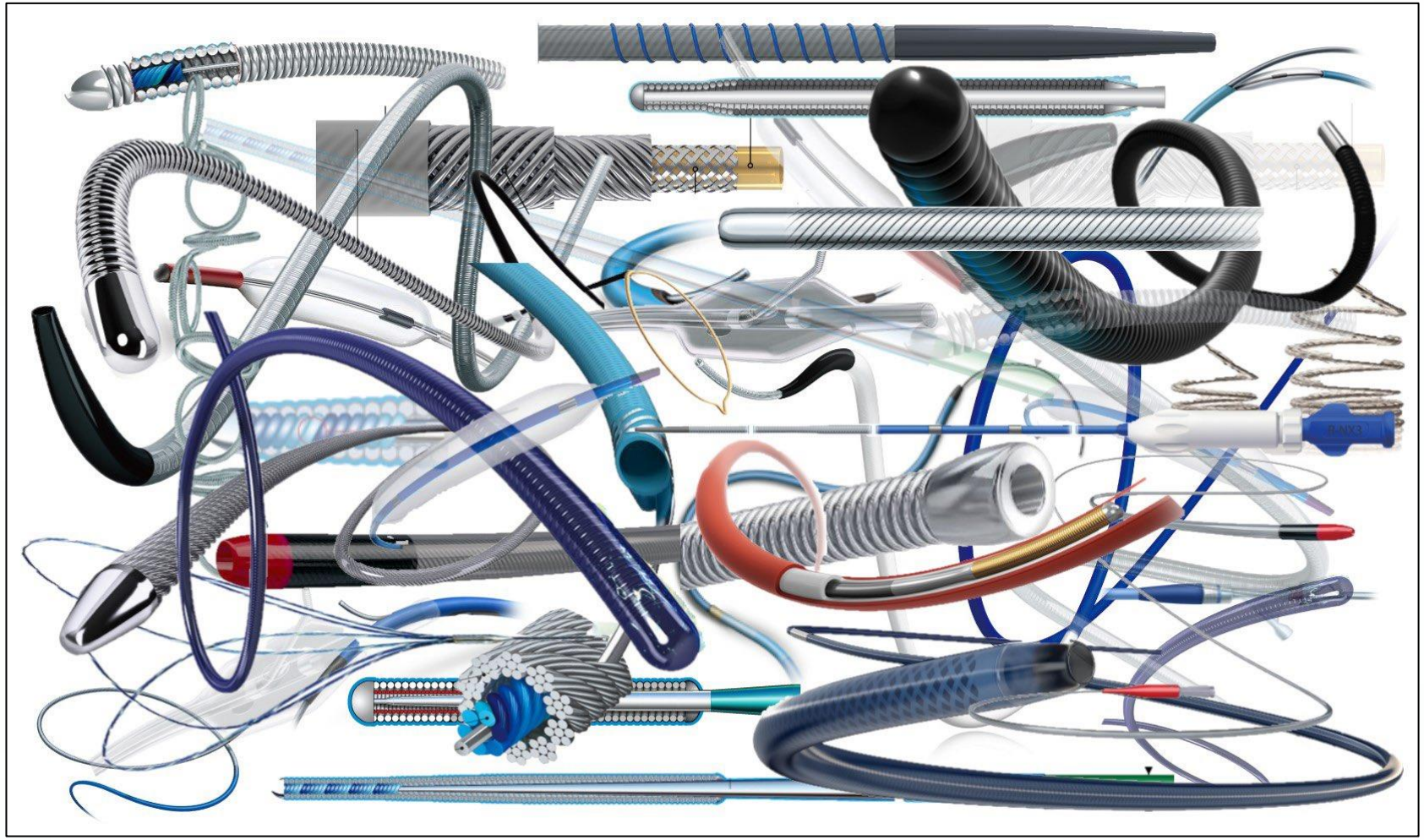
Disclosure

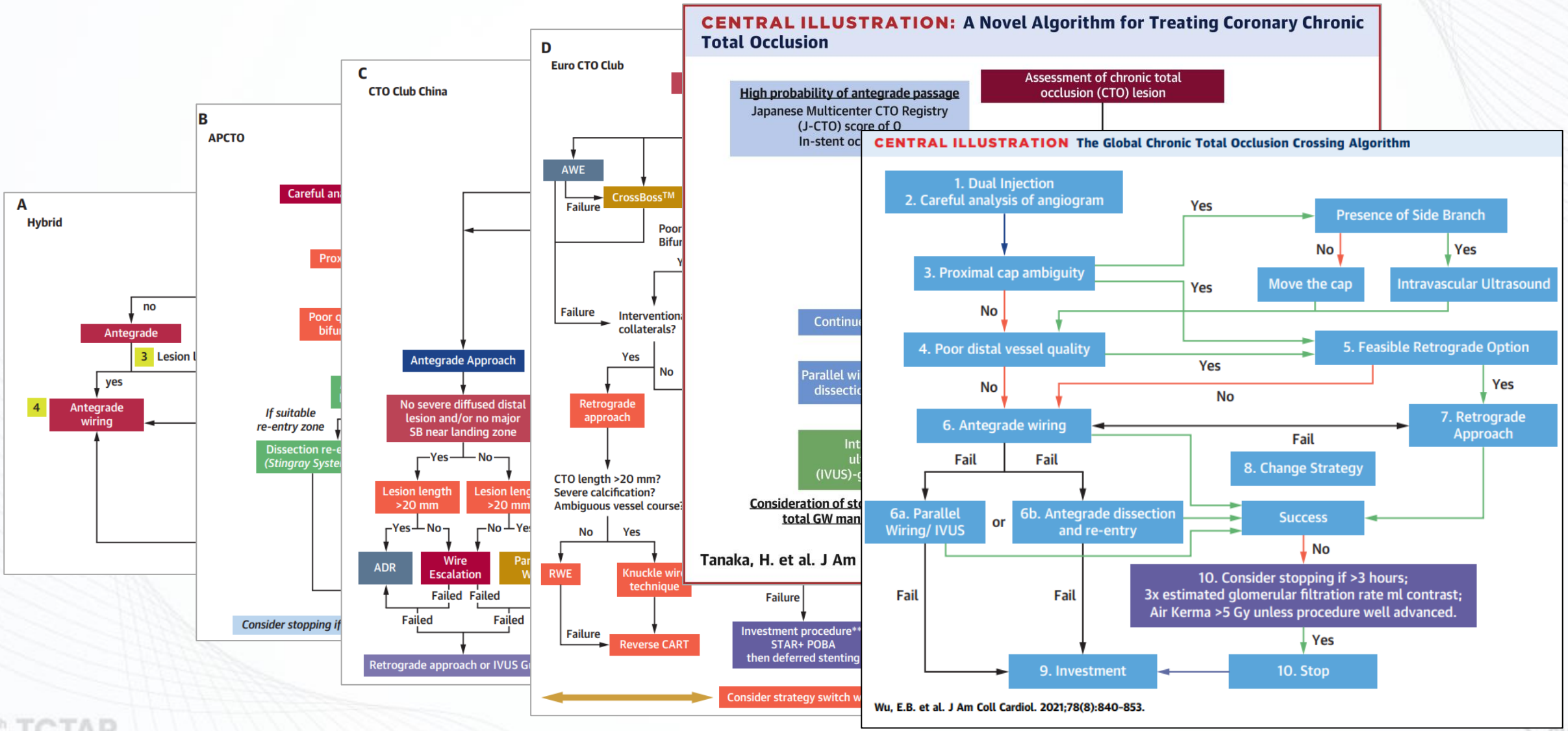
- I am ***FFR-Believer*** and ***IVUS-Holic.***
- I have been a ***Complex PCI Interventionist*** including LM and bifurcation.
- I have been an ***Antegrade Only CTO Interventionist*** for a long time.
- I am recently trying retrograde approach.

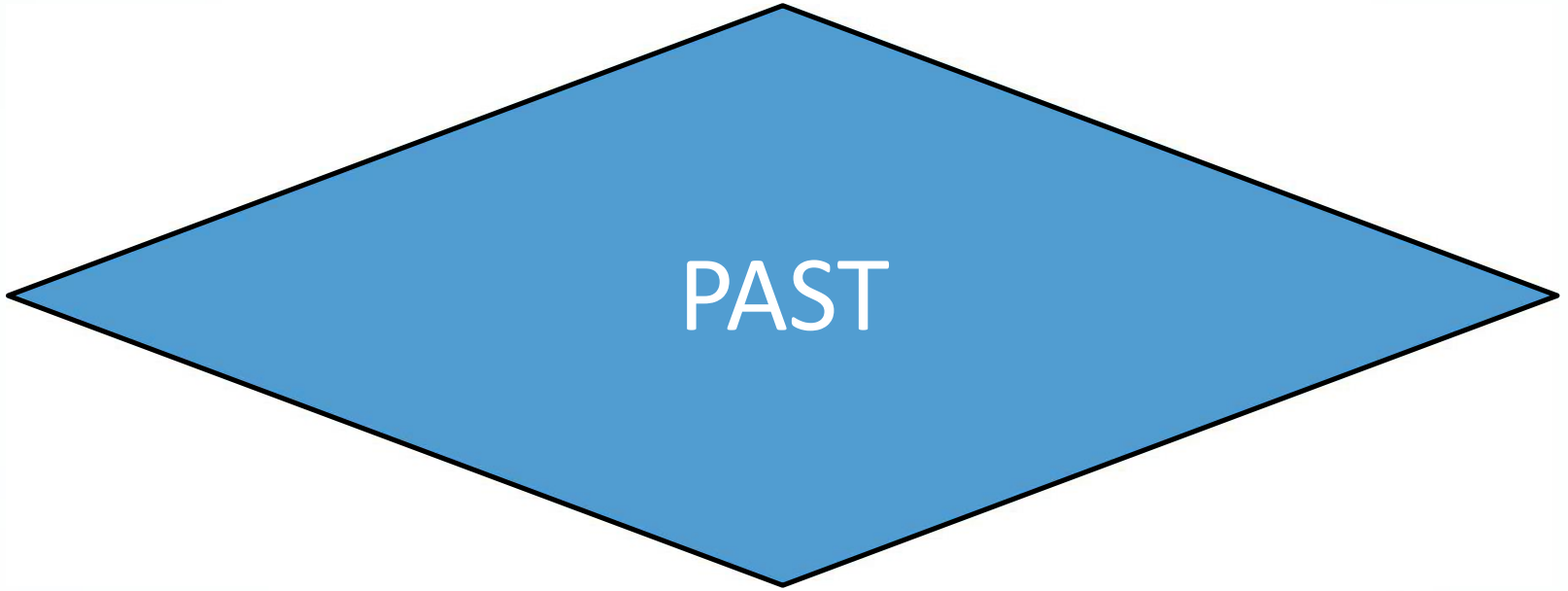
CTO-Tool kit



2nd edition of CTO toolbox@KovacicMihajlo

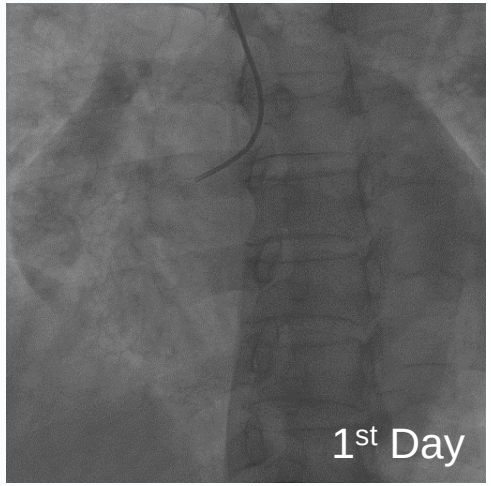
Establishment of CTO Crossing Algorithms

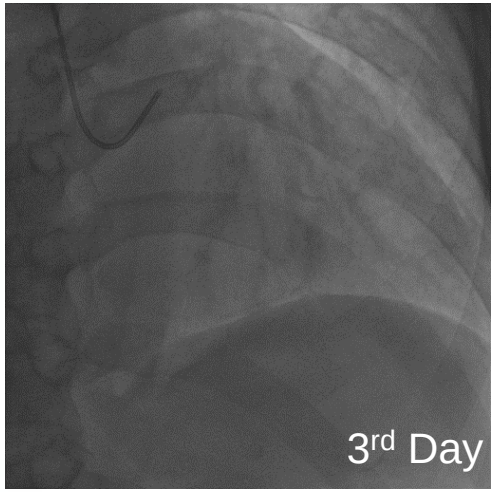


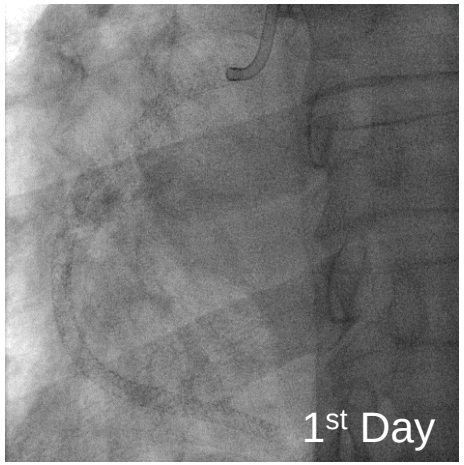

PAST

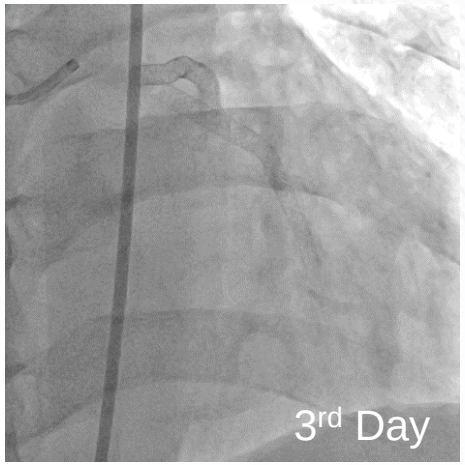
My CTO Case (1) : Go Antegrade, Only !

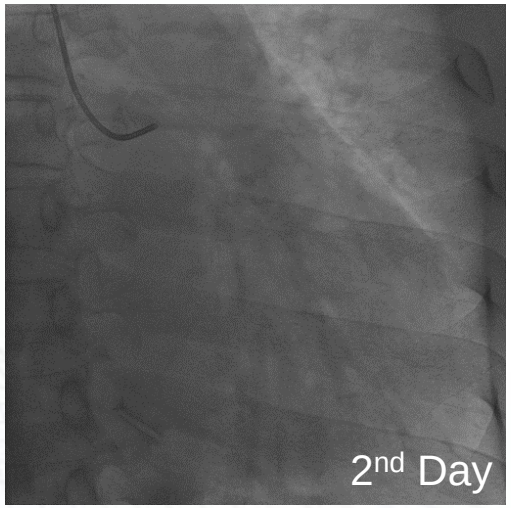
63 YO/M, EF= 18%, iCMP, on maximal HF management





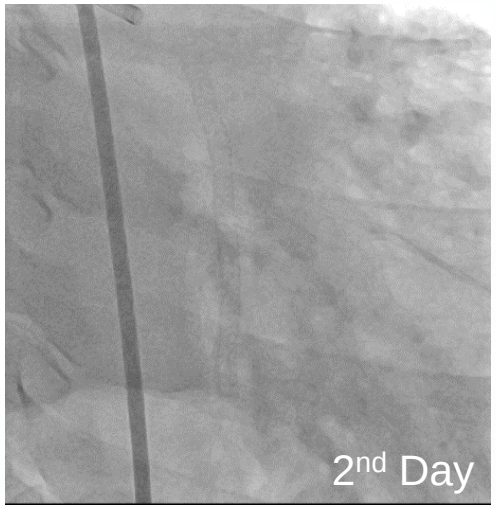






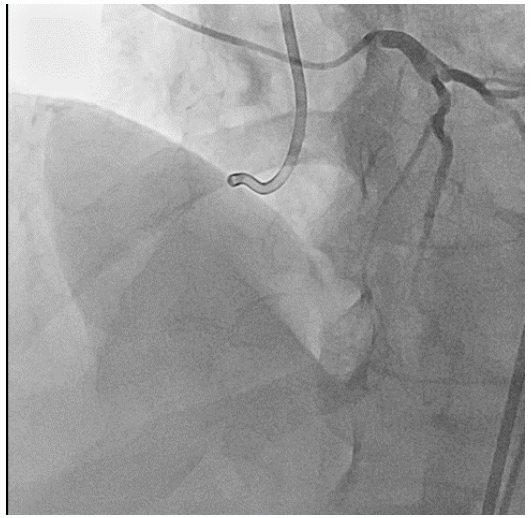
Staged PCI for 3 Days

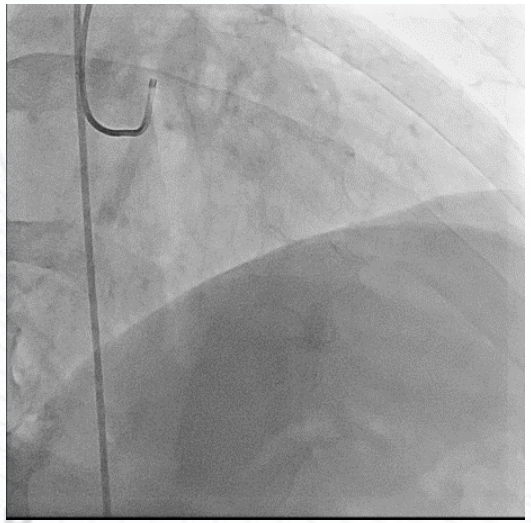
Stent
pdRCA: Xience Alpine 4.0(38)+3.5(38)+3.0(38)
dLCX: Xience Alpine 3.25(18)+2.75(38)
mdLAD: Xience Alpine 3.5(18)+2.75(28)
Balloon:
Tazuna 2.5(15), Nimbus NC 3.5(17), Ikazuchi 2.0(20), Raiden3 3.0(20), Emerge 2.5(20), Nimbus Salvo 3.0(17)
Contrast: 150+280+150, total 580 cc
Wire: Fielder XT #4, BMW #3, Sion, Gaia2 with Corsair #3
Procedure time: 52m+46m+30m, total 2h8m



My CTO Case (2) : Retrograde ….

65 YO/M, EF= 53%, Stable angina





Antegrade failure and
Retrograde approach

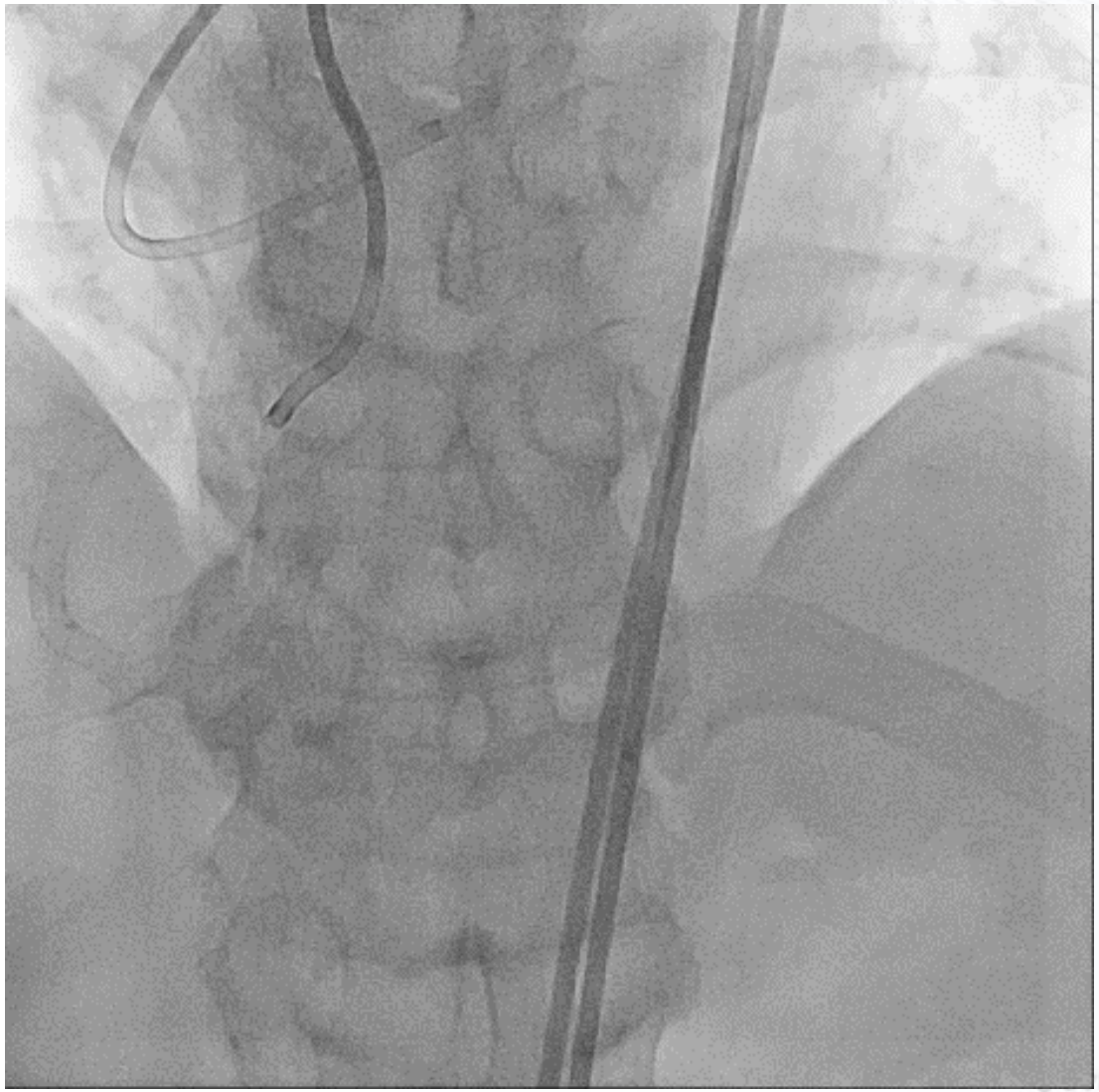
Stent:
Xience Xpedition 3.5(48),
Xience Xpedition 3.5(48),
Xience Xpedition 3.0(48)

Balloon:
Ryurei 1.5(15)
NC Trek 2.5(15)
Sapphire NC 3.5(15)
Selethru NC 4.0(20)
Selethru 5.0(10)

Contrast: 450 cc

Wire:
Fielder XT-R, Fielder XT, Sion #2, Gaia2 #3, SUOH 03, RG3 with Corsair, Caravel

Procedure time: 2h 43m



Can Opening CTO Save the Life?

Can Opening CTO Save the Life?

Success vs. Failure

Study	No. of Patients	Success	Duration of Follow-up, y	Mortality, %		
				PCI Success	PCI Failure	*P*
Mid America Heart Institute[58]	2007	1491 (74.4%)	10	26.6	35.0	0.001
British Columbia Cardiac Registry[59]	1458	1118 (76.7%)	1	10.0	19.0	<0.001
TOAST-GISE[22]	369	286 (77.5%)	6	1.1	3.6	0.13

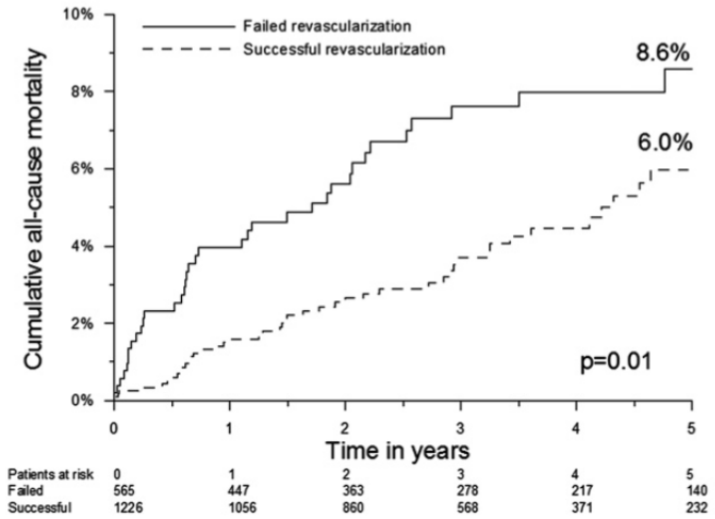
J Am Coll Cardiol. 2001;38:409 – 414

Circulation. 2001;104:II-415. Abstract

J Am Coll Cardiol. 2003;41:1672–1678

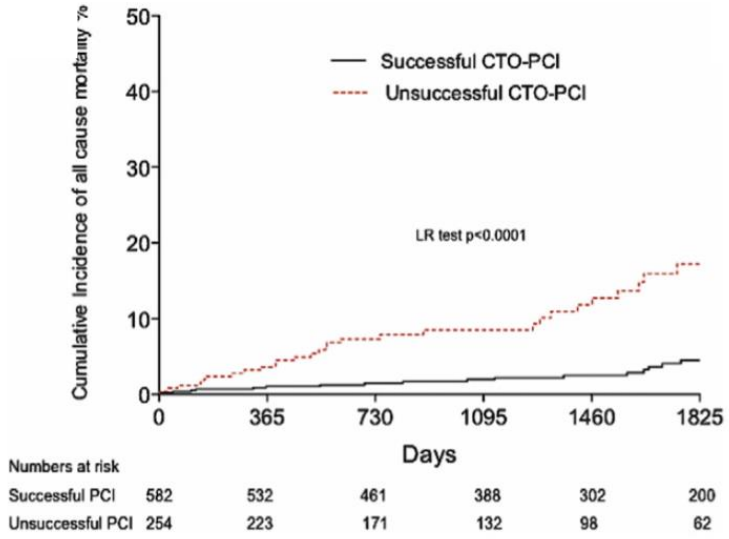
Can Opening CTO Save the Life?

Multinational CTO Registry



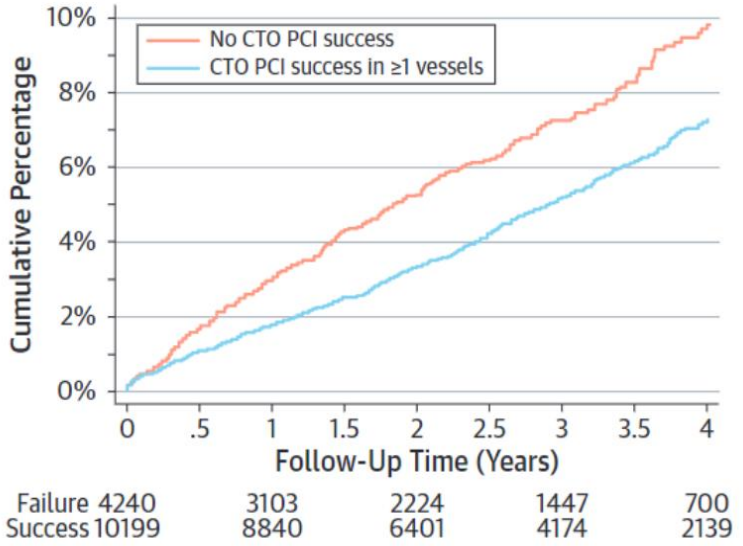
J Am Coll Cardiol Intv 2011;4:952–61

Single Center CTO Registry



J Am Coll Cardiol Intv 2012;5:380 – 8

U.K. Central Cardiac Audit Database



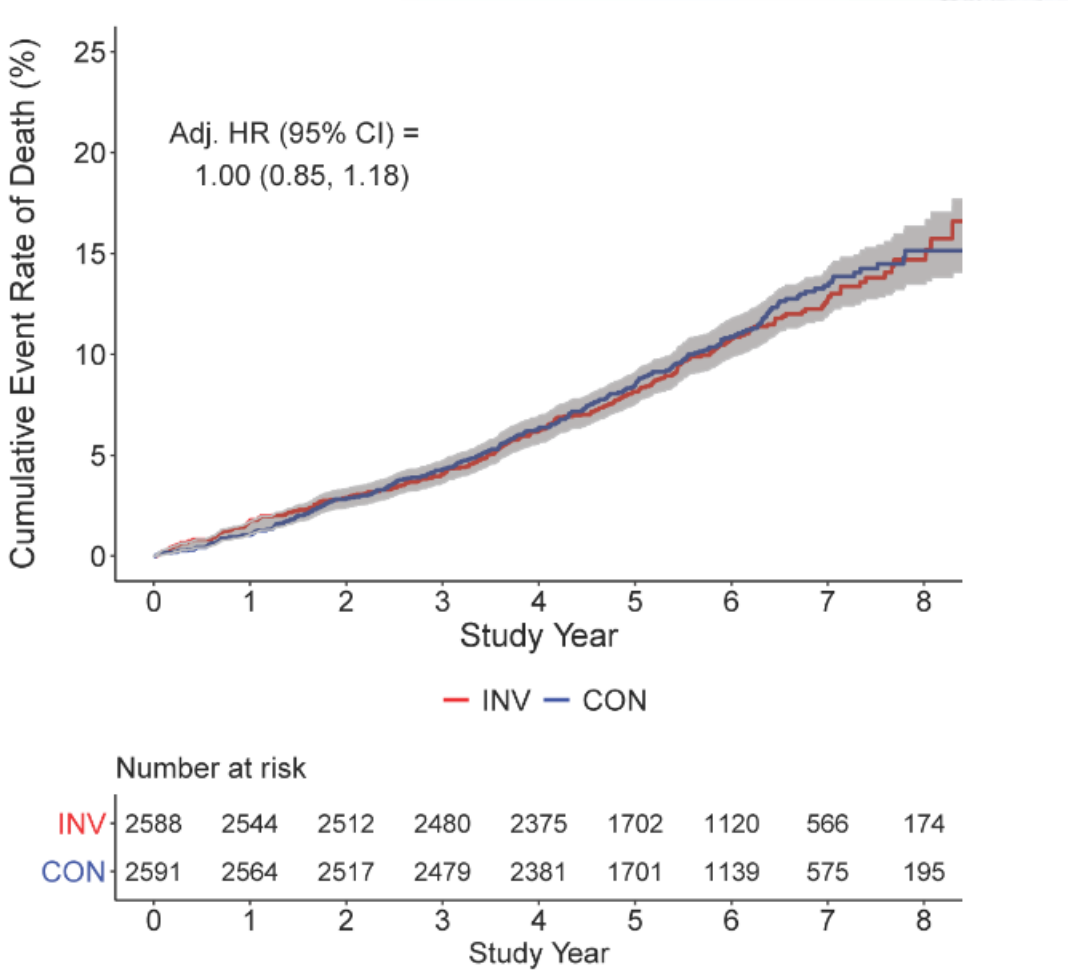
J Am Coll Cardiol 2014;64:235–43

Can Opening CTO Save the Life?

- **Success of PCI**
- **Failure of PCI**

ISCHEMIA-EXTEND Follow-up Study

All Cause Mortality



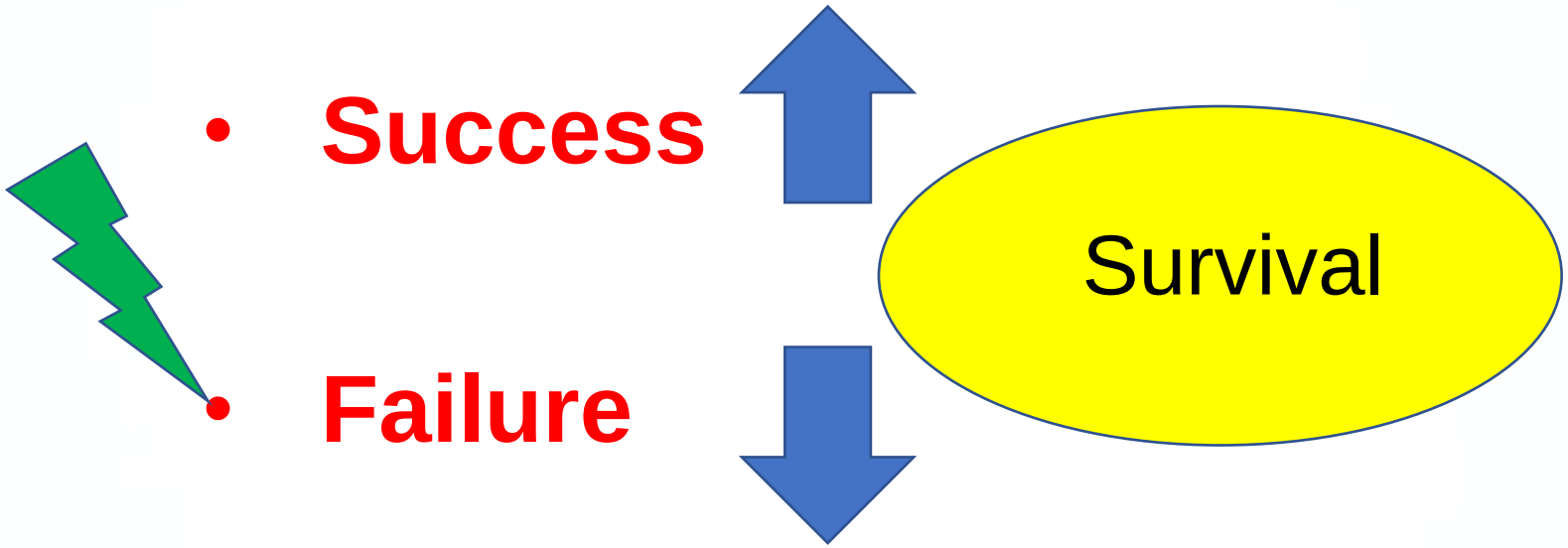
CTOs are inherently **STABLE**

Because these vessels are already occluded, there is no rush to treat them, and medical therapy / other options can be explored

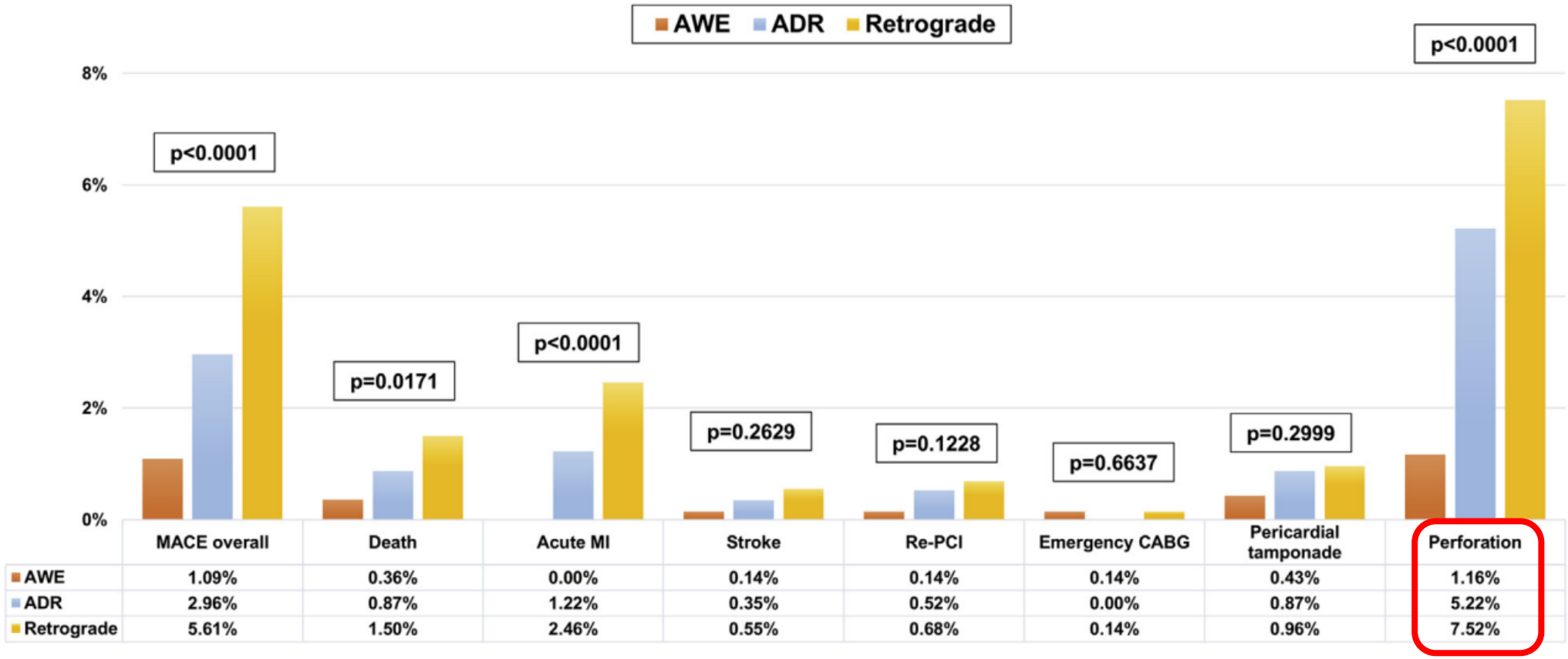
Courtesy of Ajay J. Kirtane

https://doi.org/10.1161/CIRCULATIONAHA.122.062714Circulation. 2022;0

Can Opening CTO Save the Life?



PROGRESS CTO Registry: In-Hospital Complications



	MACE overall	Death	Acute MI	Stroke	Re-PCI	Emergency CABG	Pericardial tamponade	Perforation
AWE	1.09%	0.36%	0.00%	0.14%	0.14%	0.14%	0.43%	1.16%
ADR	2.96%	0.87%	1.22%	0.35%	0.52%	0.00%	0.87%	5.22%
Retrograde	5.61%	1.50%	2.46%	0.55%	0.68%	0.14%	0.96%	7.52%

J Am Coll Cardiol Intv 2018;11:1325–35

Contemporary Series of CTO-PCI

Authors	Acronym	Study Period	Centers	Cases	Technical Success	Procedural Success	Overall MACE	Death	Acute MI	Stroke	TVR	Tamponade
Konstantinidis et al[89]	EURO-CTO registry	2008–2015	53	17626	85%	–	0.6%	0.2%	–	–	–	0.4%
Habara et al[88]	Japanese Retrograde Summit Registry	2012–2013	56	3229	–	88%	0.5%	0.2%	0.1%	0.1%	–	0.3%
Tajti et al[60]	PROGRESS-CTO	2012–2017	20	3055	87%	85%	3.0%	0.3%	0.7%	0.1%	0.2%	0.5%
Suzuki et al[31]	Japanese CTO-PCI Expert Registry	2014–2015	41	2846	90%	89%	<2%	0.2%	1.2%	0.2%	0.2%	0.4%
Maeremans et al[61]	RECHARGE	2014–2015	17	1253	89%	86%	2.6%	0.2%	0.2%	2.2%	0.1%	1.3%
Wilson et al[62]	UK Hybrid	2012–2014	7	1156	90%	—	1.6%	0.0%	0.8%	0.4%	0.0%	0.7%
Sapontis et al[3]	OPEN-CTO	2013–2017	12	1000	86%	85%	7.0%	0.9%	2.6%	0.0%	0.1%	–

14.5% of patients experienced at least 1 complication from OPEN CTO registry
(Salisbury et al, JACC CV Intv 2019)

Emmanouil S. Brilakis, CTO-PCI A Global Expert Consensus Document, Circulation 2019

JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 10, NO. 15, 2017

ISSN 1936-8798/$36.00
http://dx.doi.org/10.1016/j.jcin.2017.06.053

EDITORIAL COMMENT

Thousand Registries Are Not Worth a Randomized Trial

Also True for Chronic Total Occlusions?*

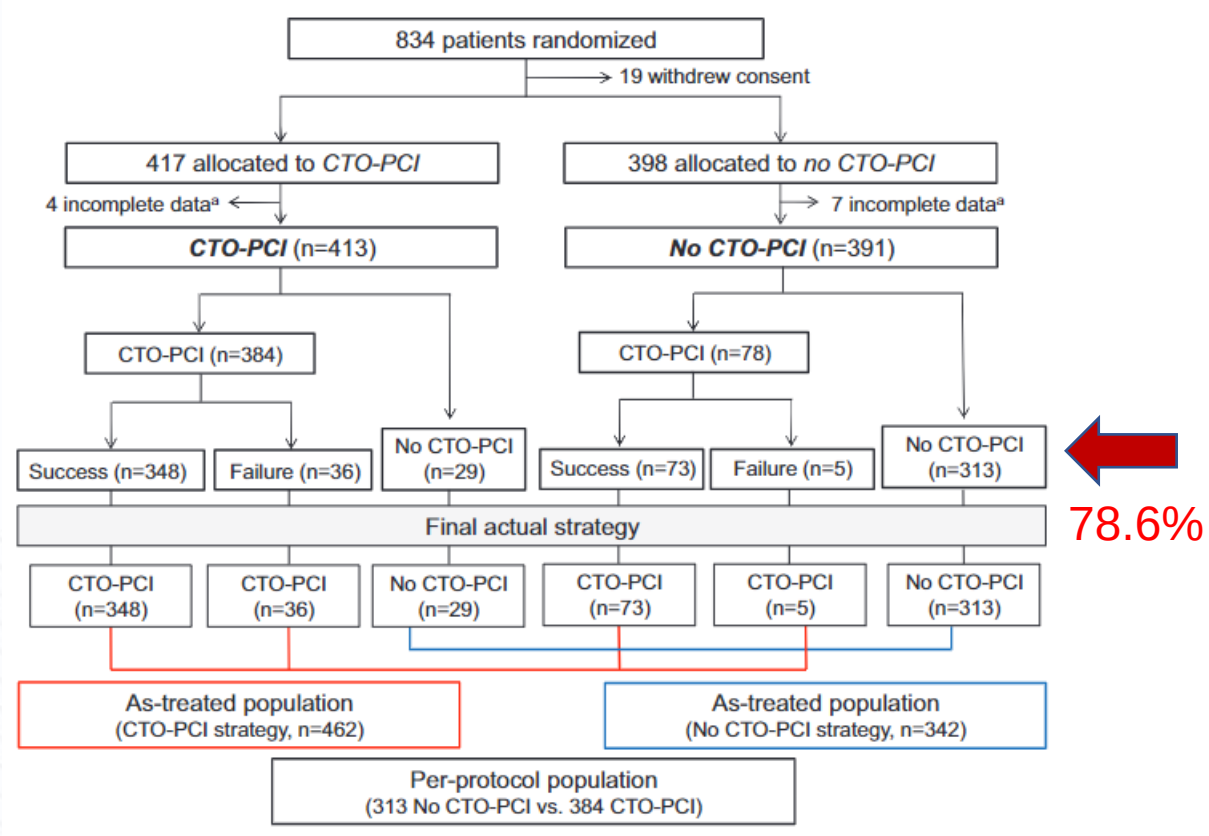
Carlo Di Mario, MD, PhD,[a,b] Carlotta Sorini Dini, MD,[a] Gerald S. Werner, MD, PhD[c]

The generally accepted principle is that registries complement the information provided by randomized trials, but only the rigor of the randomization process can eliminate the confounding factors, including the placebo effect, so frequent after interventional treatments, and ensure that true differences are present between conventional and novel therapies. Frequently, the large and significant differences observed in randomized trials lose some of their shine when applied to all-comers groups including suboptimal candidates for the tested therapies.

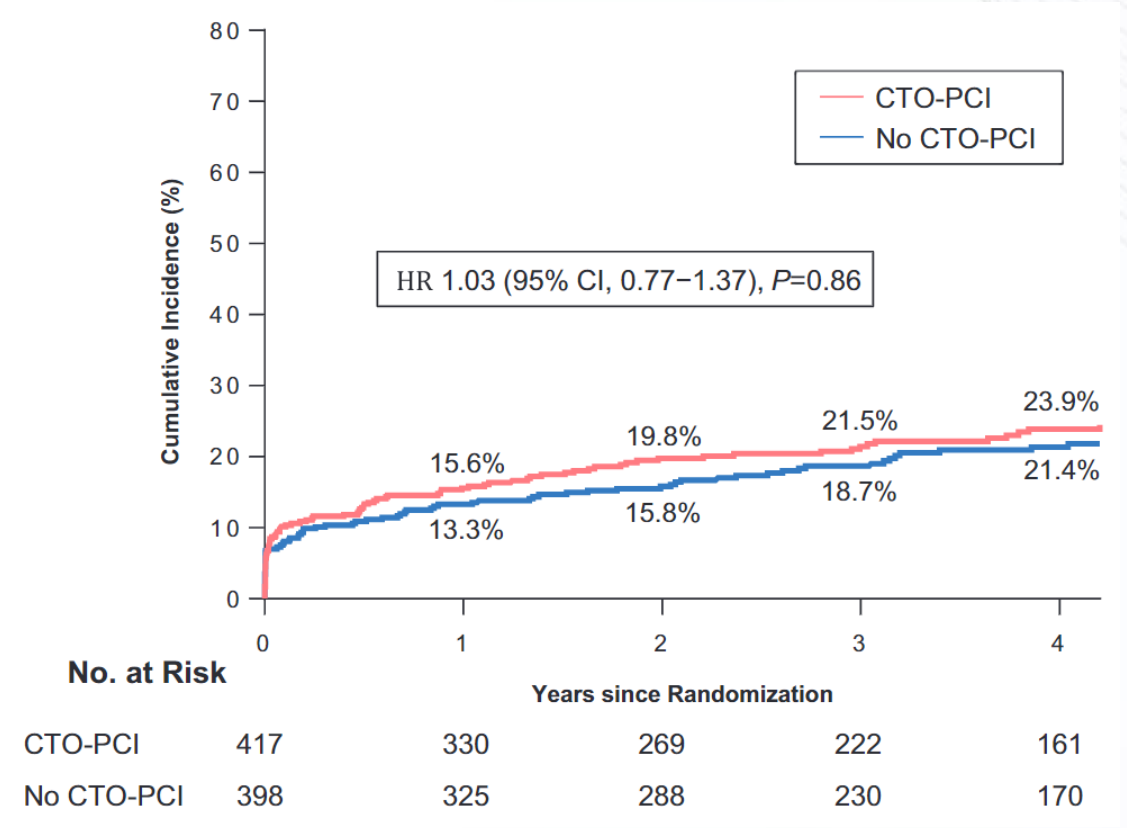
SEE PAGE 1523

complications than in this registry, DECISION CTO showed no difference in quality of life (QoL). In the OPEN-CTO (Outcomes, Patient Health Status, and Efficiency IN in Chronic Total Occlusion Hybrid Procedures) registry (5) in this issue of *JACC: Cardiovascular Interventions*, the stunning 90% technical success and 85% procedural success reported by the investigators are trimmed to 86% and 81%, respectively, by the core lab reviewing all angiograms. This is still a remarkable performance considering the

DECISION-CTO Trial



78.6%



Lee SW, Lee PH, Ahn JM, Park SJ et al Circulation. 2019;139:1674–1683

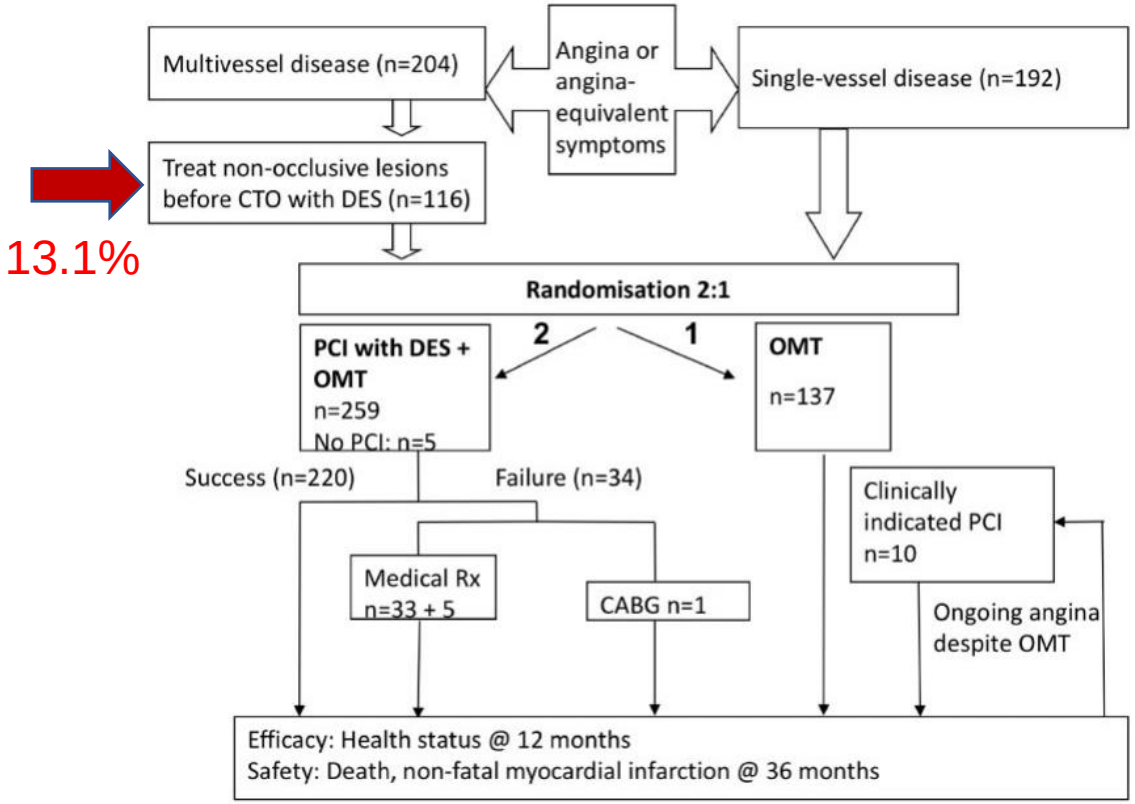
DECISION-CTO Trial

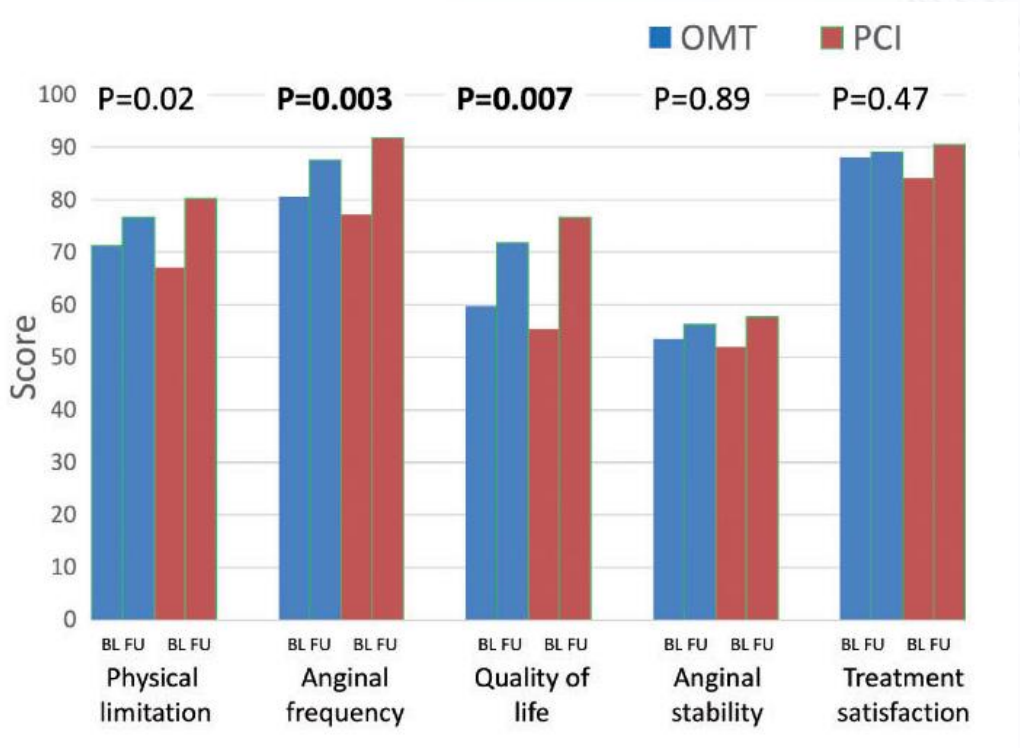
	CTO-PCI (n=417)	No CTO-PCI (n=398)	Crude HR (95% CI)	*P* Value
Primary end point: death, MI, stroke, or any revascularization	93 (22.3)	89 (22.4)*	1.03 (0.77–1.37)	0.86
Secondary end points				
Death	15 (3.6)	21 (5.3)	0.70 (0.36–1.37)	0.30
Cardiac cause	8 (1.9)	14 (3.5)	0.56 (0.24–1.34)	0.19
Noncardiac cause	7 (1.7)	7 (1.8)	0.99 (0.35–2.82)	0.99
Myocardial infarction	47 (11.3)	34 (8.5)	1.39 (0.90–2.15)	0.14
Periprocedural MI	41 (9.8)	30 (7.5)	1.37 (0.816–2.18)	0.19
Spontaneous MI	7 (1.7)	7 (1.8)	0.88 (0.30–2.57)	0.82
Stroke	6 (1.4)	10 (2.5)	0.61 (0.23–1.65)	0.33
Any revascularization	46 (11.0)	42 (10.6)	1.14 (0.75–1.73)	0.55
CTO vessel	33 (7.9)	30 (7.5)	1.13 (0.69–1.84)	0.63
Non-CTO vessel	29 (7.0)	23 (5.8)	1.34 (0.77–2.31)	0.30
Death, MI, or stroke	66 (15.8)	61 (15.3)	1.07 (0.75–1.51)	0.72
Cardiac death, MI, stroke, or any revascularization	86 (20.6)	82 (20.6)	1.02 (0.76–1.39)	0.88
Death, spontaneous MI, stroke, or any revascularization	64 (15.3)	69 (17.3)	0.91 (0.65–1.30)	0.59

Lee SW, Lee PH, Ahn JM, Park SJ et al Circulation. 2019;139:1674–1683

EURO-CTO Trial

The change in health status assessed by SAQ between baseline and 12 months





European Heart Journal (2018) 39, 2484–2493

EURO-CTO Trial

36 Months FU

	OMT (N=137)	PCI (N=259)	P value
Safety events	4 (2.9)	13 (5.0)	0.32
Cardiovascular death	2 (1.5)	7 (2.7)	0.42
Non-fatal MI	2 (1.5)	6 (2.3)	0.56
Ischemia-driven revascularization	25 (18.2)	19 (7.3)	0.0035
Cerebrovascular event	1 (0.7)	5 (1.9)	0.27
Stent thrombosis	0	1 (0.4)	
All cause death	***3 (2.2)***	***14 (5.4)***	***0.14***

TCT 2019

EXPLORE: MRI-Assessed LVEF at 4 months

280 STEMI pts with CTO randomized: CTO PCI (***73% success***) vs. no CTO PCI

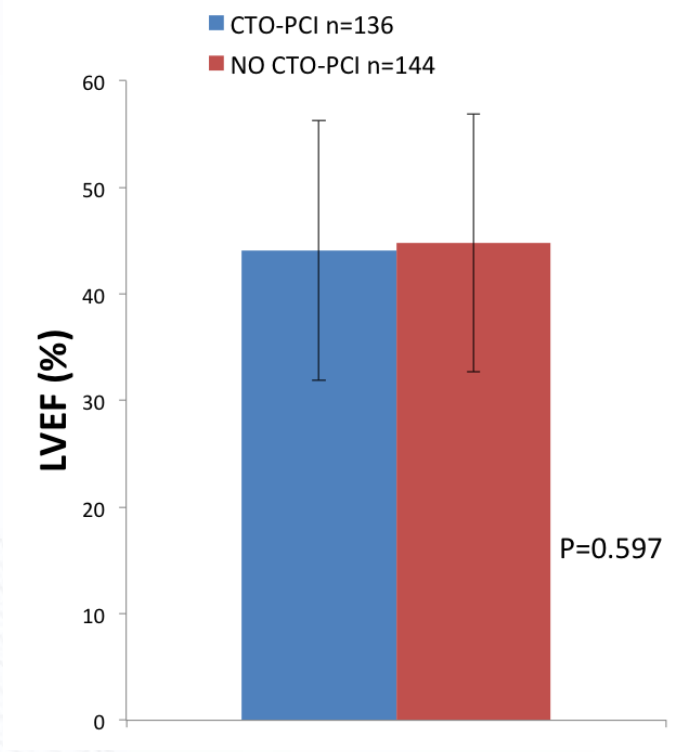


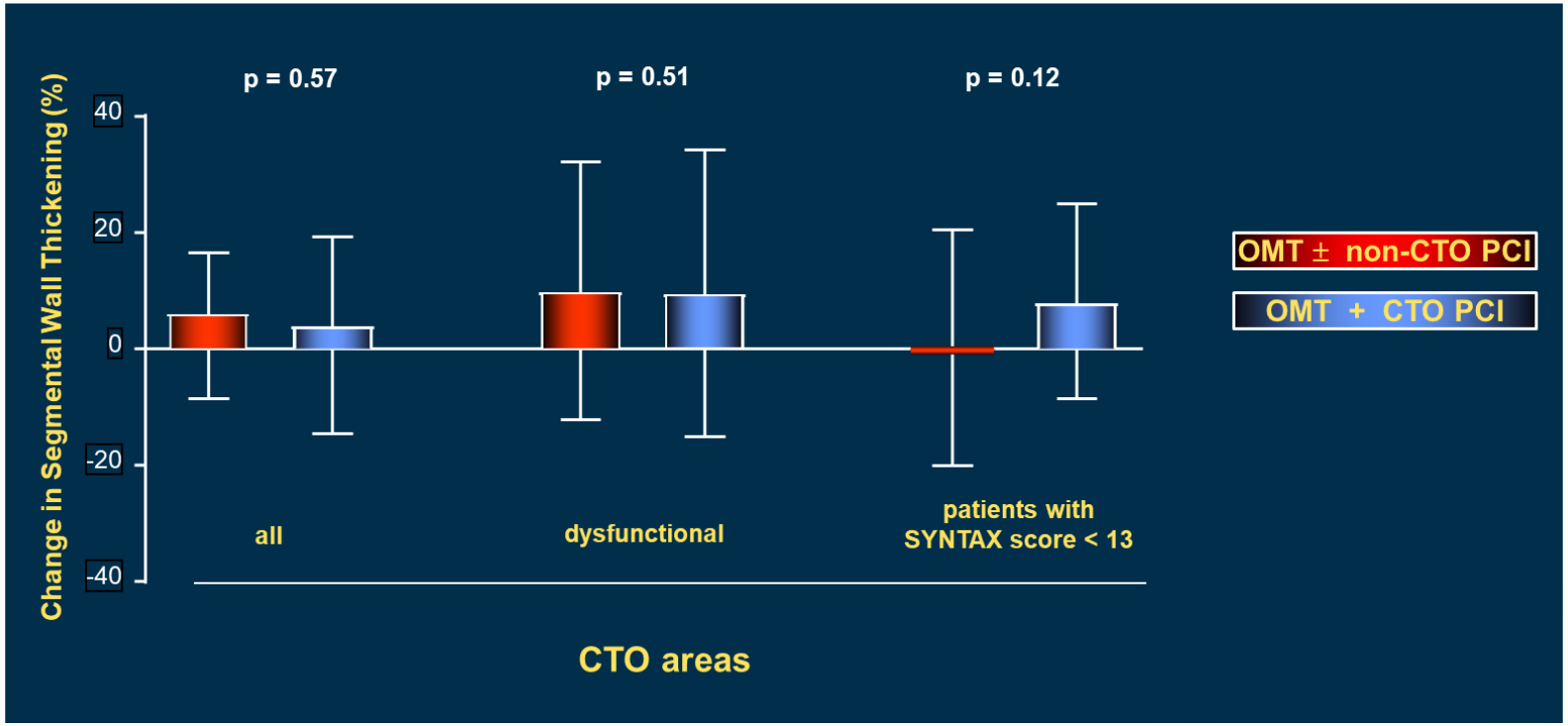
TABLE 4 Adjudicated Clinical Outcomes From Randomization to 4-Month Follow-Up

	CTO PCI (n = 148)	No CTO PCI (n = 154)	p Value
Major adverse cardiac events			
Cardiac death	4 (2.7)	0 (0.0)	0.056
Myocardial infarction	5 (3.4)	3 (1.9)	0.49
Periprocedural*	4 (2.7)	1 (0.6)	–
Spontaneous or recurrent	2 (1.4)	2 (1.3)	–
CABG operation	–	1 (0.6)	–
MACE	8 (5.4)	4 (2.6)	0.25

J Am Coll Cardiol 2016;68:1622–32

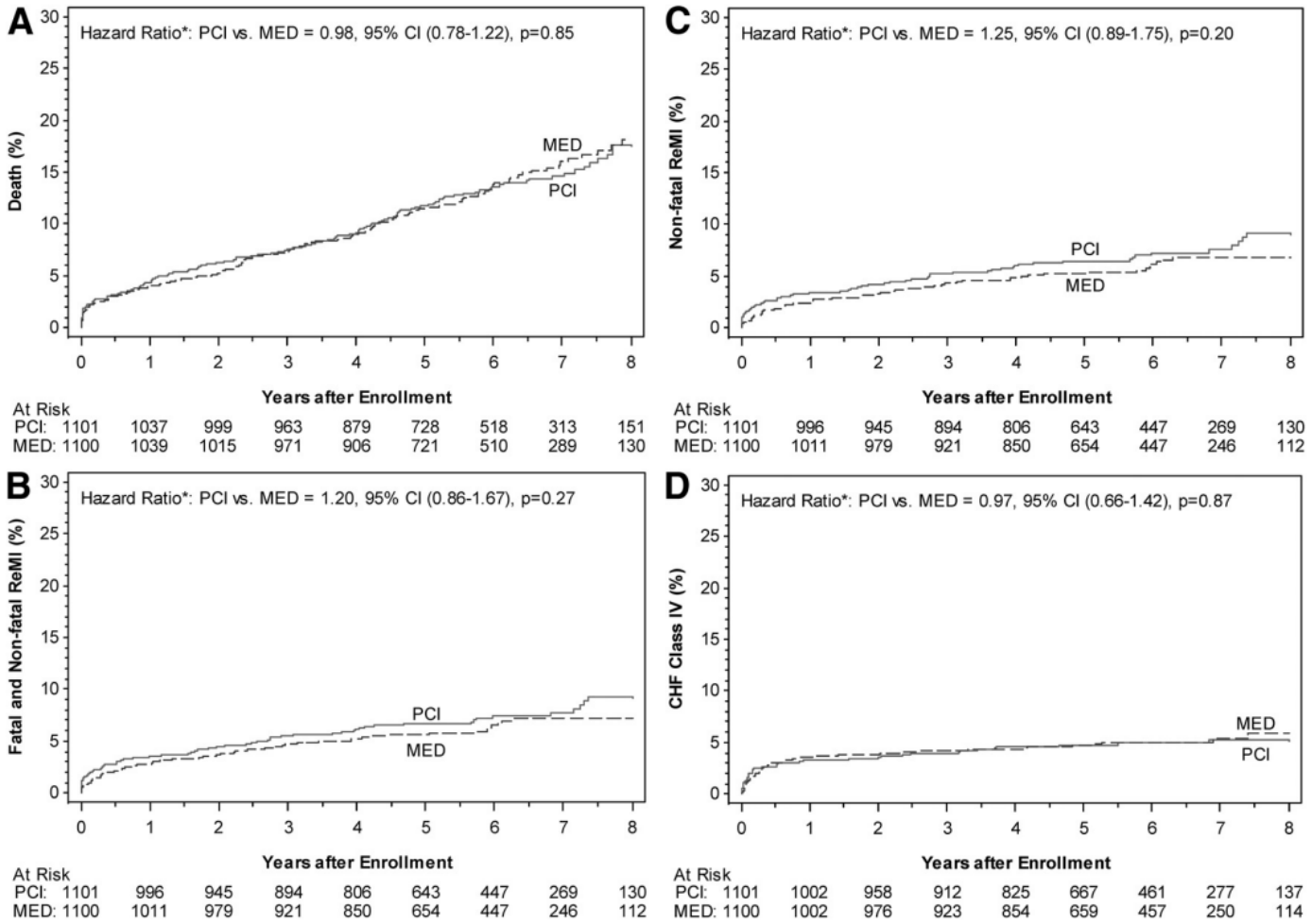
REVASC: Change in Segmental Wall Thickening at 6 Mo

205 CTO patients randomized to CTO PCI vs. no CTO PCI
(no CTO PCI group included 60% non-CTO PCI)
Mean EF 54.7% vs. 59.6%
Baseline SYNTAX Score 14 vs. 16; rSS 2 vs. 11



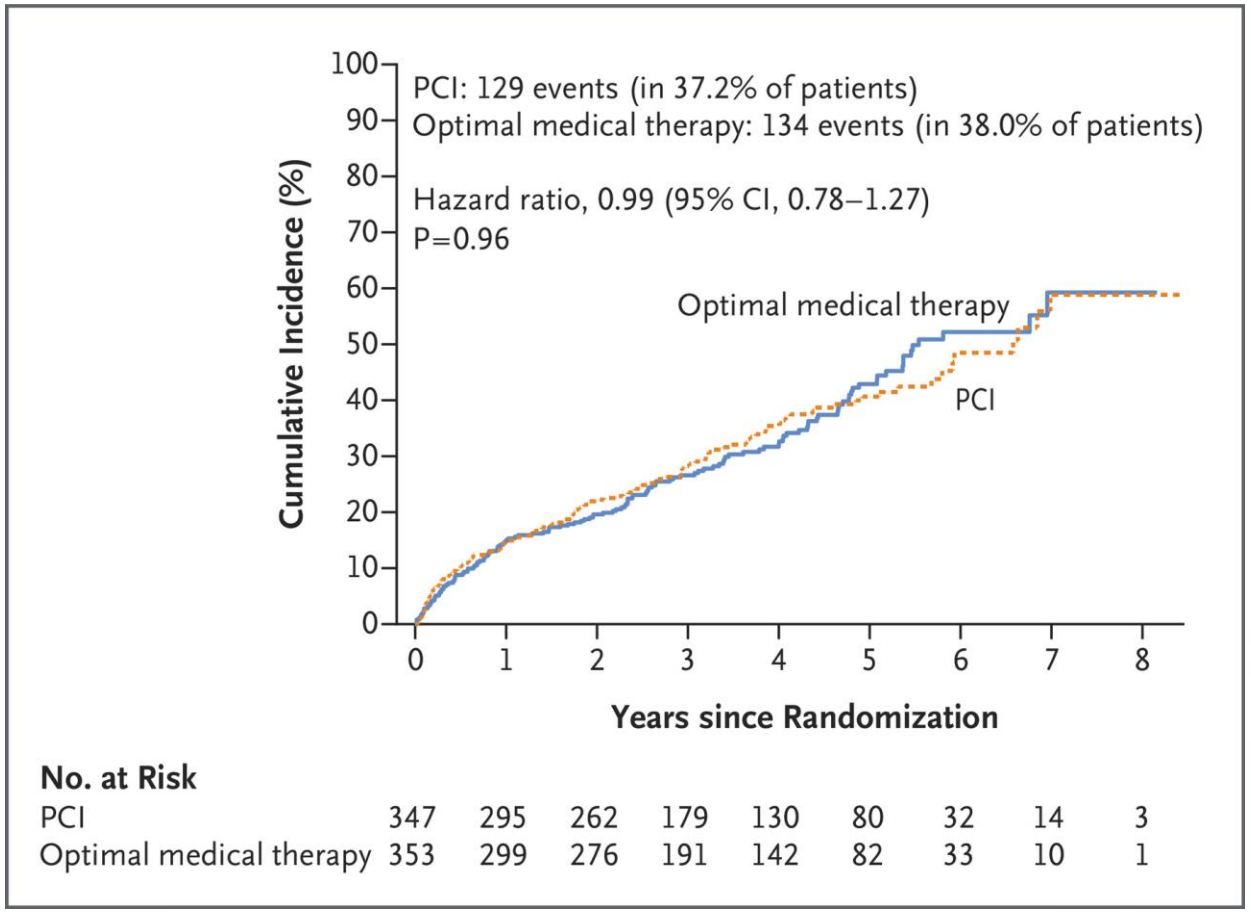
J Am Coll Cardiol Intv 2018;11:1982–91

OAT Trial: PCI vs. OMT for IRA TO >24 hours



Circulation. 2011;124:2320-2328

REVIVED-BCIS2: PCI vs. OMT in iCMP



N Engl J Med 2022; 387:1351-1360

Treatment of CTO

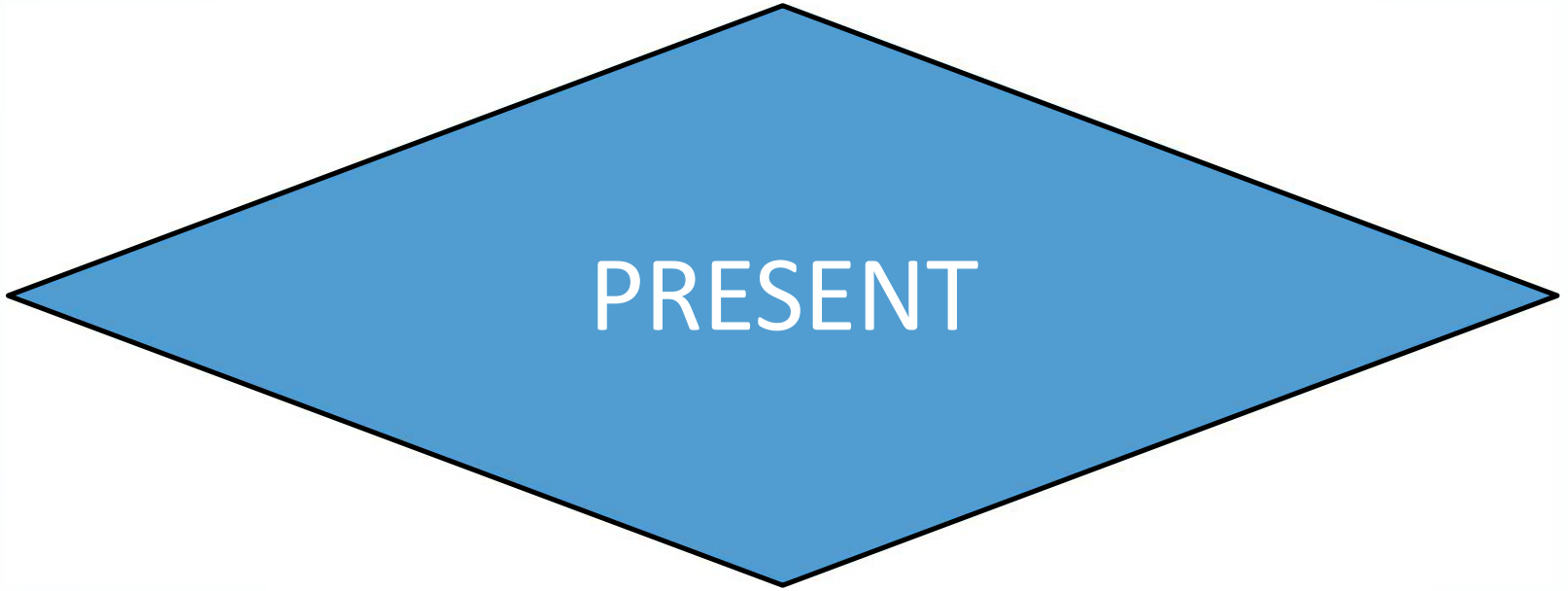
COR	LOE	Recommendation
2b	B-R	**In patients with suitable anatomy who have refractory angina on medical therapy, after treatment of non-CTO lesions, the benefit of PCI of a CTO to improve symptoms is uncertain.**

"Enthusiasm for treating these lesions was fueled by retrospective data suggesting improved outcomes for those patients who underwent successful recanalization compared with those who had failed. However, RCTs have not demonstrated improved function and have been equivocal with regard to symptoms."

CLASS 2b (WEAK)	Benefit ≥ Risk
Suggested phrases for writing recommendations: • May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain or not well-established	

LEVEL B-R	(Randomized)
• Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs	

- ❑ EUROCTO and DECISION CTO
- ❑ EXPLORE and REVASC


PRESENT

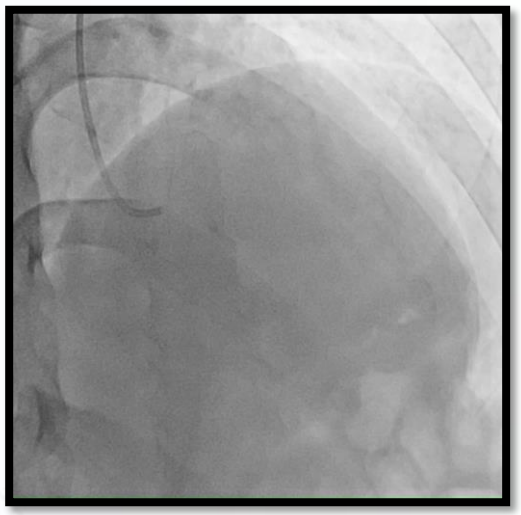
My Thought

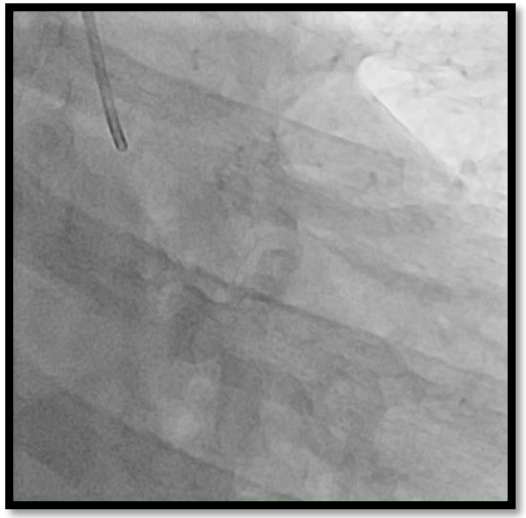
- The data in favor of CTO PCI are entirely for symptom relief. The CTO PCI was not associated with the improvement of survival or clinical outcomes.

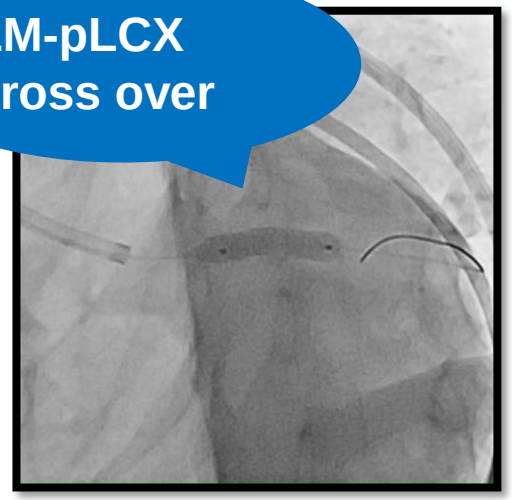
- The non-CTO, ischemia producing significant stenosis would be more relevant and safer target for symptom relief.

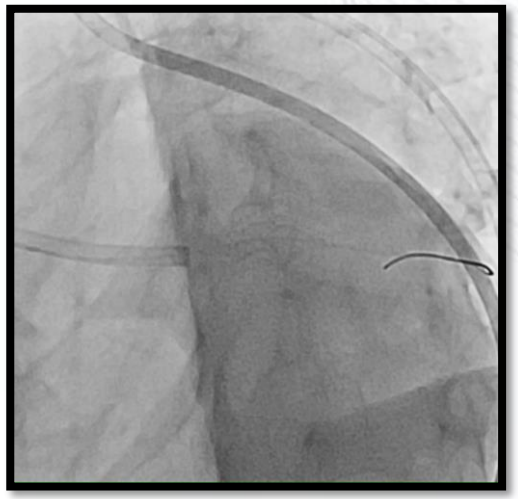
My CTO Case (3) : Non-CTO PCI, First

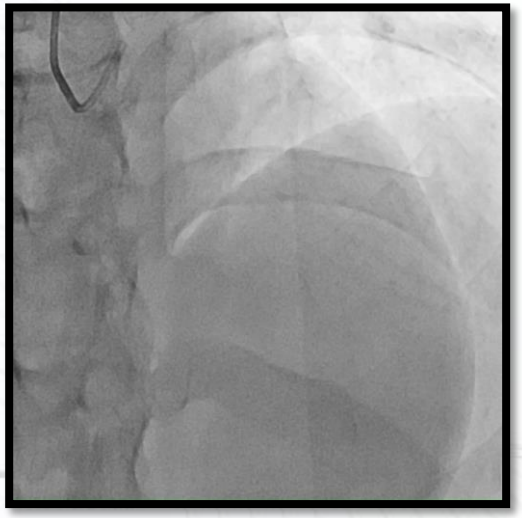
40 YO/F, EF= 55%, minimal effort chest pain

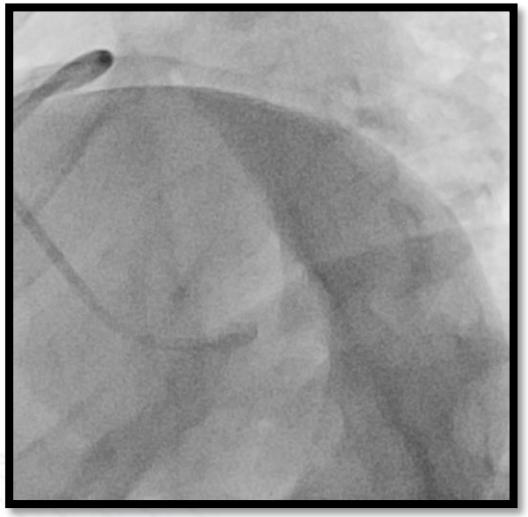






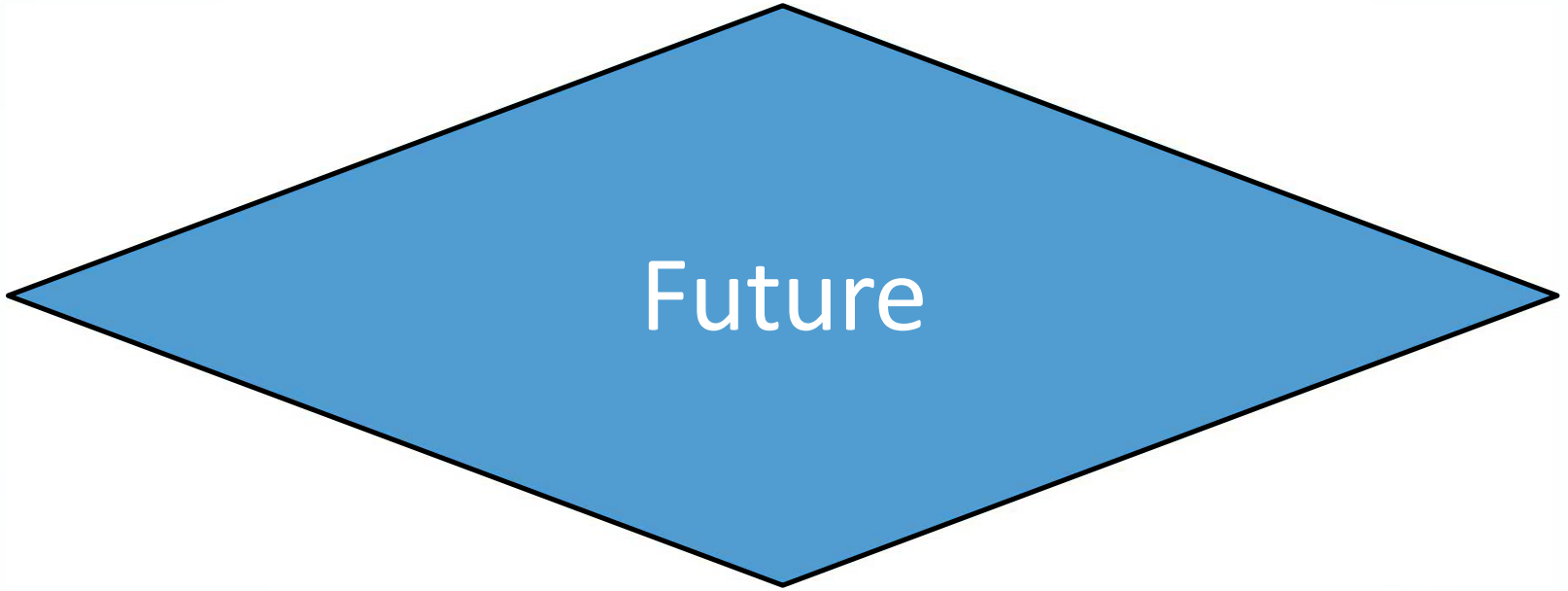






Sustained angina even after LM-LCX PCI -> MICAB

Fortunately, patient is doing very well without angina.

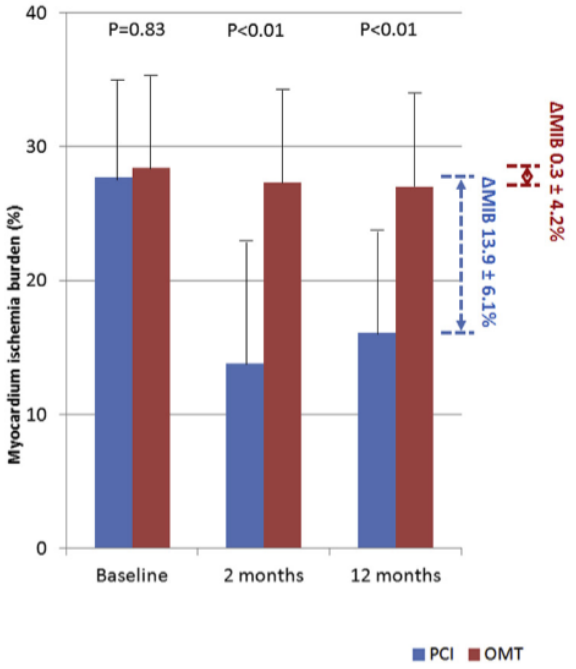

Future

The IMPACTOR-CTO Trial

39 patients in the PCI and 33 patients in OMT arms with Isolated RCA CTO

FIGURE 1 Changes in Inducible Myocardial Ischemia Burden and Quality-of-Life Parameters in the Percutaneous Coronary Intervention and Optimal Medical Therapy Groups

A



B

	Baseline			At 2 months			At 12 months		
	PCI group (n=39)	OMT group (n=33)	p	PCI group (n=39)	OMT group (n=33)	p	PCI group (n=39)	OMT group (n=33)	p
Physical Functioning, median (IQR)	40 (23; 45)	40 (30; 45)	0.42	45 (45; 75)*	41 (31; 45)	<0.01	45 (45; 70) *	40 (30; 45)	<0.01
Role Physical Functioning, median (IQR)	25 (0; 50)	25 (0; 75)	0.17	75 (50; 75) *	25 (25; 75)	<0.01	75 (50; 75) *	25 (25; 50)	<0.01
Bodily pain, median (IQR)	41 (22; 41)	41 (22; 51)	0.15	62 (41; 62) *	40 (40; 51)	<0.01	51 (41; 62) *	41 (32; 51)	<0.01
General Health, median (IQR)	25 (20; 45)	40 (25; 50)	0.07	50 (35; 57)	45 (20; 50)	0.02	50 (45; 55) *	40 (20; 50)	<0.01
Vitality, median (IQR)	30 (20; 38)	33 (25; 45)	0.22	45 (35; 50) *	35 (25; 45)	<0.01	45 (40; 50) *	33 (25; 40)	<0.01
Social Functioning, median (IQR)	50 (25; 54)	50 (25; 63)	0.43	75 (50; 75) *	50 (38; 75)	<0.01	63 (50; 75) *	50 (37; 63)	<0.01
Role-Emotional, median (IQR)	36 (33; 67)	38 (36; 69)	0.57	100 (67; 100) *	40 (34; 68)	<0.01	100 (66; 100) *	67 (33; 67)	<0.01
Mental Health, median (IQR)	40 (30; 46)	40 (32; 52)	0.22	52 (44; 62) *	40 (32; 52)	<0.01	52 (48; 60) *	40 (32; 48)	<0.01

(A) Inducible myocardial ischemia burden (MIB) at baseline and 2 and 12 months. **(B)** Short Form-36 Health Survey parameters at baseline and 2 and 12 months. *In comparison with baseline values ($p < 0.05$). IQR = interquartile range; OMT = optimal medical therapy; PCI = percutaneous coronary intervention.

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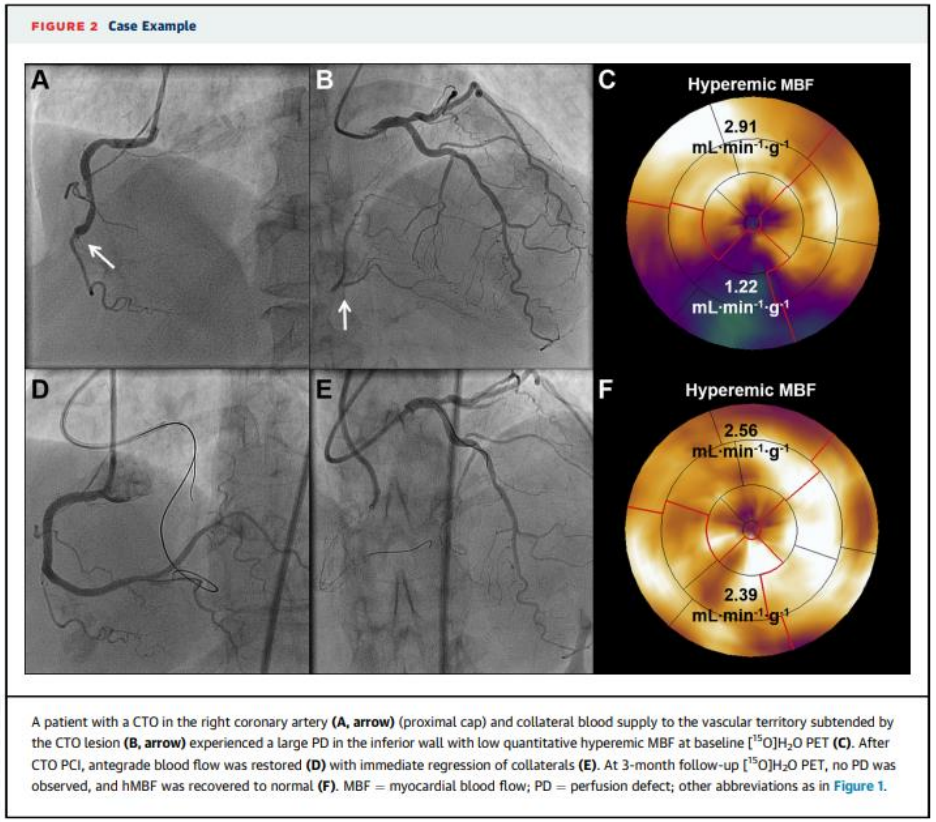
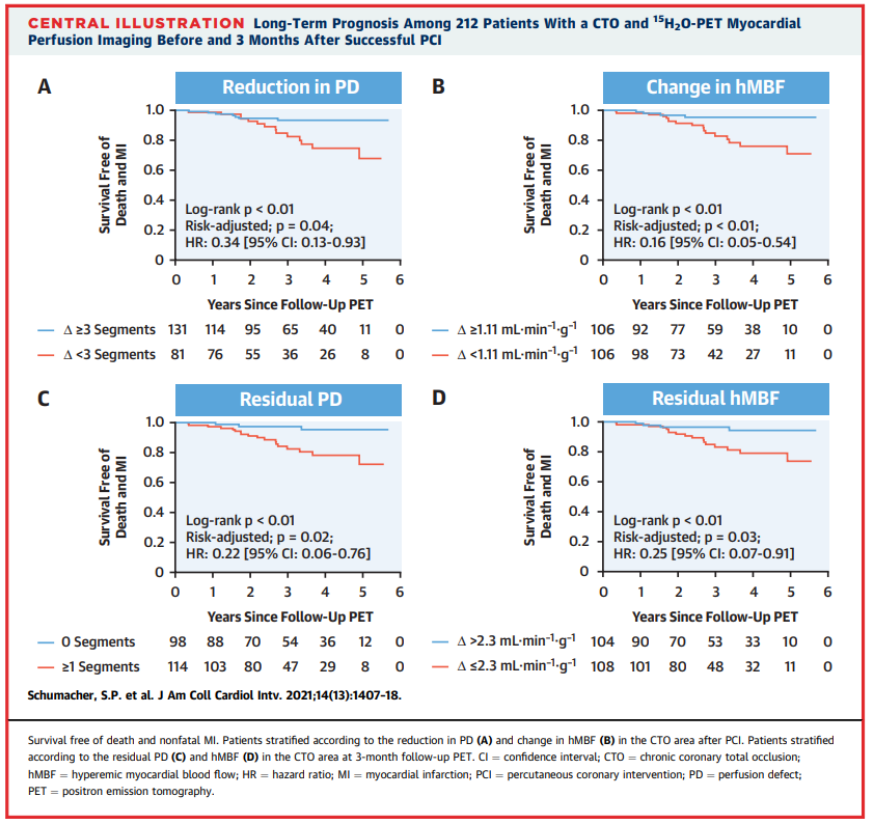
Ischemic Burden Reduction and Long-term Outcomes After CTO PCI





Patients with extensive ischemic burden reduction and no residual ischemia after CTO PCI had lower rates of ***All-Cause Death*** and ***Nonfatal MI***

J Am Coll Cardiol Intv 2021;14:1407–18

Ongoing Randomized Trials

ISCHEMIA-CTO Trial (NCT03563417)

Cohort A (N=1200)

- Population
  Asymptomatic (CCS < 2 and SAQ QoL>60) patients with ***myocardial ischemia (≥10%) in a territory supplied by CTO***
- Primary Endpoint: MACCE at 5 years

Cohort B (N=360)

- Population
  Symptomatic patients (CCS class ≥ 2 and/or SAQ QoL score≤60 after treating non-CTO lesions and after OMT) with ***myocardial ischemia (≥ 5%) in a territory supplied a CTO***
- Primary Endpoint: Quality of Life, SAQ at 6 months

NOBLE-CTO Trial (NCT03392415)

Randomized registry with option of crossover after 6months

Primary Outcome Measures (N=2000)

- All-cause mortality with minimum 6 months follow-up
- Quality of life assessment (SF-12v2) at: 6 months

Inclusion Criteria

- ≥1 CTO lesion amenable to PCI.
- Stable and stabilized coronary artery disease
- ***Symptoms and/or signs of reversible perfusion defect and/or angiographic/echocardiographic indication of reversible ischemia.***
- CTO lesion in a major coronary vessel supplying a significant myocardial territory (vessel diameter usually ≥3mm).