

CTO-PCI

Rationale and Evidences

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Agenda

- **Background on CTO**
 - Definition
 - Prevalence
 - The three unfavorable features of CTO
- **The six rationale against CTO revascularization**
 - Response
- **How should patients with CTOs be treated?**

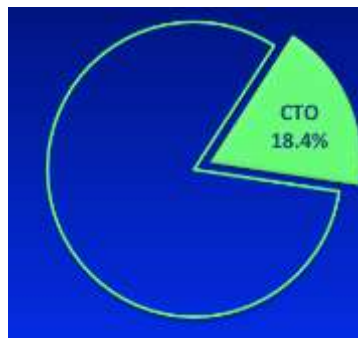
Definition

- An occluded coronary segment with coronary TIMI flow 0 for ≥ 3 months duration

EuroIntervention 2012;8:139–145

Incidence

14,439 coronary angiography



*The Canadian Multicenter Chronic Total Occlusions Registry.
J Am Coll Cardiol 59:991–997, 2012*

Prevalence

Selected subgroups	incidence
ACS	47%
CABG	89%
ICM	45%

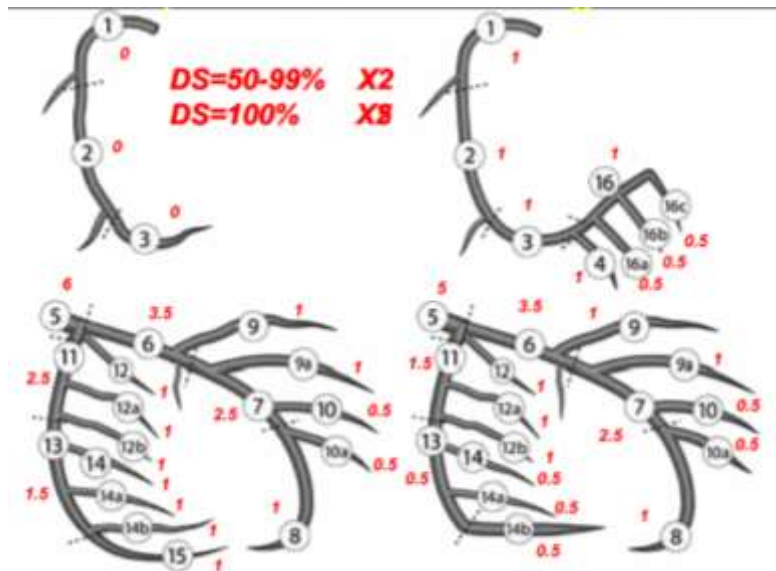
J Am Coll Cardiol 59:991–997
 Int J Cardiol 168:250–254
 Catheter Cardiovasc Interv 84:637–643
 Am J Cardiol 116:1358–1362

Feature # 1. CTO patients: High risk profile

	CTO Group (n = 1,697)	Control Group (n = 7,680)	p Value
Age, yrs	66 ± 11	64 ± 12	<0.001
Male	1,365 (80)	5,391 (70)	<0.001
Diabetes mellitus	573 (34)	1,975 (26)	<0.001
Hypertension	1,254 (75)	5,115 (68)	<0.001
Hyperlipidemia	1,374 (82)	5,826 (78)	<0.001
Prior MI	654 (40)	1,704 (23)	<0.001
Prior PCI	376 (22)	1,631 (22)	0.51
Smoker			
Current	419 (33)	1,611 (24)	<0.001
Heart failure	204 (12)	677 (9)	<0.001
Peripheral vascular disease	129 (8)	310 (4)	<0.001
Cerebrovascular disease	144 (9)	499 (7)	0.003
Dialysis	31 (2)	107 (1)	0.18
Malignancy	72 (4)	372 (5)	0.52
Indication type			
Acute coronary syndrome	752 (46)	4,352 (67)	<0.001
Stable coronary disease	881 (54)	2,163 (33)	<0.001

The Canadian Multicenter Chronic Total Occlusions Registry. J Am Coll Cardiol 59:991–997, 2012

Feature # 2: CTO lesions are complex



Feature # 2: CTO lesions are complex

- Among patients with CTO(s) the CTO lesion(s) accounted for 67%±26% of the total SS
- The proportion of patients with a CTO
 - 12% (478/3838) among pts with low SS (<22)
 - 54% (240/445) among pts with intermediate SS (≥22 and <32)
 - 64% (116/180) among pts with high (≥32) SS

Feature # 3: CTO -PCI is challenging

CTO → non-CTO

PCI to non-CTO

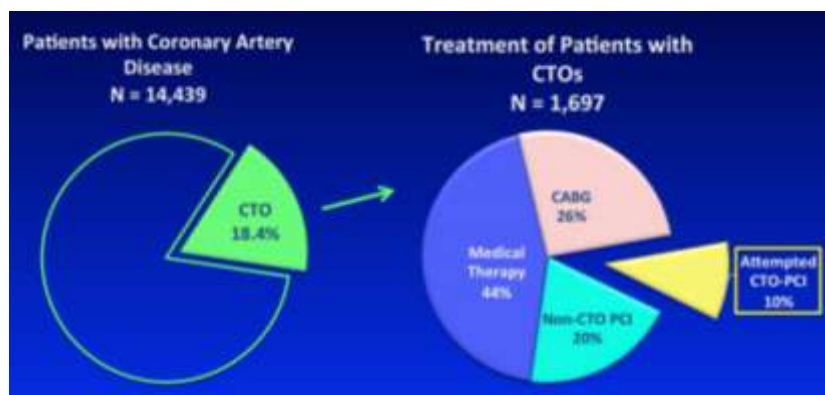
- Bifurcation
- Calcification
- Tortuous
- Diffuse disease

PCI to other lesions

Complications

- Perforation
- Tamponade
- Bleeding
- Thrombosis

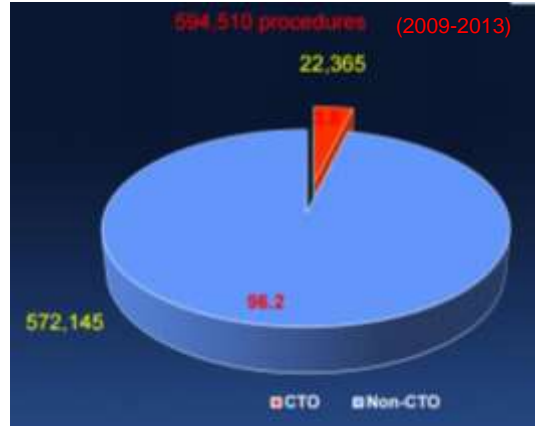
Feature # 3: CTO -PCI is challenging



*The Canadian Multicenter Chronic Total Occlusions Registry.
J Am Coll Cardiol 59:991-997, 2012*

Feature # 3 : CTO -PCI is challenging

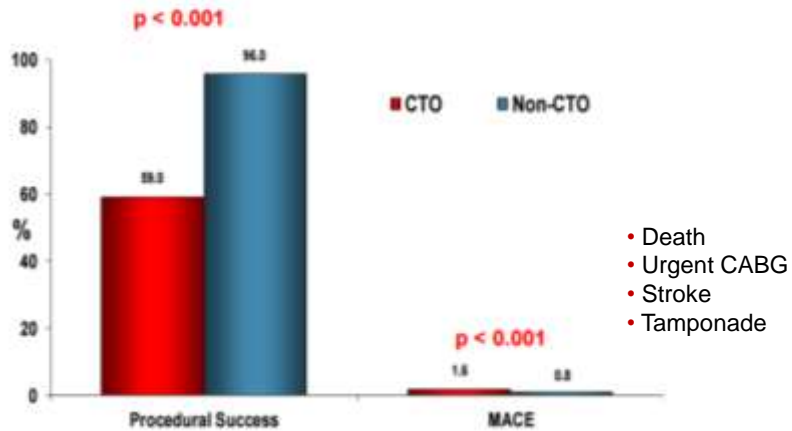
CTO PCI represents 3.8% of the total PCI volume for SIHD



J Am Coll Cardiol Intv 2015;8:245-53

Feature # 3 : CTO -PCI is challenging

594,510 procedures (2009-2013)



J Am Coll Cardiol Intv 2015;8:245-53

Feature # 3: CTO -PCI is challenging

NCDR (2009 – 2013): 22,365 CTO

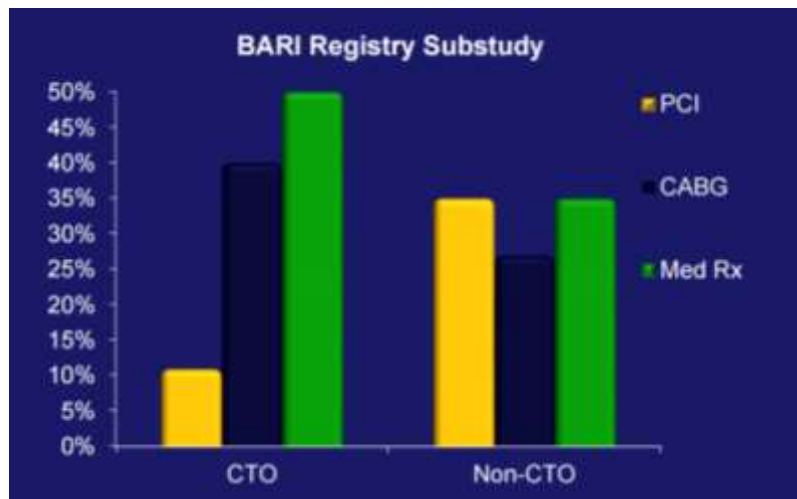
TABLE 2 Success and MACE Rates of CTO PCI Over Time

Outcome	Total (N = 22,365)	2009 (n = 2,695)	2010 (n = 6,373)	2011 (n = 6,161)	2012 (n = 5,650)	2013 (n = 1,486)	p Value
CTO PCI as percentage of total PCI volume	22,365 of 594,510 (3.8)	2,695 of 84,483 (3.2)	6,373 of 183,649 (3.5)	6,161 of 160,072 (3.8)	5,650 of 135,331 (4.2)	1,486 of 30,975 (4.8)	<0.001
Procedural success	13,077 (58.5)	1,495 (55.5)	3,637 (57.1)	3,645 (59.2)	3,380 (59.8%)	920 (61.9)	<0.001
MACE	357 (1.6)	50 (1.9)	103 (1.6)	104 (1.7)	81 (1.4)	19 (1.3)	0.108



J Am Coll Cardiol Intv 2015;8:245–53

CTO: CABG referral



Christofferson et al. Am J Cardiol 2005

CTO-PCI: study data

A Weighted Meta-Analysis of 18,061 Patients From 65 Studies

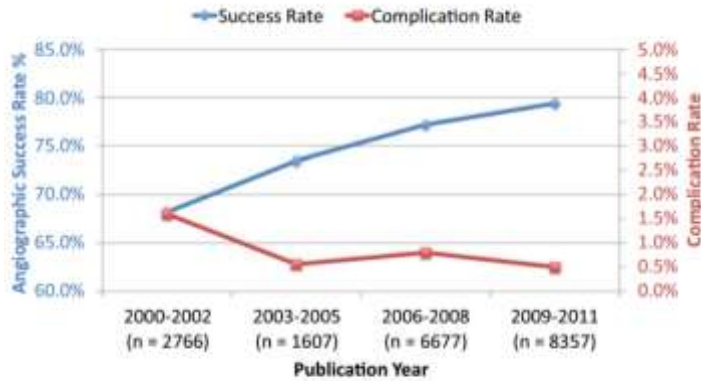


Figure 3. Temporal Trends in Cumulative Angiographic Success Rates and Major Procedural Complication Rates

J Am Coll Cardiol Intv 2013;6:128–36

Angiographic Success and Procedural Complications in Patients Undergoing Percutaneous Coronary Chronic Total Occlusion Interventions

A Weighted Meta-Analysis of 18,061 Patients From 65 Studies

Conclusions CTO PCI is currently performed infrequently in the United States for stable coronary artery disease and is associated with lower procedural success and higher complication rates compared with non-CTO PCI. Procedural success was associated with several patient factors and operator experience. (J Am Coll Cardiol Intv 2015;8:245-53)

- Patients: heterogeneous
- Operators: variable experience
- Selection bias
- Treatment bias

Procedural Success and Complications in Patients Undergoing Percutaneous Coronary Chronic Total Occlusion Interventions: A Report From the National Cardiovascular Data Registry (NCRD) CathPCI Registry

CONCLUSIONS CTO PCI is currently performed infrequently in the United States for stable coronary artery disease and is associated with lower procedural success and higher complication rates compared with non-CTO PCI. Procedural success was associated with several patient factors and operator experience. (J Am Coll Cardiol Intv 2015;8:245-53) © 2015 by the American College of Cardiology Foundation.

J Am Coll Cardiol Intv 2015;8:245–53

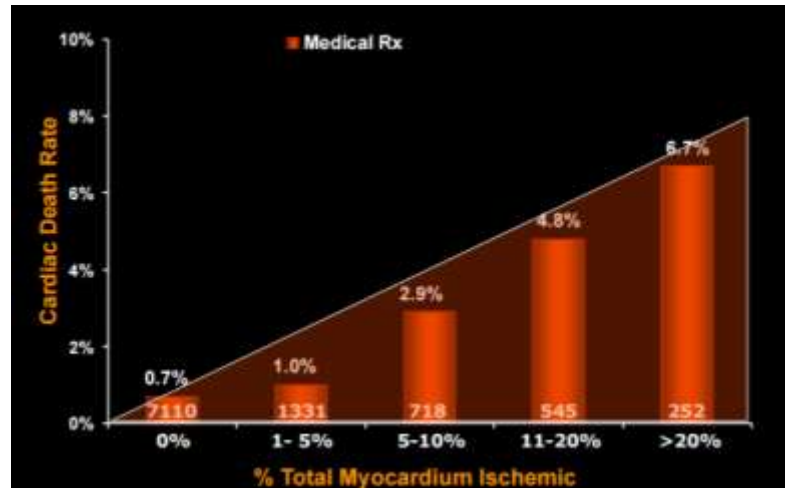
CTO-PCI: no need...

1. CTOs can not get any worse ; therefore pts are not at risk
2. CTOs represent stable CAD (COURAGE patients)
3. CTOs is well collateralized; therefore carry minimal risk
4. I have turned a MVD into a single vessel disease
5. No RCT to show benefit
6. CTO- PCI procedure: complex, complications, cost

CTO-PCI: no need...

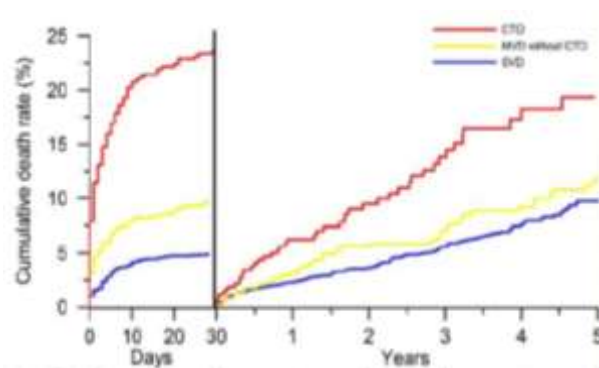
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1. Ischemia



Circulation. 2003;107:2900-2907

2. Improved Tolerability of ACS



	30 day mortality	5 year mortality
CTO	3.6 (2.6-4.7)*	1.9 (1.4-2.8)*
MVD without CTO	1.6 (1.2-2.2)*	1.1 (0.8-1.6)

* p ≤ 0.01

J Am Coll Cardiol Intv 2009;2:1128-34

3. Arrhythmia Risk

VACTO study

162 ICM patients with ICD for 1st prevention (CTO in 44%)

Table 2. Cumulative Event Rates for Appropriate ICD Therapy

Primary Prevention, % (95% CI)	
Global	No. CTO
1 y	13 (8-16)
2 y	16 (10-23)
3 y	23 (15-31)

Table 3. Univariable and Multivariable Predictors of ICD Therapy

Variable	Univariable		Multivariable	
	HR (95% CI)	P	HR* (95% CI)	P
CTO	2.9 (1.3-6.2)	0.007	3.5 (1.5-8.3)	0.003

Table 4. Multivariable Predictors of Mortality

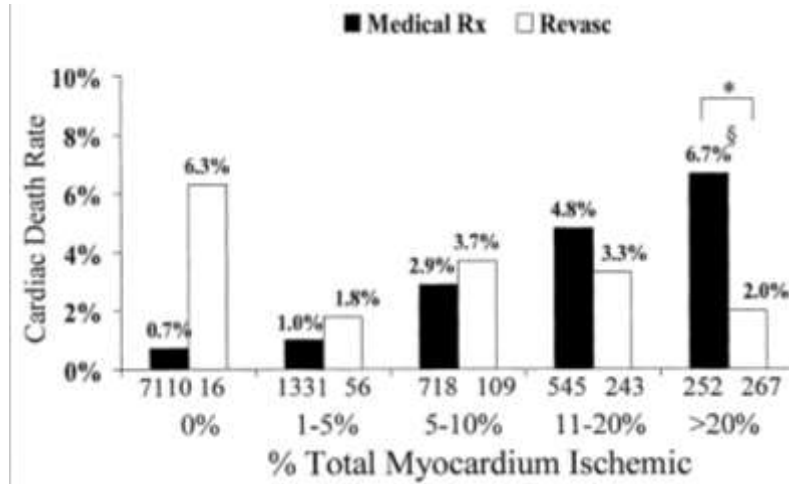
Variable	Multivariable Analysis	
	HR (95% CI)	P
Absence of β -blocker	6.3 (1.4-28.0)	0.02
CTO	5.6 (1.4-21.8)	0.01
NYHA class \geq III	4.7 (1.3-17.1)	0.02
Age (per 5-y increase)	1.5 (1.0-2.3)	0.05

Circ Arrhythm Electrophysiol 2012;5:147-54

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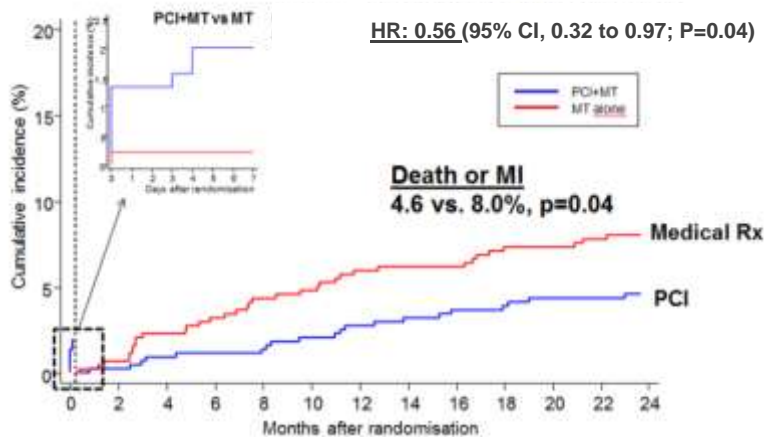
Ischemia



Circulation. 2003;107:2900-2907

Fractional Flow Reserve–Guided PCI for Stable Coronary Artery Disease

FAME 2: Two years FU



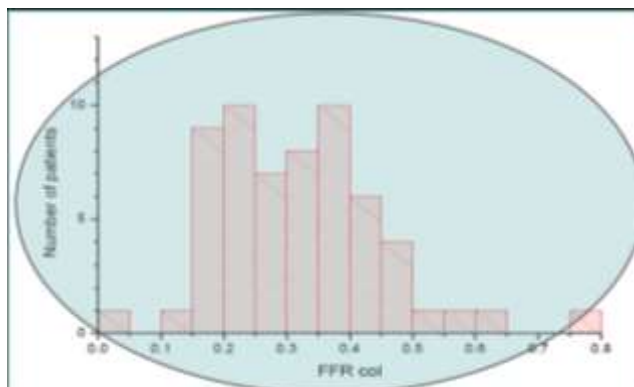
NEJM 2014; 371:13

CTO-PCI: no need...

1. Can not get any worse ; therefore not at risk for ACS/AMI
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3. **CTOs is well collateralized; therefore carry minimal risk**
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Ischemia

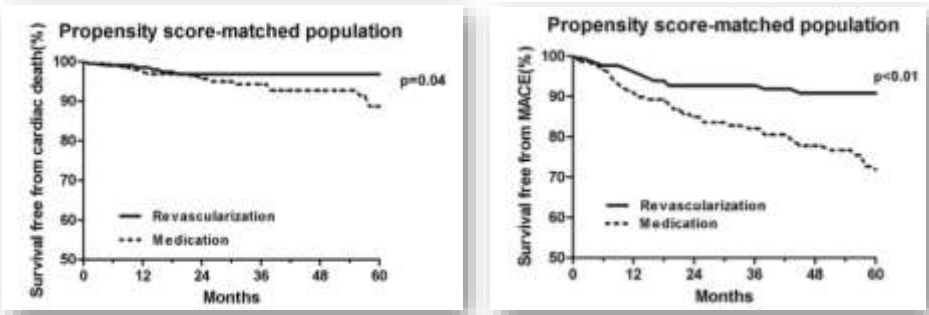
CTO is well collateralized and therefore minimal risk



Werner GS et al, European Heart Journal 2006

Collaterals..

738 CTO patients with well developed collaterals
Revascularized (n= 502) vs. medical (n= 236)



Cardiac death (HR: 0.27; 95% CI: 0.09 to 0.80; p = 0.02)
MACE (HR: 0.44; 95% CI: 0.23 to 0.82; p= 0.01)

J Am Coll Cardiol Intv 2015;8:271-9

Collaterals..

738 CTO patients with well developed collaterals
Revascularized (n= 502) vs. medical (n= 236)

TABLE 4 Clinical Outcomes in Propensity-Matched Patients (n = 430)

	Medication (n = 215)	Revascularization (n = 215)	HR (95% CI)	p Value
All-cause death	39 (18.1)	16 (7.4)	0.23 (0.10-0.53)	<0.01
Cardiac death	20 (9.3)	9 (4.2)	0.27 (0.09-0.80)	0.02
MI	1 (0.5)	2 (0.9)	2.00 (0.18-22.06)	0.57
Repeat revascularization*	33 (15.3)	14 (6.5)	0.59 (0.27-1.29)	0.18
MACE†	53 (24.7)	23 (10.7)	0.44 (0.23-0.82)	0.01

Values are n (%). *Repeat revascularization included target vessel revascularization-PCI, non-target vessel revascularization-PCI, and CABG. †Major adverse cardiac events (MACE) included cardiac death, MI, and repeat revascularization with PCI or CABG.

J Am Coll Cardiol Intv 2015;8:271-9

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Complete revascularization

Meta-analysis : 28 studies ; 83,695 patients with MVD ; Fu: 4.7 years.

Meta-analysis: Outcomes Based on Revascularization Strategy for Multivessel Disease

	RR	95% CI
All-Cause Mortality		
Overall	0.73	0.66-0.81
CABG Subgroup	0.76	0.63-0.90
PCI Subgroup	0.73	0.64-0.82
MI	0.74	0.64-0.85
Repeat Revascularization	0.77	0.66-0.88

Catheter Cardiovasc Interv. 2016;87:3-12

CTO and IR

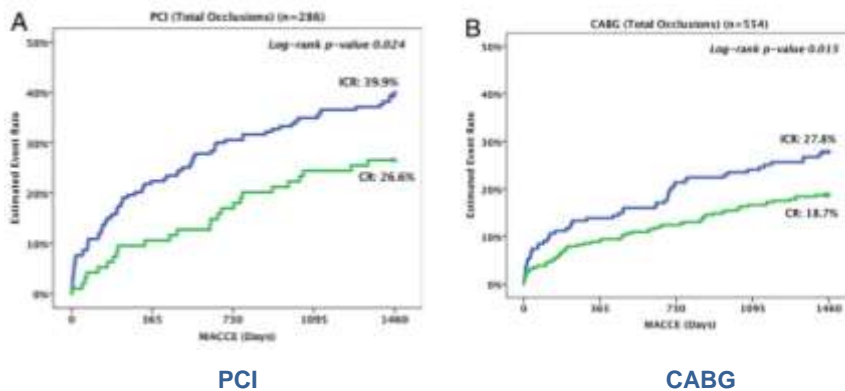
Independent predictors of IR in all comers PCI SYNTAX population

Anatomical/Clinical Characteristic	OR (95% CI)	p Value
PCI-treated patients		
TO	2.70 (1.98-3.67)	<0.001
Any RCA lesion	2.12 (1.33-3.38)	0.002
Left arterial dominance	1.81 (1.26-2.60)	0.001
Additive EuroSCORE ≥ 6	1.58 (1.18-2.13)	0.002
Number of lesions*	1.44 (1.29-1.59)	<0.001
Hyperlipidemia	1.49 (1.08-2.06)	0.015
Any tortuosity	1.39 (1.04-1.86)	0.025
Total bifurcation/trifurcations*	1.32 (1.13-1.53)	<0.001

J Am Coll Cardiol 2013;61:282-94

CTO and IR

CTO patients with IR: more MACCE over 4 year FU
(both PCI and CABG)



J Am Coll Cardiol 2013;61:282-94

CABG is not a default option

SYNTAX CTO sub-study

	PCI	CABG
CTO	27%	27%
Successful CTO revascularization	49.4%	68.1%
Complete revascularization		49.6%

J Am Coll Cardiol 2013;61:282–94

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Guidelines downgraded CTO-PCI

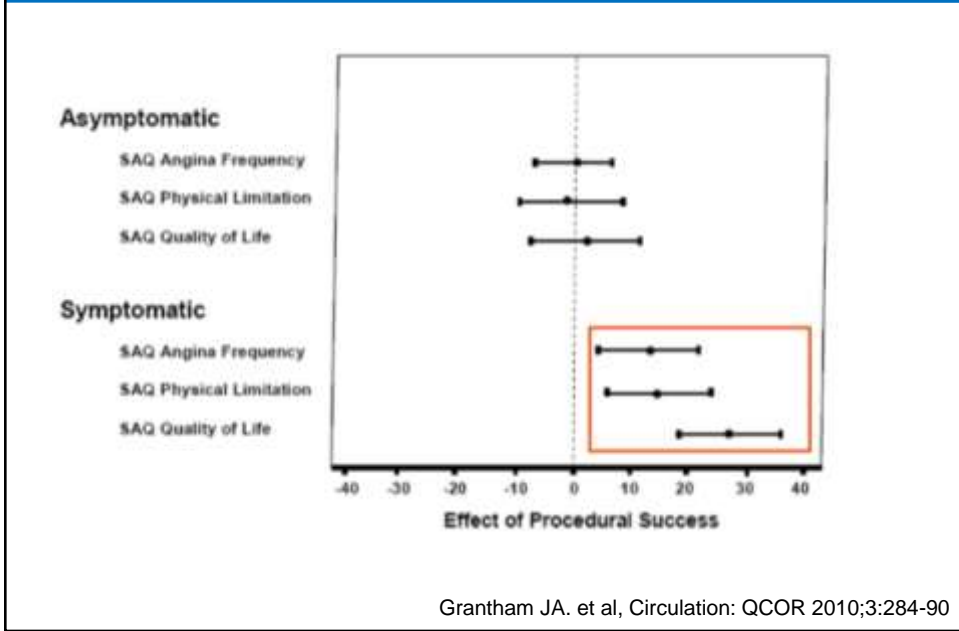
Table 4 CTO PCI in recent European and North American guidelines

Guidelines	Specific CTO guidelines	Class of recommendation	Level of evidence	Recommendations
European	Yes	IIa	B	• 'Percutaneous recanalization of CTOs should be considered in patients with expected ischaemia reduction in a corresponding myocardial territory and/or angina relief'
		IIb	C	• 'Retrograde recanalization of CTOs may be considered after a failed antegrade approach or as the primary approach in selected patients'
American	Yes	IIa	B	• 'PCI of a CTO in patients with appropriate clinical indications and suitable anatomy is reasonable when performed by operators with appropriate expertise'

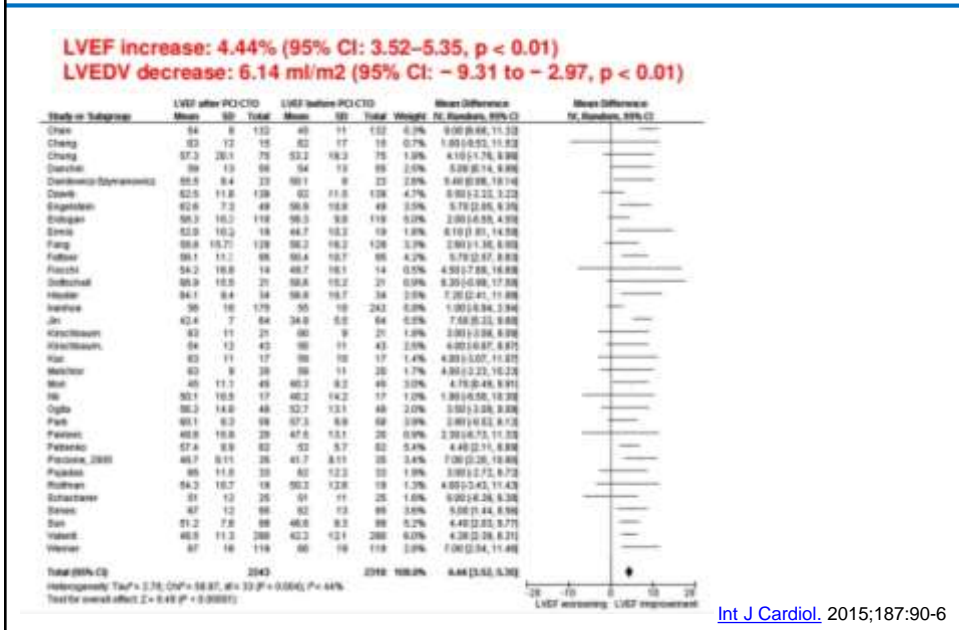
Is this true?!!

- Lack of evidence of benefit does not mean evidence of lack of benefit ...

1. Angina & QOL

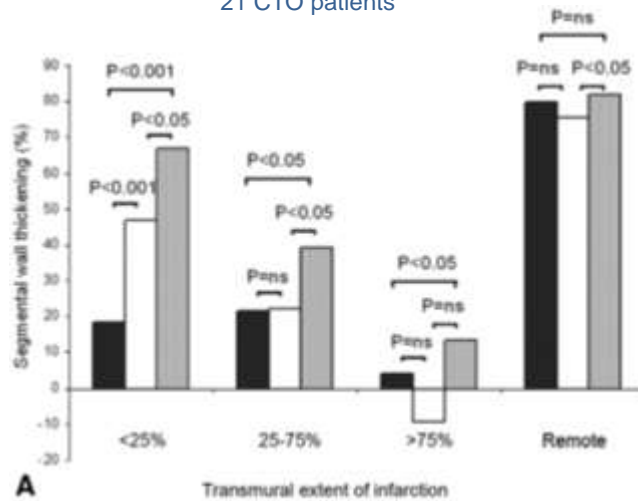


2. LV function



2. LV function

Relation between functional recovery after recanalization and Transmural scar by CMR
21 CTO patients



Am J Cardiol 2008;101:179-185

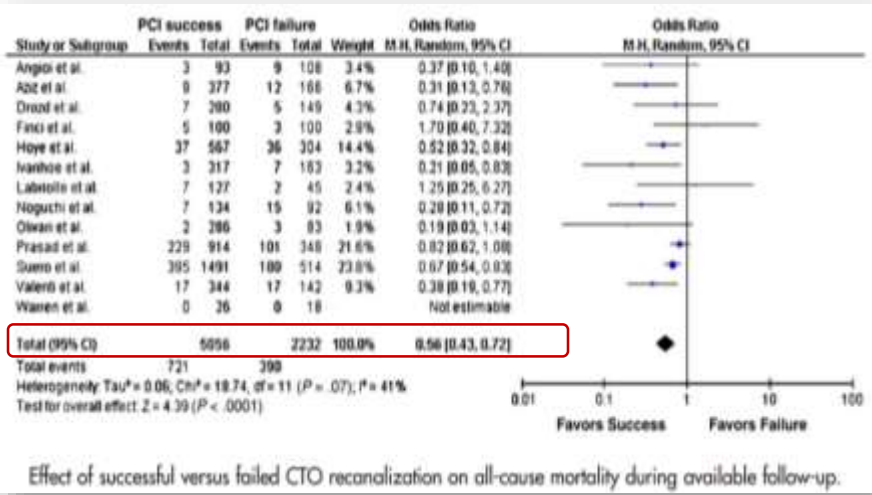
3. Mortality

Table 1. Effect of Successful Versus Failed CTO PCI in All-Cause Mortality During Long-Term Follow-Up

First Author, Year (Ref. #)	Follow-Up (yrs)	PCI Success (n)	PCI Failure (n)	OR/HR, 95% CI
Finci et al., 1990 (5)	2	100	100	OR: 1.70, 0.40-7.32
Warren et al., 1990 (10)	2.6	26	18	N/A
Ivanhoe et al., 1992 (6)	4	317	163	OR: 0.21, 0.05-0.83
Angioi et al., 1995 (11)	3.6	93	108	OR: 0.37, 0.10-1.40
Noguchi et al., 2000 (12)	4.3	134	92	OR: 0.28, 0.11-0.72
Suero et al., 2001 (13)	10	1,491	514	OR: 0.67, 0.54-0.83
Olivari et al., 2003 (7)	1	289	87	OR: 0.19, 0.03-1.14
Hoye et al., 2005 (14)	4.5	567	304	OR: 0.52, 0.32-0.84
Droad et al., 2006 (15)	2.5	298	161	OR: 0.74, 0.23-2.37
Aziz et al., 2007 (16)	1.7	377	166	OR: 0.31, 0.13-0.76
Prasad et al., 2007 (17)	10	914	348	OR: 0.82, 0.62-1.08
Valenti et al., 2008 (4)	1	344	142	OR: 0.38, 0.19-0.77
de Labriolle et al., 2008 (20)	2	127	45	OR: 1.25, 0.25-6.27
Mehran et al., 2011 (18)	2.9	1,226	565	HR: 0.63, 0.40-1.0
Jones et al., 2012 (19)	3.8	582	254	HR: 0.28, 0.15-0.52
Joyal et al., 2010* (9)		5,056	2,236	OR: 0.56, 0.43-0.72

Effectiveness of recanalization of chronic total occlusions: A systematic review and meta-analysis

13 study: 7,288 CTO

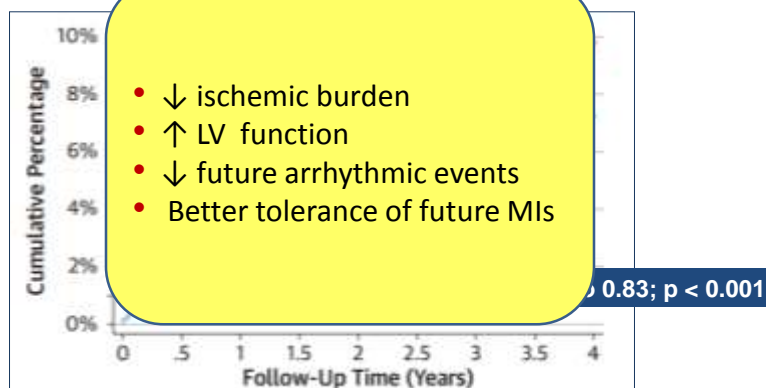


Am Heart J 2010;160:179-87

Long-Term Follow-Up of Elective Chronic Total Coronary Occlusion Angioplasty

Analysis From the U.K. Central Cardiac Audit Database

CTO-PCI to 13,443 patients; FU: 2.65 year



J Am Coll Cardiol 2014;64:235-43

RCT in CTO

- **DECISION-CTO** (DES vs OMT ; 3-year outcome)
- **EURO-CTO** (revascularization vs OMT; 1-3 year outcome)

But:

- Heterogeneity (pts ; lesions)
- Operator experience
- Selection bias
- Treatment cross over
- Mortality as a 1st endpoint

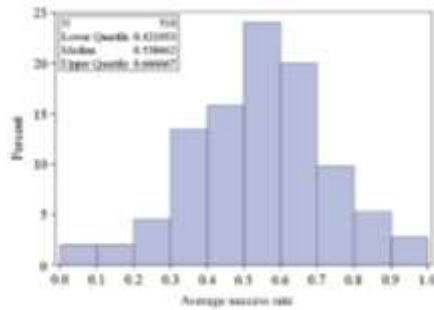
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CTO operators ; CTO centers

TABLE 3 Procedural Success and MACE Rates as a Function of Annual CTO PCI Volume

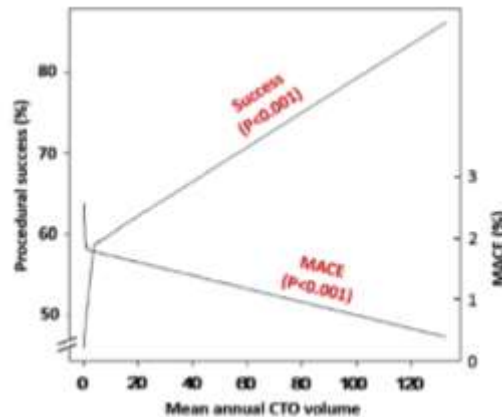
Outcome	Total (N = 22,225)	<5 CTO PCI per Year (n = 14,934)	5-10 CTO PCI per Year (n = 2,881)	>10 CTO PCI per Year (n = 4,410)	p Value
Procedural success	13,010 (58.5)	7,934 (53.1)	1,788 (62.1)	3,288 (74.6)	<0.001
MACE	356 (1.6)	260 (1.7)	34 (1.2)	62 (1.4)	0.050



J Am Coll Cardiol Intv 2015;8:245–53

CTO operators ; CTO centers

Each 10 CTO-PCI per year → 5% increase in success rate



J Am Coll Cardiol Intv 2015;8:245–53

CTO-PCI: centre of excellence



PROspective Global REgistry for the Study of CTO interventions

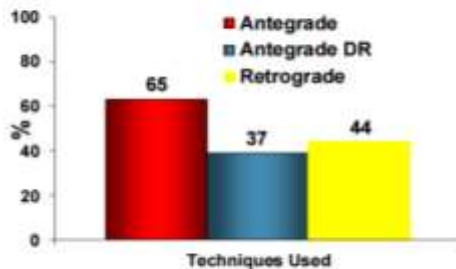
•Appleton Cardiology, WI
 •Dallas VAMC/UTSW, TX
 •Peaceheath Bellingham, WA
 •Piedmont Heart Institute, GA
 •St Luke's Mid America Heart Institute, MO
 •Torrance Medical Center, CA

1/2012 to 2/2014

n=632

Technical success: **92.4%**

Major complications: **1.9%**



Successful technique



Christopoulos, Kampilotis, Alizwad, Wynan, Lombardi, Grantham, Thompson, Brilakis et al, JIC 2014

How should patients with CTOs be treated ?

Indications for revascularization

- Symptoms (despite OMT)
- Large ischemic burden (> 10%)
- LV dysfunction (viability)

PCI vs CABG vs Hybrid

- SYNTAX score
- Ability to achieve CR
- Guideline
- Operator experience
- Operative risk
- Socioeconomic
- Patients wishes

Thank You

