

Peri-Procedural Myocardial Injury in Chronic Total Occlusion Interventions

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Background

- CTO intervention tended to damage myocardium during procedure
 - sub-intimal wiring/multiple wiring
 - harder and stiffer wire manipulation
 - retrograde approach (using large, both guiding catheter)
 - distal embolization (intra-lesional thrombus or plaque)
 - side branch compromise
 - longer procedure time and higher amount of contrast
 - high atherosclerotic burden (need more stents)

Background

- Successful recanalization of coronary CTO could provide considerable clinical benefits.
- Myocardial injury might be considered as a inevitable phenomenon during CTO procedure.
- However, the clinical implications of periprocedural myocardial injury (PMI) in patients undergoing CTO-PCI have not yet been systematically evaluated.

Objective

- To evaluate the determinants of PMI during CTO-PCI
- To evaluate the long-term prognostic implication of PMI in patients who received successful DES implantation for coronary CTOs.

Patients / Procedure

- All patients who underwent successful PCI for at least one CTO lesion **between March 2003 and June 2014** were included in this study.
- All patients received aspirin (a loading dose of 200 mg followed by 100 or 200 mg/day indefinitely) and clopidogrel (a loading dose of 300 or 600 mg, followed by 75 mg/day for at least 12 months).
- The use of specialized devices or techniques and the choice of type of DES were left to the operator's discretion.
- Restoration of TIMI 3 flow with residual stenosis <30%, as determined on visual assessment, was achieved in all stented lesions.

Definition

- The absolute levels of **creatinine kinase myocardial band (CK-MB)** isoenzyme were measured by sandwich immunoassay (Bayer corporation, Tarrytown, NY, USA, **normal range <5 ng/ml**) at the baseline (1-3 h before PCI) and at 6 h after the PCI.
- In cases of CK-MB value elevation or chest pain, further re-measurement was performed at 12 h after PCI.
- Additional measurements were optionally performed at the discretion of the attending physician, and the peak CK-MB value could be determined in all study cases.
- **PMI was defined as elevations of CK-MB >3 times** the upper reference limit (URL) in cases of normal baseline CK-MB values.
- **If the baseline CK-MB value was elevated, a CK-MB increase >3 × URL as well as a rise of CK-MB >20% relative to the baseline was required with documentation that the values were decreasing or at nadir before PCI.**

Baseline Clinical Characteristics

	All patients (N=1,058)	PMI (N=121)	Non-PMI (N=937)	P value
Age, years	59.5 ± 10.5	60.7 ± 10.7	59.3 ± 10.5	0.16
Sex, male	873 (82.5)	98 (81.0)	775 (82.7)	0.73
Body mass index, kg/m ²	25.5 ± 3.1	25.3 ± 2.6	25.5 ± 3.2	0.35
Hypertension	637 (60.2)	80 (66.1)	557 (59.4)	0.19
Diabetes	322 (30.4)	35 (28.9)	287 (30.6)	0.78
Diabetes using insulin	50 (4.7)	7 (5.8)	43 (4.6)	0.50
Hyperlipidemia	686 (64.8)	77 (63.6)	609 (65.0)	0.85
Current smoker	273 (25.8)	31 (25.6)	242 (25.8)	1.00
Previous PCI	270 (25.5)	33 (27.3)	237 (25.3)	0.72
Previous CABG	31 (2.9)	6 (5.0)	25 (2.7)	0.16
History of MI	105 (9.9)	13 (10.7)	92 (9.8)	0.87
History of heart failure	105 (9.9)	13 (10.7)	92 (9.8)	0.87

Baseline Clinical Characteristics

	All patients (N=1,058)	PMI (N=121)	Non-PMI (N=937)	P value
History of stroke	66 (6.2)	15 (12.4)	51 (5.4)	0.008
Peripheral vascular disease	20 (1.9)	4 (3.3)	16 (1.7)	0.27
Chronic lung disease	26 (2.5)	5 (4.1)	21 (2.2)	0.21
Renal dysfunction†	20 (1.9)	7 (5.8)	13 (1.4)	0.005
Clinical diagnosis				<0.001
Stable angina	787 (74.4)	73 (60.3)	714 (76.2)	
NSTE-ACS	271 (25.6)	48 (39.7)	223 (23.8)	
Atrial fibrillation	19 (1.8)	3 (2.5)	16 (1.7)	0.47
Left ventricular ejection fraction, %	57.8 ± 8.3	57.6 ± 8.7	57.9 ± 8.2	0.76
Antiplatelet therapy at discharge				
Aspirin	1057 (99.9)	121 (100)	936 (99.9)	1.00
Clopidogrel	1053 (99.5)	120 (99.2)	933 (99.6)	0.46
Cilostazol	273 (25.8)	31 (25.6)	242 (25.8)	1.00

Lesion Characteristics

	All patients (N=1,058)	PMI (N=121)	Non-PMI (N=937)	P value
* Values for 1076 lesions (122 vs. 954)				
Multi-vessel disease	576 (54.4)	85 (70.2)	491 (52.4)	<0.001
Left main disease	43 (4.1)	7 (5.8)	36 (3.8)	0.32
Multiple CTOs	82 (7.8)	12 (9.9)	70 (7.5)	0.44
Restenotic CTO*	68 (6.3)	6 (4.9)	62 (6.5)	0.69
CTO located in*				0.23
Left anterior descending artery	482 (44.8)	48 (39.3)	434 (45.5)	
Left circumflex artery	151 (14.0)	16 (13.1)	135 (14.2)	
Right coronary artery	439 (40.8)	57 (46.7)	382 (40.0)	
Left main	2 (0.2)	0	2 (0.2)	
Saphenous vein graft	2 (0.2)	1 (0.8)	1 (0.1)	
Collateral Flow, Rentrop scale*				0.82
0 / 1	226 (21.0)	27 (22.1)	199 (20.9)	
2	407 (37.8)	48 (39.3)	359 (37.6)	
3	443 (41.2)	47 (38.5)	396 (41.5)	
CTO length, mm*	13.8 ± 9.2	16.7 ± 11.7	13.5 ± 8.7	0.005
Lesion length, mm*	39.4 ± 19.4	45.0 ± 22.3	38.7 ± 18.9	0.005

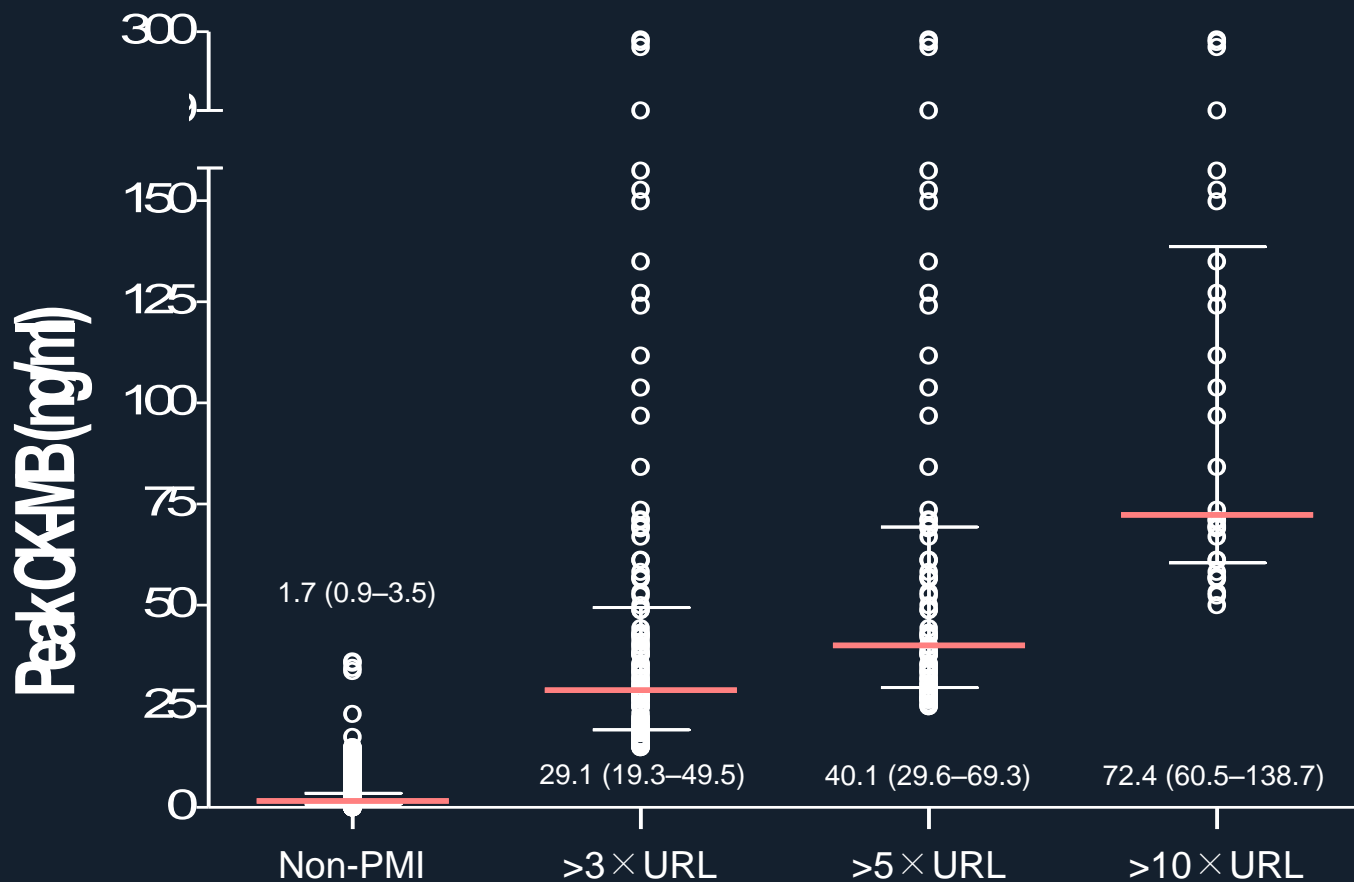
Procedural Characteristics

* Values for 1076 lesions (122 vs. 954)	All patients (N=1,058)	PMI (N=121)	Non-PMI (N=937)	P value
Stent type*				0.87
1st generation DES	491 (45.6)	57 (46.7)	434 (45.5)	
2nd generation DES	585 (54.4)	65 (53.3)	520 (54.5)	
Number of stents*	1.78 ± 0.78	1.98 ± 0.87	1.76 ± 0.76	0.003
Length of stent, mm*	50.7 ± 23.3	55.9 ± 25.3	50.1 ± 23.0	0.009
Average stent diameter, mm*	3.15 ± 0.33	3.17 ± 0.28	3.14 ± 0.33	0.34
Retrograde attempt*	124 (11.5)	26 (20.5)	99 (10.4)	0.002
Retrograde success*	93 (8.6)	21 (17.2)	72 (7.5)	0.001
Double coronary injection*	362 (33.6)	44 (36.1)	318 (33.3)	0.62
Intravascular ultrasound use*	948 (88.1)	106 (86.9)	842 (88.3)	0.77
Contrast volume, ml	400 (300–520)	460 (310–655)	400 (300–510)	0.002
Fluoroscopy time, min	33 (19–53)	56 (27–89)	31 (19–49)	<0.001
Non-target lesion intervention	358 (33.8)	54 (44.6)	304 (32.4)	0.01

Key Predictors of Periprocedural Myocardial Injury

Variables	Univariate	<i>P</i>	Multivariate	<i>P</i>
Age (per-year increment)	1.013 (0.995–1.032)	0.16		
Female gender	1.123 (0.692–1.823)	0.64		
Diabetes Mellitus	0.922 (0.608–1.398)	0.70		
Renal dysfunction*	4.364 (1.706–11.164)	0.002	4.251 (1.592–11.348)	0.004
Clinical presentation of ACS†	2.105 (1.420–3.122)	<0.001	2.181 (1.447–3.286)	<0.001
Collateral flow (per-1 Rentrop scale)	0.927 (0.724–1.188)	0.55		
Double coronary injection	1.115 (0.750–1.657)	0.59		
Stent length of the target vessel (per-1mm increment)	1.010 (1.002–1.018)	0.011		
Stent number of the target vessel	1.409 (1.117–1.777)	0.004	1.379 (1.075–1.769)	0.011
Retrograde attempt	2.229 (1.370–3.629)	0.001	2.267 (1.338–3.840)	0.002
Non-target lesion intervention	1.678 (1.144–2.463)	0.008	1.741 (1.171–2.587)	0.006

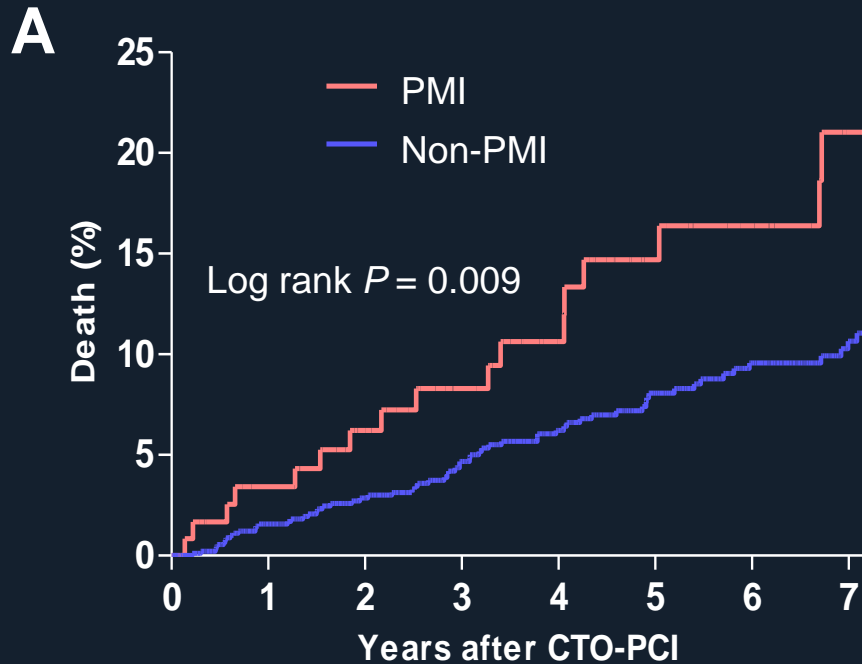
Distribution of the Post-PCI Peak CK-MB values



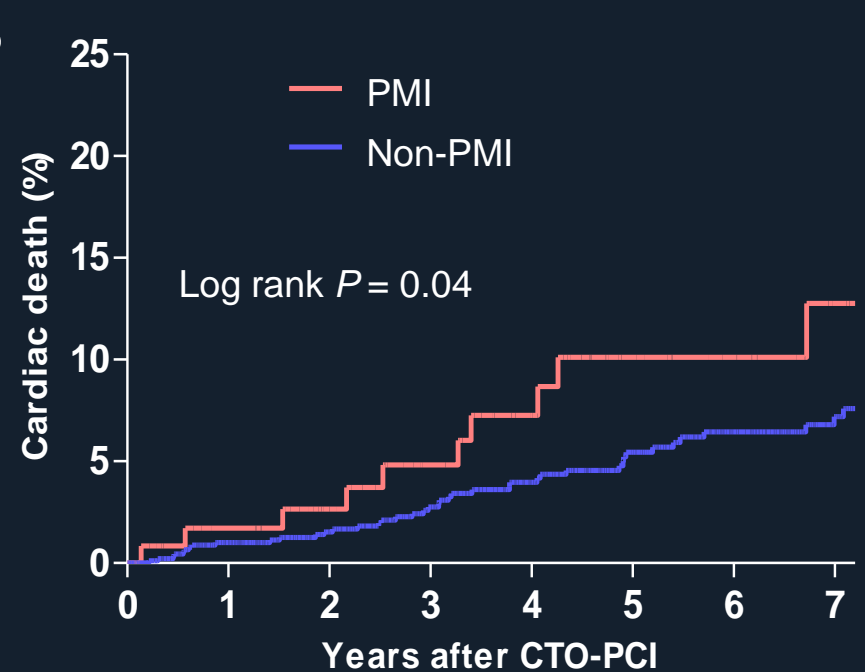
Unadjusted Kaplan-Meier Curve

Median 4.4 years (IQR 2.1 – 7.0)

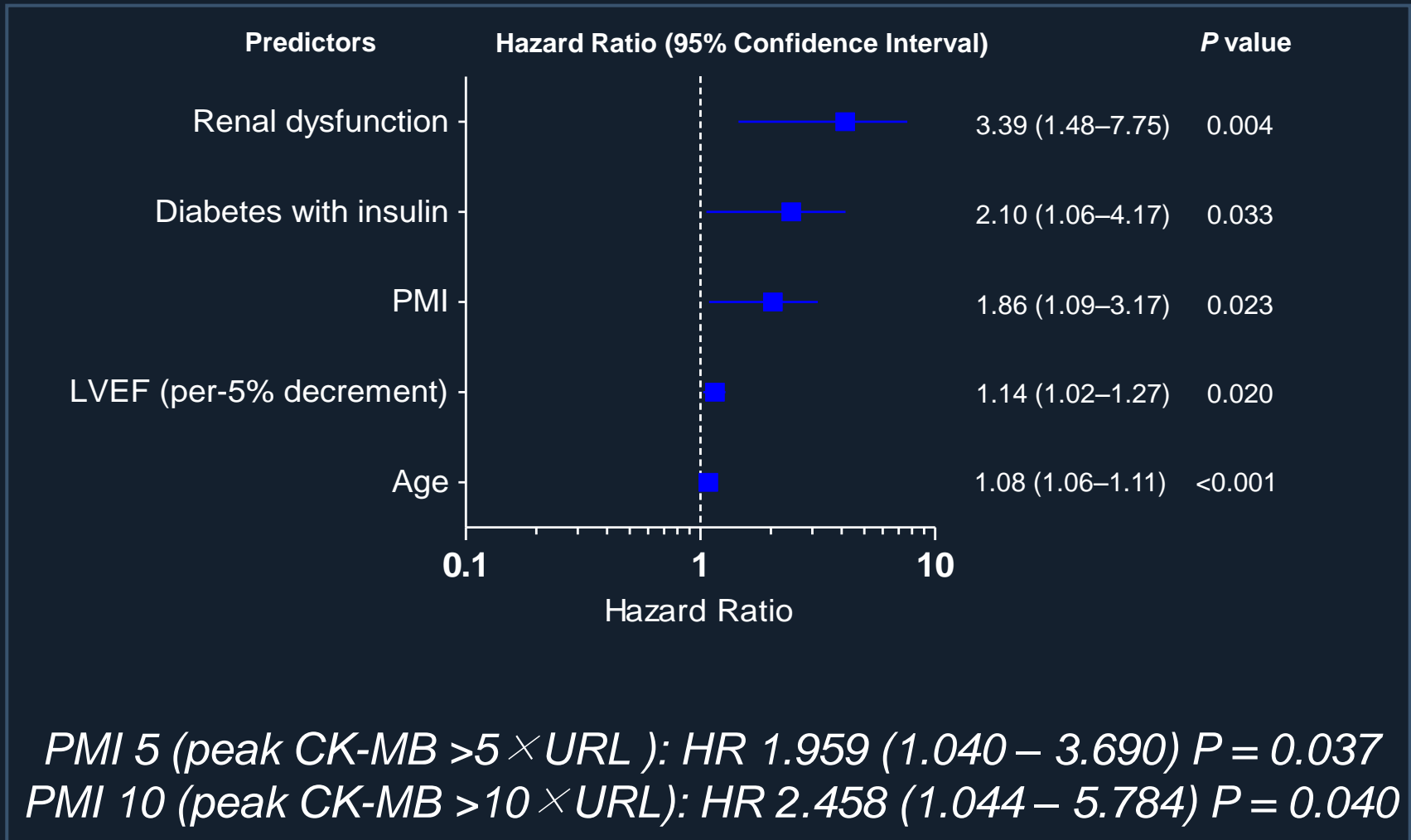
Death



Cardiac death



Predictors of Cumulative Death



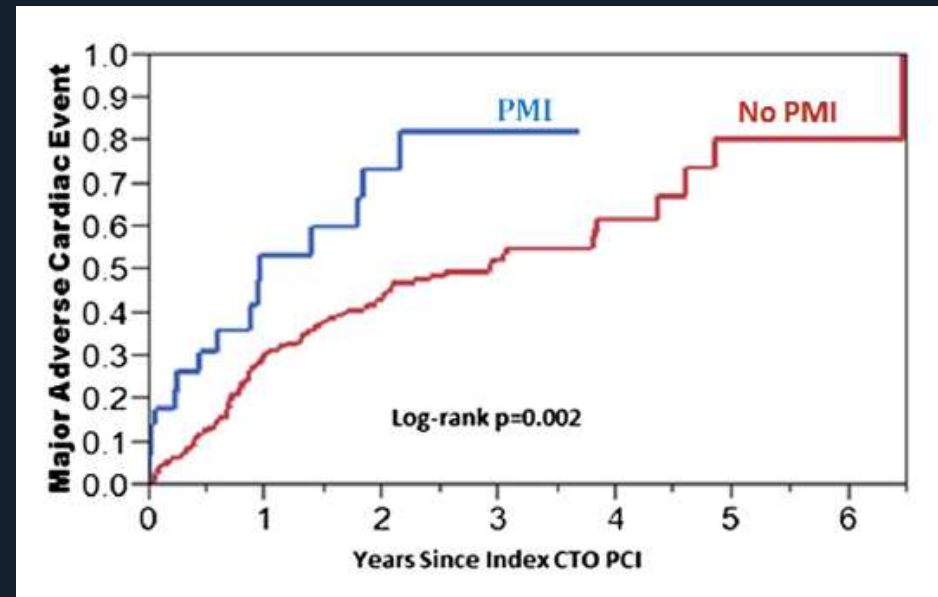
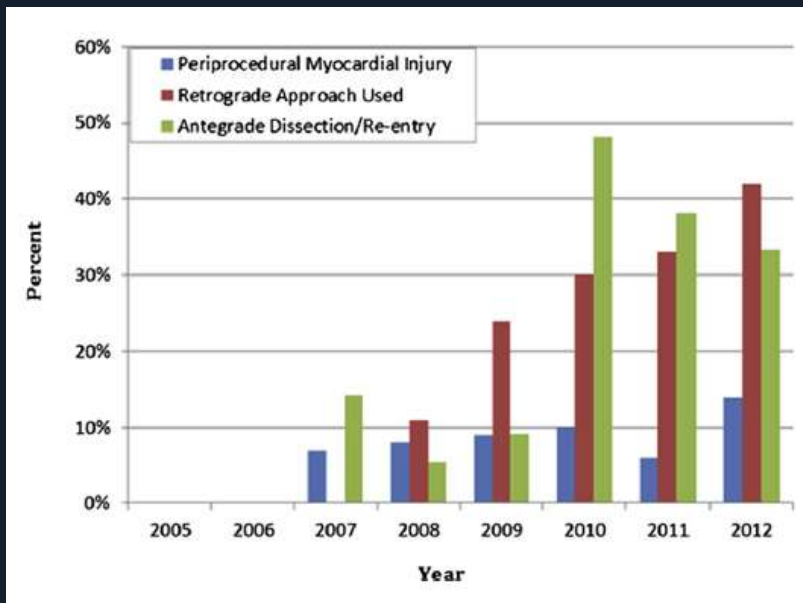
Summary

- PMI (11.8%) was determined by clinical and procedural factors including renal dysfunction, clinical presentation of acute coronary syndrome, the number of stents used, attempted retrograde approach, and concomitant, non-target lesion intervention.
- PMI was also associated with an increased risk of long-term mortality even in patients who underwent successful CTO-PCI.

Other evidences

PeriMI during CTO PCI

Retrospectively examined PMI among 325 consecutive CTO PCI performed at Dallas and Arlington, Texas between 2005 and 2012



PMI occurs in **8.6%** of patients, is more common with the retrograde approach, and is associated with worse subsequent clinical outcomes during mid-term follow-up (2.3 years).

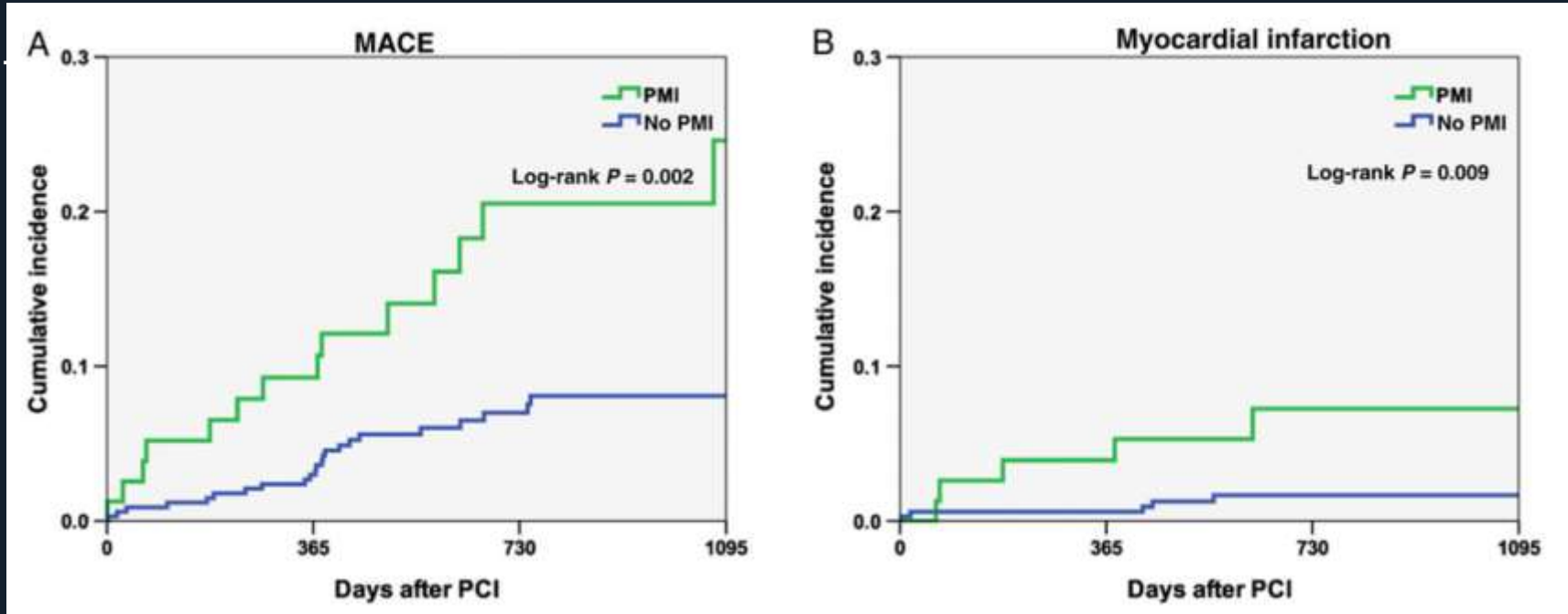
PeriMI during CTO PCI

- From January 2006 to September 2012, 715 (442) consecutive patients undergoing PCI of CTO in major native coronary arteries were screened for registry at 3 centres.
- **PMI was defined as an elevation of cTn >5 times URL** in patients with normal baseline values or a rise of cTn >20% if baseline values were elevated.
 - a) successful CTO-PCI and no-PMI (Group A, n=195);
 - b) successful CTO-PCI with PMI (Group B, n=133);
 - c) failed CTO-PCI (Group C, n=114).
- MACE rate was significantly lower in patients treated with successful CTO-PCI without PMI, and progressively increased in case of PMI or failed CTO-PCI (**Group A=9%, Group B=15%, Group C=28%, HR: 1.57 (1.24-2.18), p<0.01**).
- **Occurrence of PMI during PCI of CTO is associated with worse clinical outcome, yet superior to that of patients with failed CTO recanalization.**

PeriMI during CTO PCI

Between 2009 and 2012, a total of 437 patients who underwent successful recanalization with DESs were included. (China)

PMI was defined as an elevation of cTn >5 times URL in patients with normal baseline values.



PeriMI during CTO PCI

927 patients with CTO and stable angina who were treated with coronary artery bypass grafting CABG (n=367) or PCI (n=560)

PMI was defined as a peak CK-MB ≥ 3 times the upper limit of normal (ULN) after PCI or a CK-MB ≥ 5 times the ULN after CABG.

	PMI	No-PMI	Unadjusted HR (95% CI)	P value	Adjusted HR (95% CI) ^{ab}	P value
CTO-PCI population (n = 560)	n = 59	n = 501				
Cardiac death	3 (5.1)	18 (3.6)	1.49 (0.44–5.04)	0.53	1.72 (0.50–5.96)	0.39
All-cause death	6 (10.2)	38 (7.6)	1.38 (0.59–3.28)	0.46	1.58 (0.66–3.80)	0.31
Spontaneous MI	3 (5.1)	2 (0.4)	13.63 (2.27–81.82)	<0.01	19.41 (2.96–127.147)	<0.01
Cardiac death or MI	5 (8.5)	18 (3.6)	2.55 (0.95–6.87)	0.06	3.15 (1.13–8.78)	0.03
CVA	3 (5.1)	21 (4.2)	1.27 (0.38–4.25)	0.70	1.45 (0.43–4.98)	0.55
Repeat revascularization	6 (10.2)	65 (13.0)	0.82 (0.35–1.89)	0.64	0.83 (0.35–1.93)	0.66
MACCE	12 (20.3)	103 (20.4)	1.04 (0.57–1.89)	0.90	1.10 (0.60–2.02)	0.75
CTO-CABG population (n = 367)	n = 59	n = 308				
Cardiac death	2 (3.4)	17 (5.5)	0.66 (0.15–2.87)	0.58	0.47 (0.11–2.09)	0.32
All-cause death	8 (13.6)	38 (12.3)	1.16 (0.54–2.48)	0.71	0.86 (0.40–1.89)	0.71
Spontaneous MI	0 (0)	1 (0.3)				
Cardiac death or MI	2 (3.4)	17 (5.5)	0.66 (0.15–2.87)	0.58	0.47 (0.11–2.09)	0.32
CVA	3 (5.1)	19 (6.2)	0.89 (0.26–3.01)	0.85	0.60 (0.17–2.09)	0.42
Repeat revascularization	1 (1.7)	4 (1.3)	1.38 (0.15–12.37)	0.77	1.16 (0.12–11.02)	0.89
MACCE	14 (23.7)	56 (18.2)	1.44 (0.80–2.59)	0.22	1.18 (0.65–2.14)	0.60

PMI occurred in 118 patients (12.7% of the overall study population).

PMI may not be associated with increased cardiac mortality after coronary revascularization in patients with stable CTO.

Conclusions

- PMI is a considerable incidence during CTO PCI.
- PMI was also associated with an increased risk of long-term poor prognosis, even in patients who underwent successful CTO-PCI.
- These findings might be helpful when planning a treatment strategy for patients with CTO.
(such as intraluminal tracking, saving the side branch, shorter procedure time, etc)

Thank you for your attention !