The lessons from DECISON-CTO

Medical Therapy With or Without Stenting For Coronary Chronic Total Occlusion

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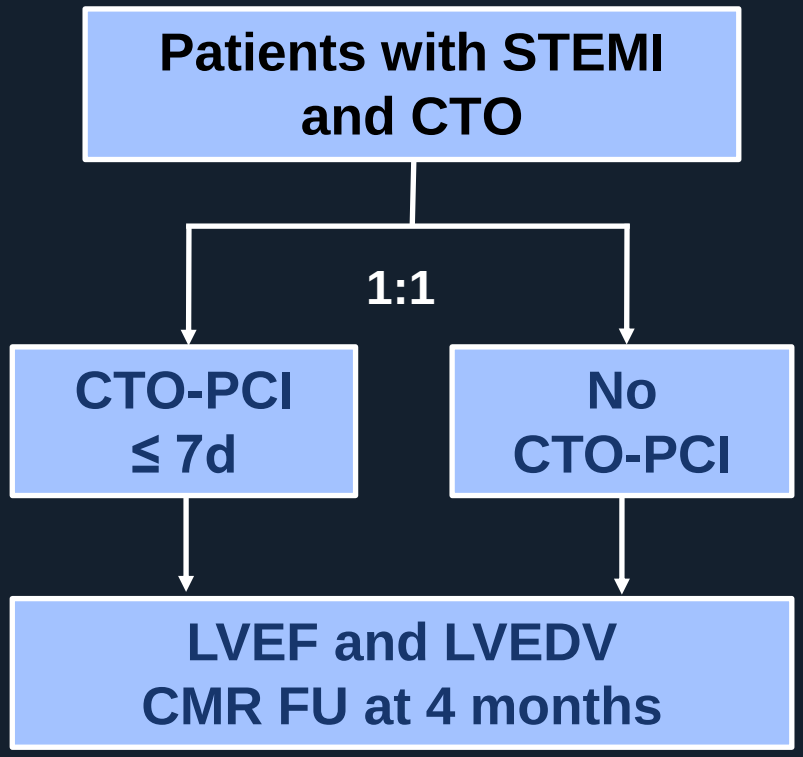
Background

- Benefits of successful CTO-PCI include reduced angina frequency and improvements in quality of life, left ventricular ejection fraction, or survival.

- However, CTO-PCI can lead to procedure-related complications. In addition, the evidence for CTO-PCI was obtained from observational studies, most of which compared successful and failed CTO-PCI without a control group receiving optimal medical treatment.

EXPLORE: Study Design



1. LVEF absolute difference of 4% (40% vs 36%, SD: 12%)
2. LVEDV absolute difference of 15 ml (185ml vs 200 ml, SD: 45 ml)
3. CTO PCI success 80% of cases

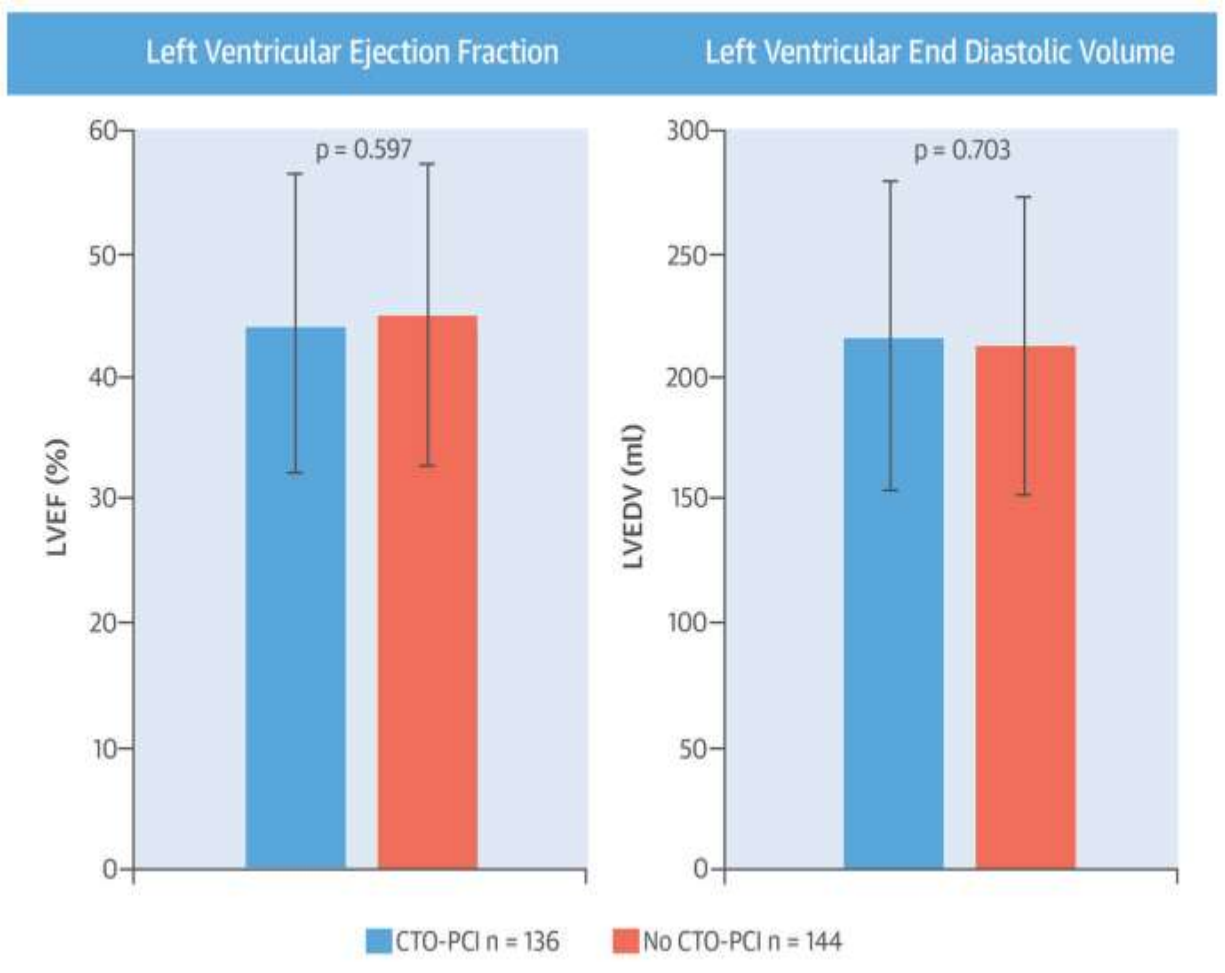
With 2 × 150 randomized patients, 80% power to detect absolute differences of 4% in LVEF and 15mL in LVEDV in favour of PCI of the CTO with two-sided alpha of 5%

CTO-PCI success rate 72%

J Am Coll Cardiol. 2016;68(15):1622-1632

Primary Outcome

Left ventricular function at 4 months



J Am Coll Cardiol. 2016;68(15):1622-1632

Long-term Results

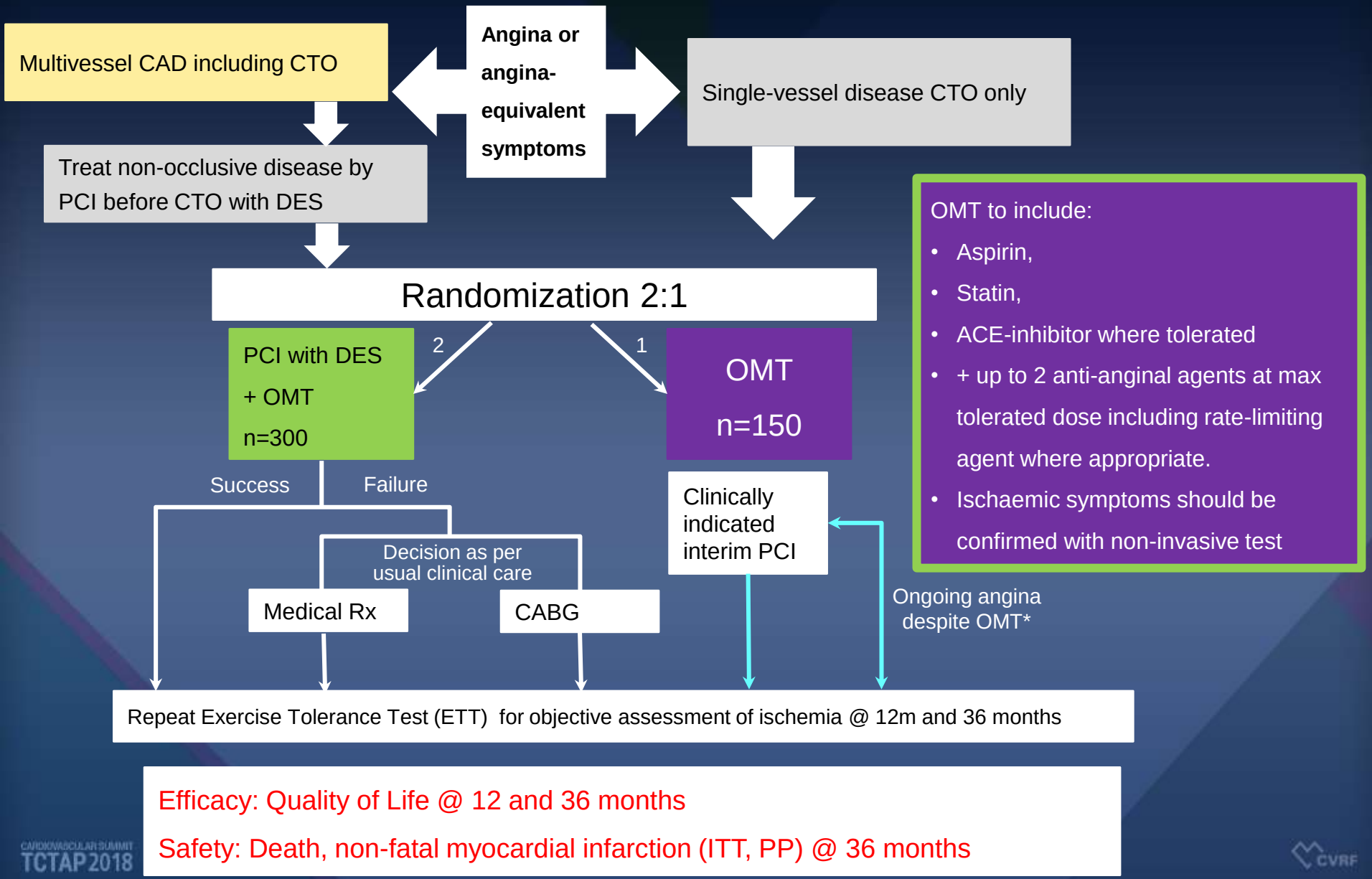
CMR @ 1 year

Intention-to treat	CTO PCI (n=45)		No-CTO PCI (n=49)		p-value
LVEF	45.5	(9.1)	44.6	(10.7)	0.66
LVEDV (ml)	198.0	(44.8)	208.1	(50.9)	0.31
LVESV (ml)	108.9	(34.8)	118.2	(46.3)	0.27

MACE (cardiac death, MI, CABG) @ 3.9 years

	CTO PCI (n=148)	No CTO PCI (n=154)	Log-rank p-value
Cardiac Death	8 (6·0%)	1 (1·0%)	0·02
Myocardial infarction	12 (9·2%)	13 (8·7%)	0·91
CABG operation	3 (2·1%)	5 (3·5%)	0·53
Composite of Cardiac death/MI/CABG	18 (13·5%)	18 (12·6%)	0·93

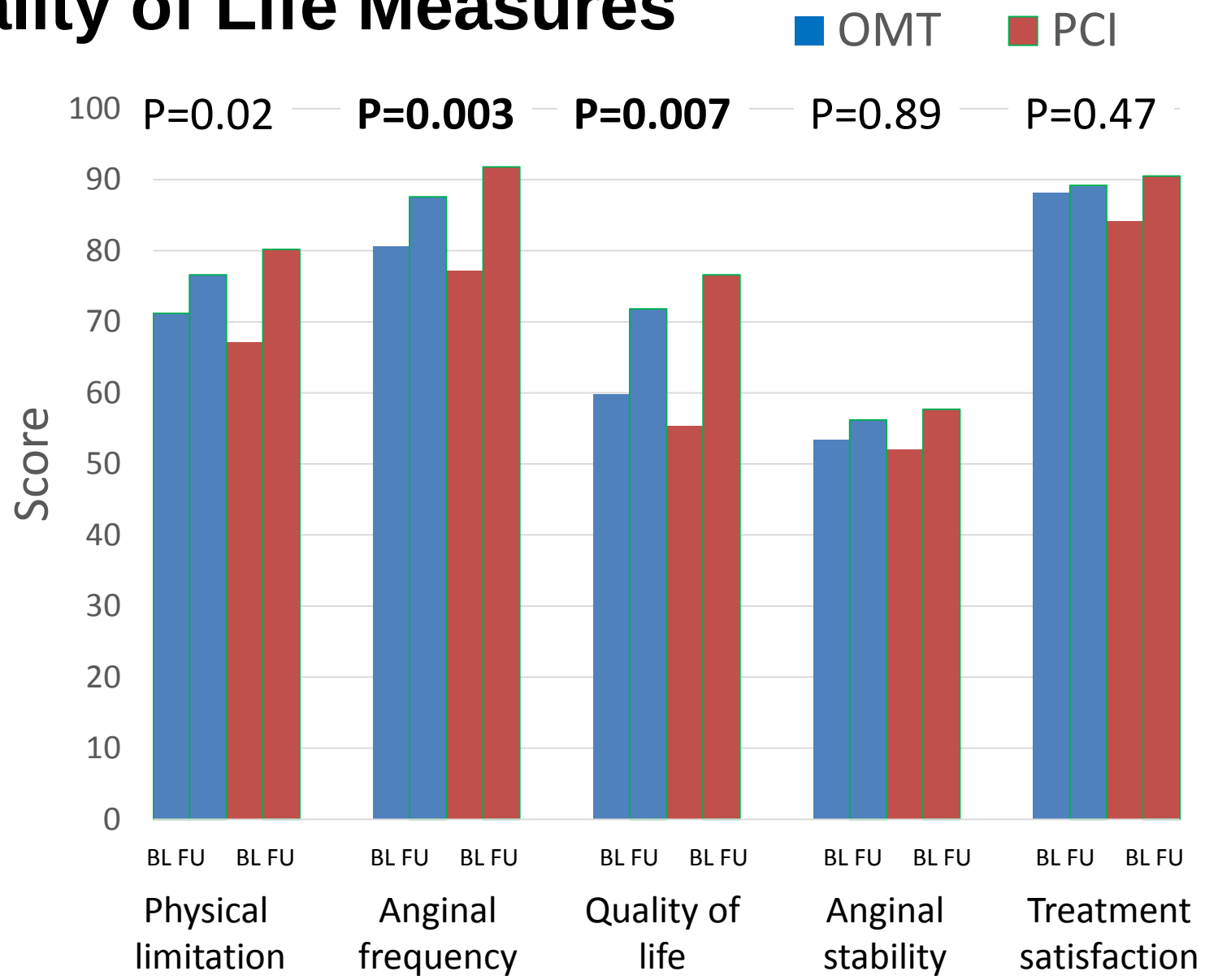
EURO-CTO: Study Design



Efficacy: Quality of Life @ 12 and 36 months

Safety: Death, non-fatal myocardial infarction (ITT, PP) @ 36 months

Quality of Life Measures

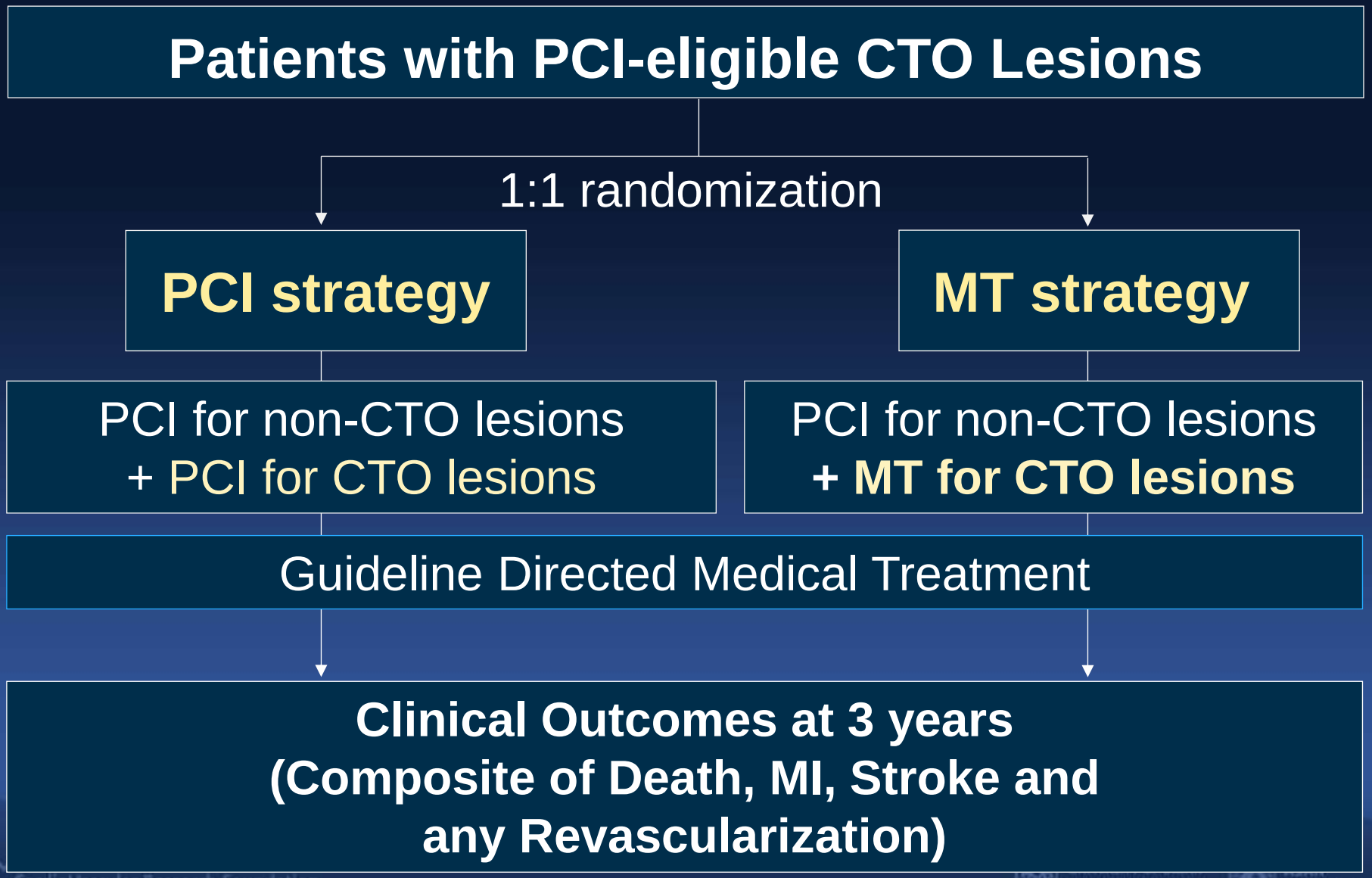


DECISION CTO Trial

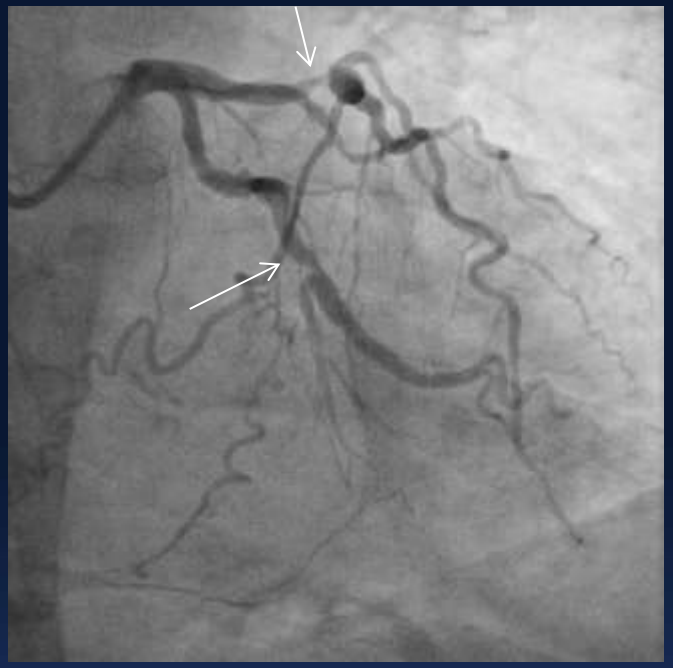
Design

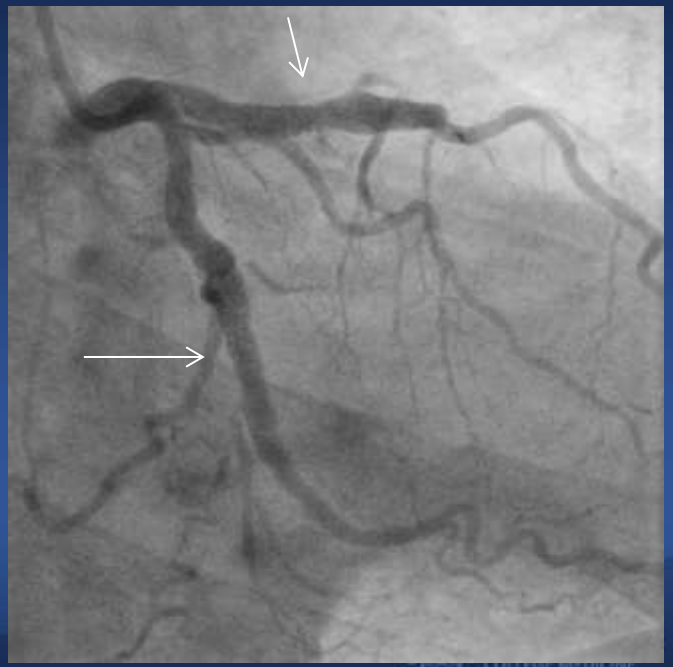
- DESIGN: a prospective, open-label, randomized trial
- OBJECTIVE: To compare the outcomes of medical treatment alone with PCI coupled with medical treatment in patients with CTO.
- PRINCIPAL INVESTIGATOR
  Seung-Jung Park, MD, PhD,
  Asan Medical Center, Seoul, Korea

DECISION-CTO



RCA CTO





Participating Centers (N=19)

Country	Site	Investigator
Korea	Asn Medical center	Seung-Jung Park
India	Ruby Hall Clinic	Shirish Hiremath
Korea	Keimyung University Dongsan Medical Center	Seung Ho Hur
Korea	Korea University Guro Hospital	Seung Un Rha
Indonesia	Medistra Hospital	Teguh Santoso
Korea	The Catholic University of Korea, Daejeon ST. Mary's Hospital	Sung-Ho Her
Korea	Chungnam National University Hospital, Daejeon	Si Wan Choi
Korea	Kangwon National University Hospital	Bong-Ki Lee
Korea	Soon Chun Hyang University Hospital Bucheon, Bucheon	Nae-Hee Lee
Korea	Kangbuk Samsung Medical Center, Seoul	Jong-Young Lee
Korea	Gangneung Asan Hospital, Gangneung	Sang-Sig Cheong,
Thailand	King Chulalongkorn Memorial Hospital	Wasan Udayachalerm
Korea	Dong-A University Hospital, Busan	Moo Hyun Kim
Korea	Chonnam National University Hospital, Gwangju	Young-Keun Ahn
Korea	Bundang Cha Medical Center, Bundang	Sang Wook Lim
Korea	Ulsan University Hospital, Ulsan	Sang-Gon Lee
Korea	Hangang Sacred Heart Hospital, Seoul	Min-Kyu Kim
Korea	Sam Anyang Hospital, Anyang	Il-Woo Suh
Taiwan	Shin Kong Hospital	Jun Jack Cheng

Major Inclusion Criteria

- Silent ischemia, stable angina, or ACS
- De novo CTO located in a proximal to mid epicardial coronary artery with a reference diameter of ≥2.5 mm
- CTO was defined as a coronary artery obstruction with TIMI flow grade 0 of at least three months' duration based on patient history.

Major Exclusion Criteria

- CTO located in
  - Distal coronary artery
  - 3 different vessel CTOs in any location
  - 2 proximal CTOs in separate coronary artery
  - left main segment
  - In-stent restenosis
  - Graft vessel
- LVEF < 30%
- Severe comorbidity

Study Procedures (1)

- Patients who were assigned to PCIs underwent CTO-PCI using DES within 30 days after randomization using standard procedures.
- In cases of failed CTO-PCI, additional attempts were allowed within 30 days after the index procedure.
- The use of specialized devices or techniques, and the choice of drug-eluting stent type were left to the operator's discretion.

Study Procedures (2)

- Revascularization for all significant non-CTO lesions within a vessel diameter of ≥2.5 mm for patients with multi-vessel coronary artery disease was recommended.
- Patients were prescribed guideline derived optimal medical treatment including aspirin, P2Y12 receptor inhibitors (>12months in case of PCI), beta-blocker, CCB, nitrate, ACEi/ARB, and statin.
- Blood pressure and diabetic control, smoking cessation, weight control, and regular exercise were recommended.

Primary End Point

At 3 year, a composite of

- Death from any cause
- Myocardial infarction
  - Periprocedural MI: CK-MB > 5 times UNL
  - Spontaneous MI: any cardiac enzyme elevation
- Stroke
- Any revascularization

Original Power Calculation

Non-inferiority Design for Primary Endpoint

- Assumed primary event rate: 17% at 3 years
- A noninferiority margin : event rate ratio 0.7
- A one-sided type I error rate : 0.025
- Power : 80%
- Dropout rate: 5%
- Assumed sample size: 1,284 patients

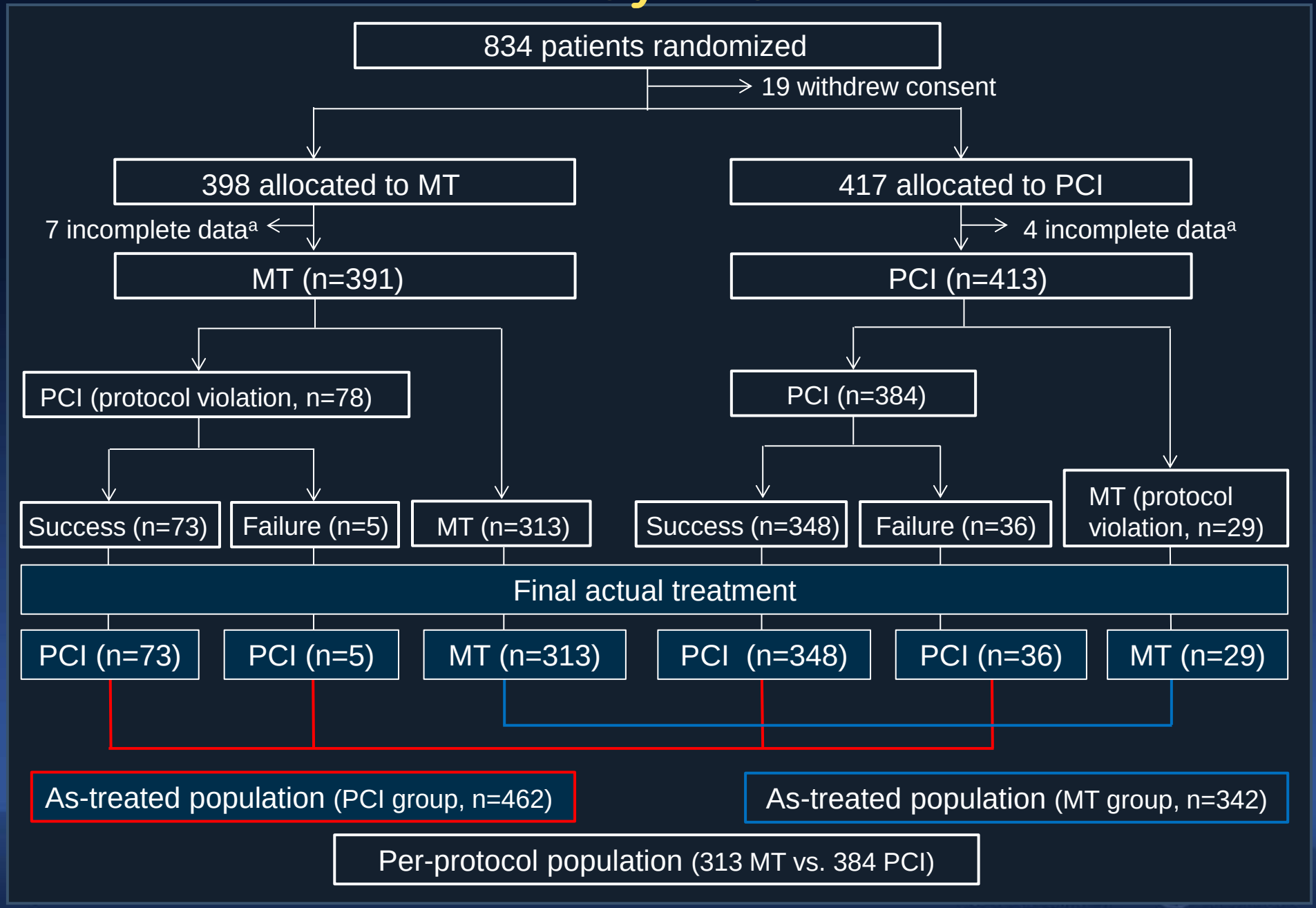
Premature Termination of Trial

- Because enrollment was slower than anticipated, enrollment was stopped in September 2016 as recommended by the data and safety monitoring board by which time 834 patients had been enrolled.
- The sponsor and study leadership were unaware of study results at the time of this decision.

Statistical Analysis

- All analyses were performed according to the intention-to-treat principle. Further sensitivity analyses were performed in the per-protocol and as-treated population.
- Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazard models, with robust standard errors that accounted for clustering effect of stratified randomization.
- Noninferiority test using the Z-test with 95% CI of difference in the 3-year event rate.
- Survival curves were estimated using Cox model and the Kaplan-Meier method
- For quality of life analysis, we assumed the missing values were missing at random, and compared mean values of two groups using Student's t-test at specific time points.
- All P-values and CIs were two-sided. SAS software version 9.3 was used for all statistical analyses.

Study Flow


834 patients randomized
19 withdrew consent
398 allocated to MT
417 allocated to PCI
7 incomplete data[a]
4 incomplete data[a]
MT (n=391)
PCI (n=413)
PCI (protocol violation, n=78)
PCI (n=384)
Success (n=73)
Failure (n=5)
MT (n=313)
Success (n=348)
Failure (n=36)
MT (protocol violation, n=29)
Final actual treatment
PCI (n=73)
PCI (n=5)
MT (n=313)
PCI (n=348)
PCI (n=36)
MT (n=29)
As-treated population (PCI group, n=462)
As-treated population (MT group, n=342)
Per-protocol population (313 MT vs. 384 PCI)

Baseline Characteristics

ITT Population

	MT Strategy (N=398)	PCI Strategy (N=417)	P value
Age (years)	62.9±9.9	62.2±10.2	0.32
Male sex	319 (81.6%)	344 (83.3%)	0.59
BMI, kg/m^2	25.5±3.3	25.6±3.5	0.59
Hypertension	238 (60.9%)	262 (63.4%)	0.50
Diabetes mellitus	134 (34.3%)	132 (32.0%)	0.54
Hypercholesterolemia	217 (55.5%)	249 (60.3%)	0.19
Current smoker	102 (26.1%)	125 (30.3%)	0.22
Previous PCI	75 (19.2%)	64 (15.5%)	0.20
Previous MI	34 (8.7%)	45 (10.9%)	0.35
Previous CABG	5 (1.3%)	4 (1.0%)	0.93
Chronic renal failure	5 (1.3%)	6 (1.5%)	>0.99
LVEF, %	57.6±9.1%	57.3±9.8%	0.68

Baseline Characteristics

ITT Population

	MT Strategy (N=398)	PCI Strategy (N=417)	P value
Clinical presentation			0.79
Stable angina	293 (75.0%)	300 (72.8%)	
Unstable angina	76 (19.4%)	84 (20.3%)	
AMI	22 (5.6%)	29 (7.0%)	
Location of CTO			0.67
LAD	163 (41.7%)	185 (44.8%)	
LCX	42 (10.7%)	42 (10.2%)	
RCA	186 (47.6%)	186 (45.0%)	
Multivessel disease	288 (73.6%)	302 (73.2%)	0.83
SYNTAX score	20.8±9.5	20.8±9.2	0.99
J-CTO score	2.2±1.2	2.1±1.2	0.16

Lesion and Procedural Characteristics

ITT Population

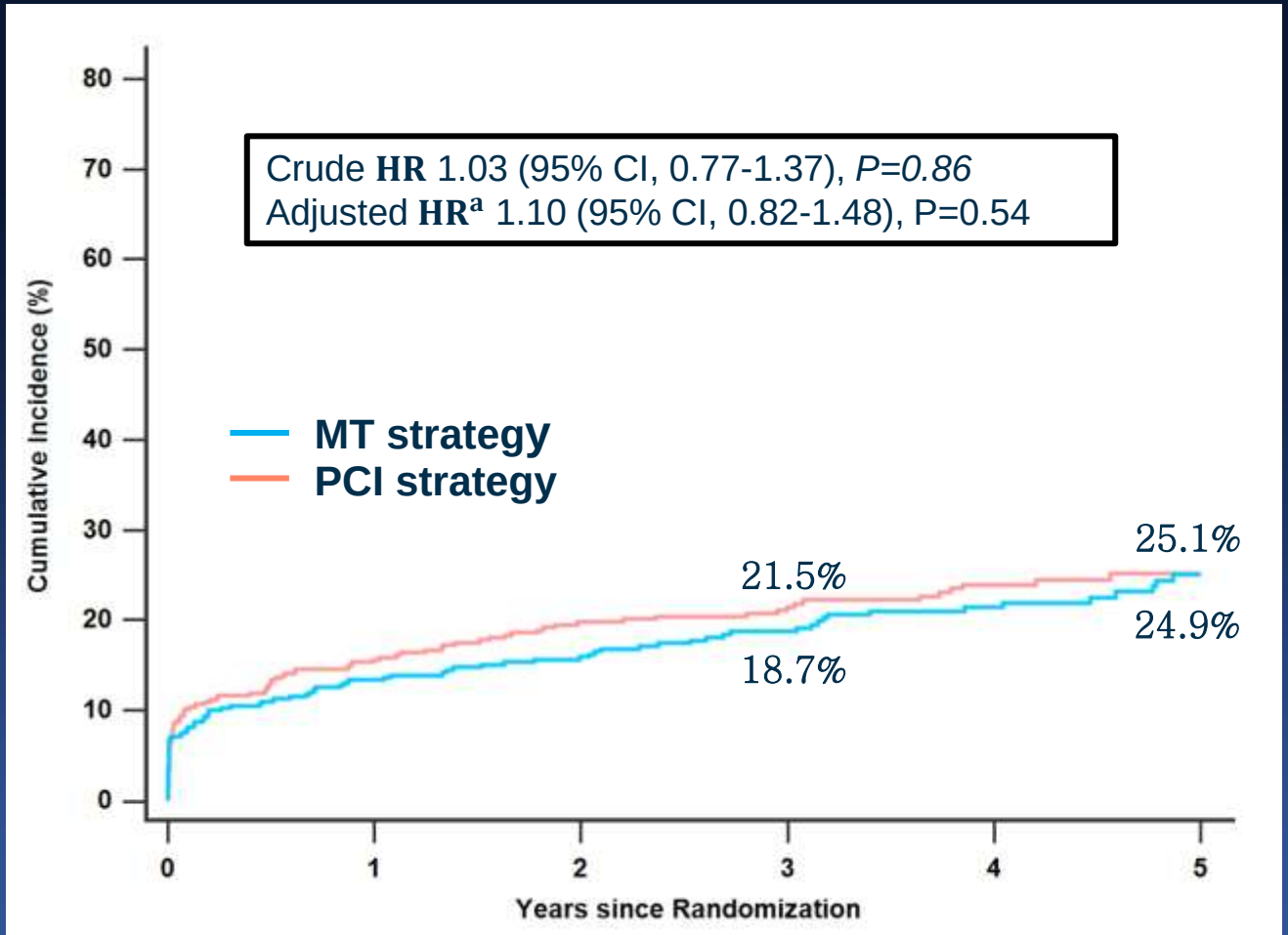
	CTO lesion			Non-CTO lesion		
Variable	MT strategy (n=398)	PCI strategy (n=417)	P	MT strategy (n=398)	PCI strategy (n=417)	P
Number of lesion[b]						0.59
0				97 (25.0)	107 (26.2)	
1		Not applicable		127 (32.7)	145 (35.5)	

	MT Strategy	PCI Strategy	P value
CR (non-CTO vs.)	302 (77.2%)	325 (78.7%)	0.67
Residual SS (non-CTO vs.)	3.7 ± 5.4	4.0 ± 5.9	0.42

Total stent length, mm	53.6 ± 39.4	71.3 ± 40.5	≤0.001	44.2 ± 28.0	41.1 ± 25.9	0.26
Stent diameter, mm	3.1 ± 0.4	3.1 ± 0.3	0.18	3.2 ± 0.4	3.2 ± 0.4	0.88
Stents			0.31			0.14
Early generation DES	4 (5.5)	13 (3.7)		10 (5.2)	7 (3.3)	
Newer generation DES	69 (94.5)	335 (96.3)		18 (94.8)	206 (96.7)	
IVUS use	7 (9.6)	203 (58.3)		108 (56.5)	114 (53.8)	0.58
Fluoroscopy time, minutes	37.2 ± 35.7	42.0 ± 34.0	0.09			
Total contrast amount, ml	337 ± 177	341 ± 157	0.78			

ITT Population

Primary End Point
(Death, MI, Stroke, Any Revascularization)



Medical therapy	398	324	287	229	169	107
PCI	417	330	268	221	159	104

[a]Adjusted for age, BMI, hypercholesterolemia, previous stroke, renal dysfunction, atrial fibrillation, clinical presentation, location of CTO, number of diseased vessels, and stratifying covariates.

ITT Population

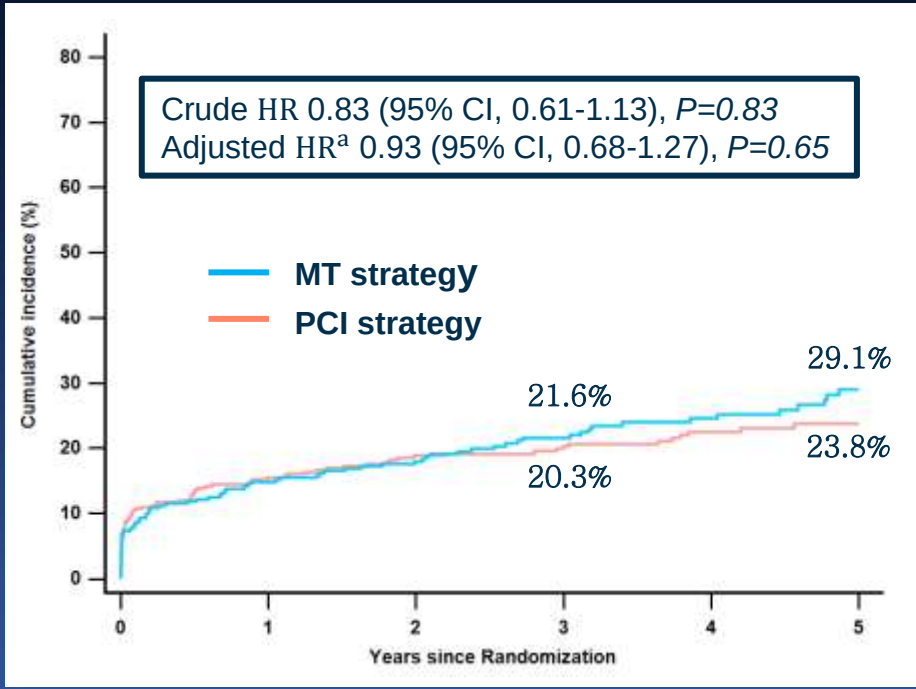
Clinical Endpoints

	MT Strategy (n=398)	PCI Strategy (n=417)	Crude HR (95% CI)	P value	Adjusted HR* (95% CI)	P value
Primary endpoint Death, MI, stroke, or any revascularization	89 (22.4)	93 (20.3)	1.03 (0.77-1.37)	0.86	1.10 (0.69-1.24)	0.54
Secondary endpoints						
Death	21 (5.3)	15 (3.6)	0.70 (0.36-1.37)	0.30	0.85 (0.42-1.72)	0.65
Cardiac cause	14 (3.5)	8 (1.9)	0.56 (0.24-1.34)	0.19	0.63 (0.24-1.63)	0.34
Noncardiac cause	7 (1.8)	7 (1.7)	0.99 (0.35-2.82)	0.99	1.16 (0.36-3.77)	0.80
Myocardial infarction	34 (8.5)	47 (11.3)	1.31 (0.85-2.04)	0.23	1.42 (0.90-2.23)	0.13
Periprocedural MI	30 (7.5)	41 (9.8)	1.30 (0.81-2.07)	0.29	1.36 (0.84-2.20)	0.22
Spontaneous MI	7 (1.8)	7 (1.7)	0.83 (0.28-2.48)	0.74	0.87 (0.27-2.77)	0.82
Stroke	10 (2.5)	6 (1.4)	0.57 (0.21-1.58)	0.28	0.97 (0.32-2.96)	0.96
Any revascularization	42 (10.6)	46 (11.0)	1.08 (0.71-1.65)	0.71	1.09 (0.71-1.68)	0.70
CTO vessel	30 (7.5)	33 (7.9)	1.01 (0.67-1.79)	0.73	1.06 (0.64-1.76)	0.81
Non-CTO vessel	23 (5.8)	29 (7.0)	1.24 (0.72-2.14)	0.44	1.31 (0.74-2.32)	0.36
Death, MI, or stroke	61 (15.3)	66 (15.8)	1.07 (0.75-1.51)	0.72	1.26 (0.88-1.80)	0.21
Cardiac death, MI, stroke, or any revascularization	82 (20.6)	86 (20.6)	1.02 (0.76-1.39)	0.88	1.08 (0.80-1.48)	0.61
Death, spontaneous MI, stroke, or any revascularization	69 (17.3)	64 (15.3)	0.91 (0.65-1.30)	0.59	1.01 (0.71-1.42)	0.98

*Adjusted for age, BMI, hypercholesterolemia, previous stroke, renal dysfunction, atrial fibrillation, clinical presentation, location of CTO, number of diseased vessels, and stratifying covariates.

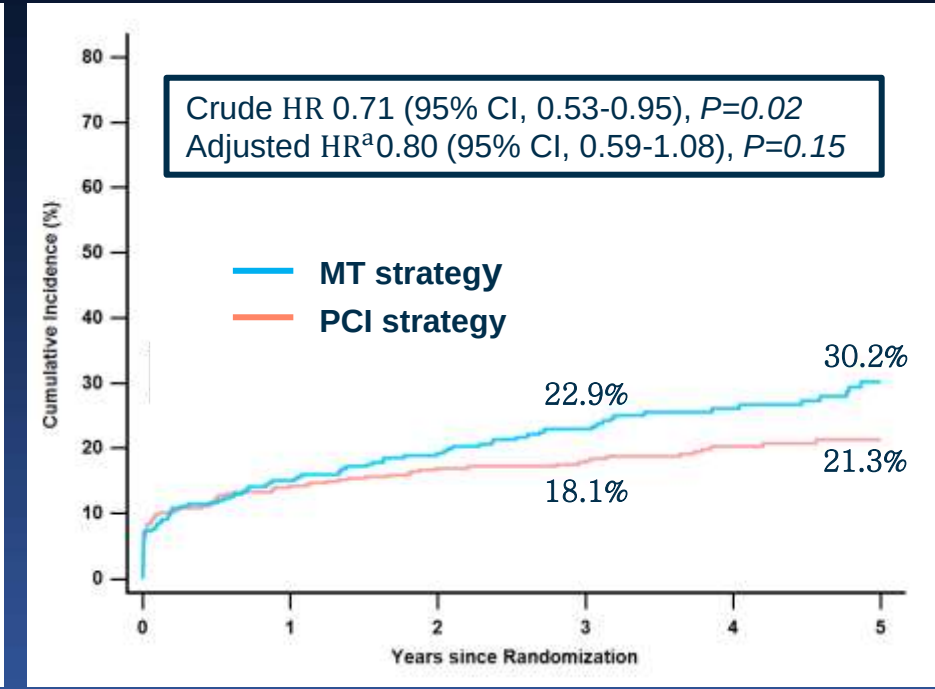
Primary End Point
(Death, MI, Stroke, Any Revascularization)

Per-protocol population



MT	313	257	224	172	125	79
PCI	384	306	254	210	152	98

As-treated population

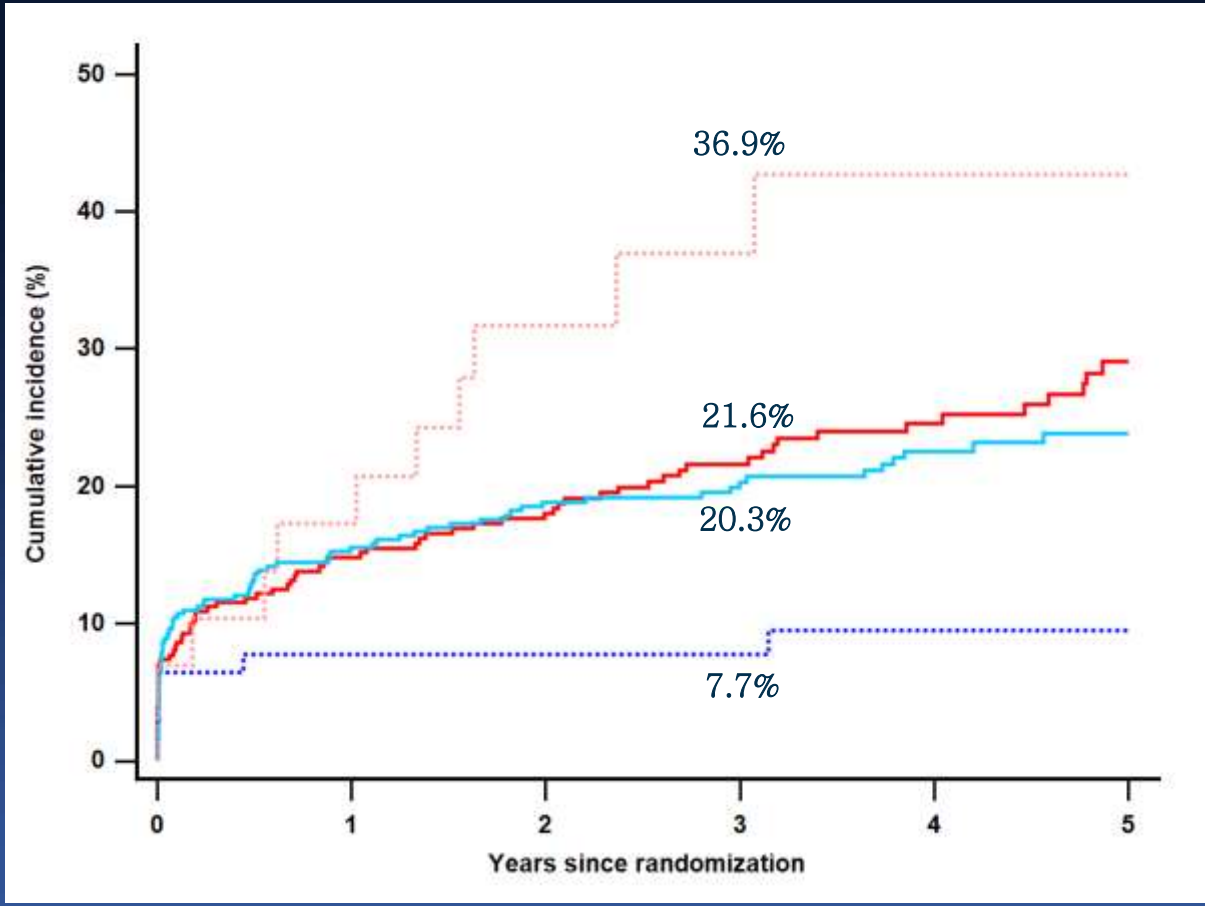


MT	342	281	239	184	134	86
PCI	462	375	318	268	197	127

[a]Adjusted for age, BMI, hypercholesterolemia, previous stroke, renal dysfunction, atrial fibrillation, clinical presentation, location of CTO, number of diseased vessels, and stratifying covariates.

Primary endpoint analyses

Stratified by the assigned and actual strategy



PCI to MT strategy

MT to MT strategy

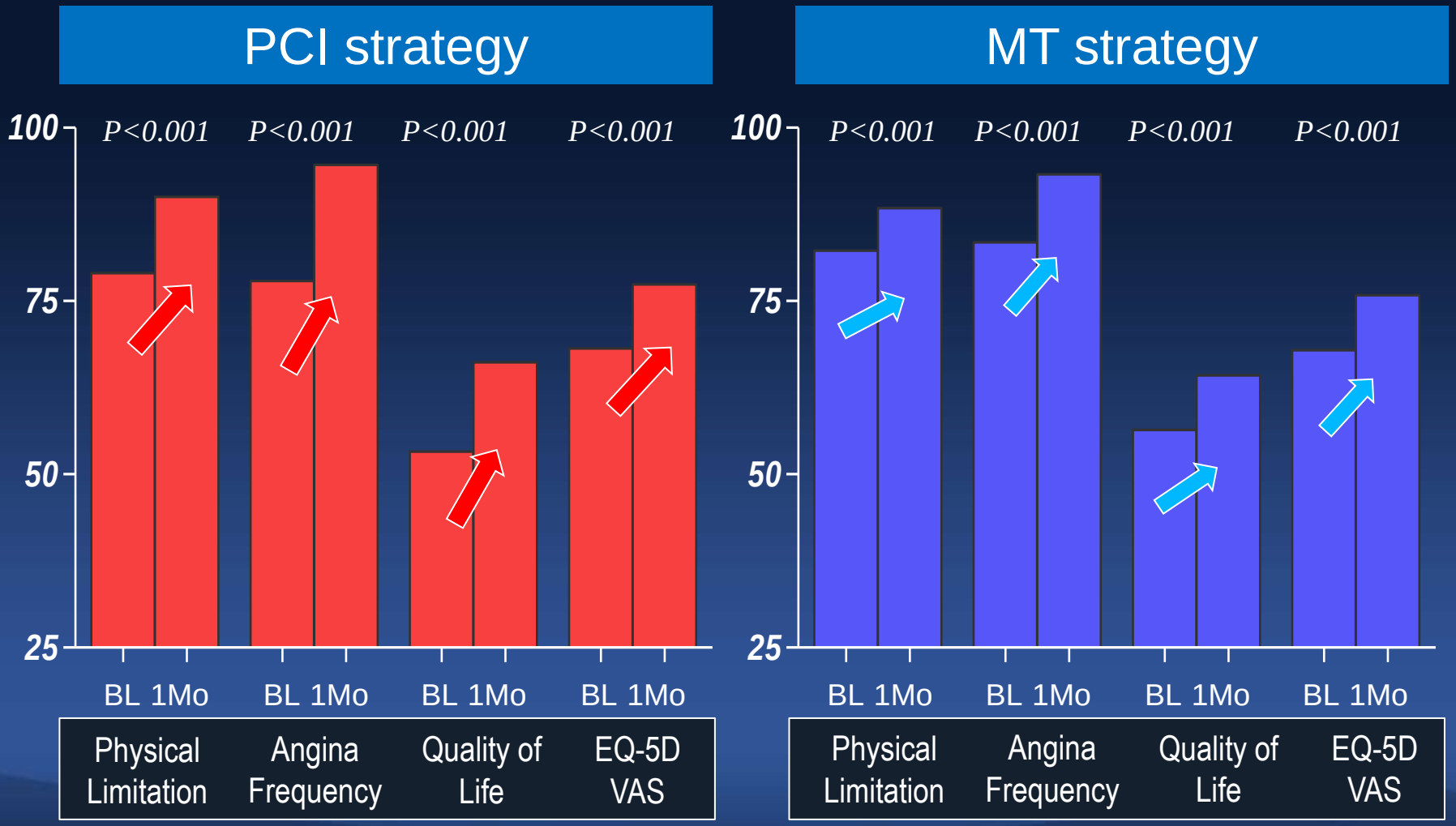
PCI to PCI strategy

MT to PCI strategy

PCI to PCI	384	306	254	210	152	98
PCI to MT	29	25	16	13	10	8
MT to PCI	78	70	65	59	46	30
MT to MT	313	257	224	172	125	78

QOL Measure Scores

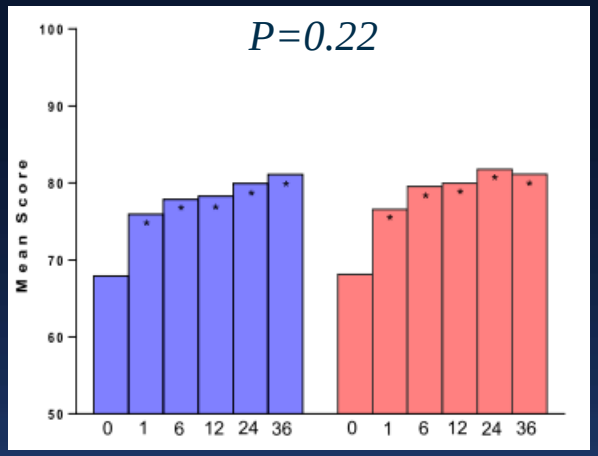
Within group changes from baseline to 1 month



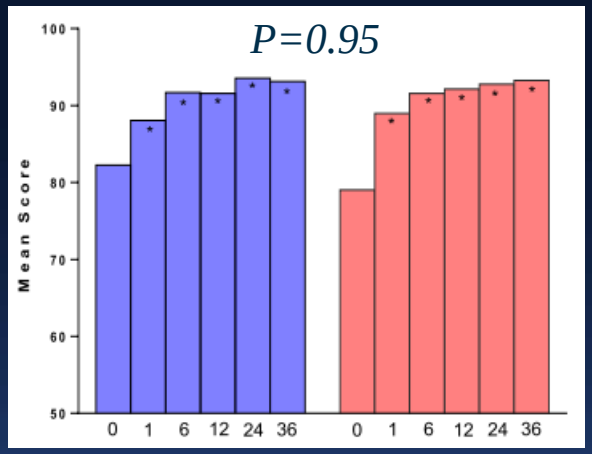
QOL Measures Over Time

Similar Trend Between Strategies

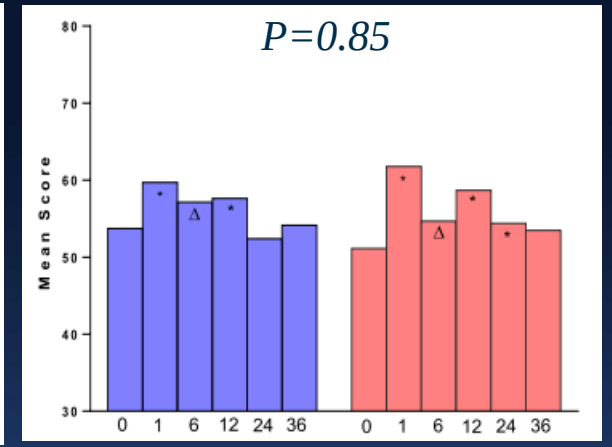
EQ-5D Visual Analogue Scale



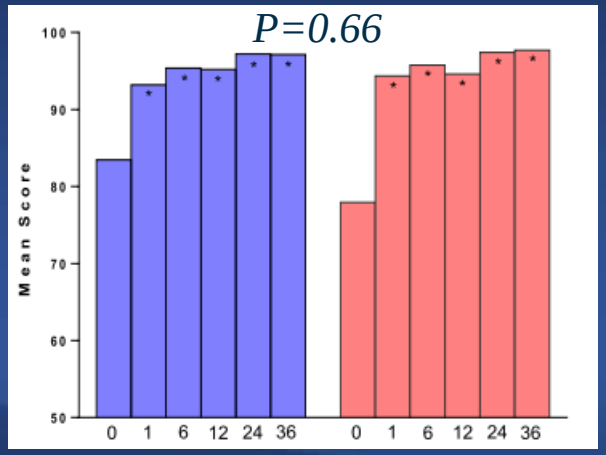
SAQ, Physical Limitation



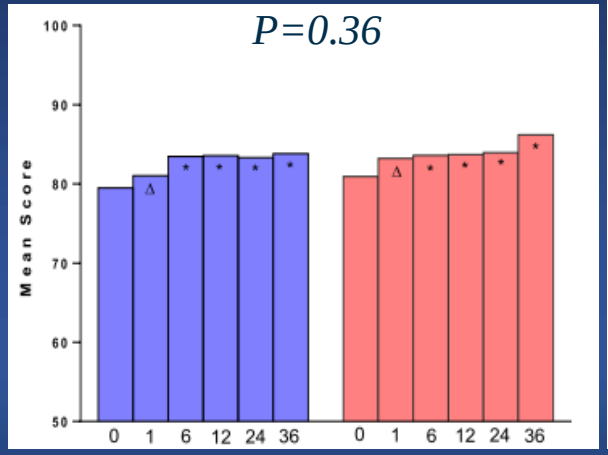
SAQ, Angina Stability



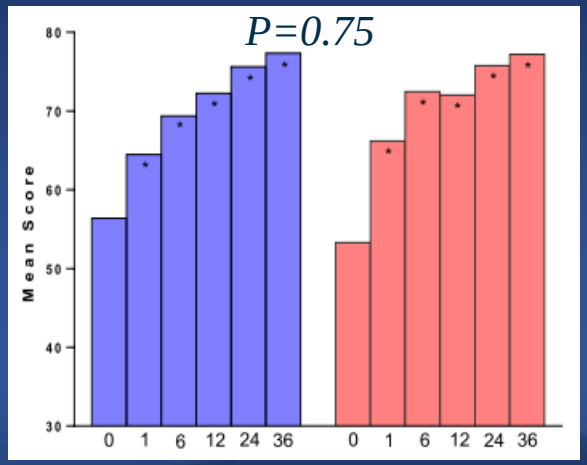
SAQ, Angina Frequency



SAQ, Treatment Satisfaction



SAQ, Quality of Life



MT strategy PCI strategy

P values are for Treatment*Time

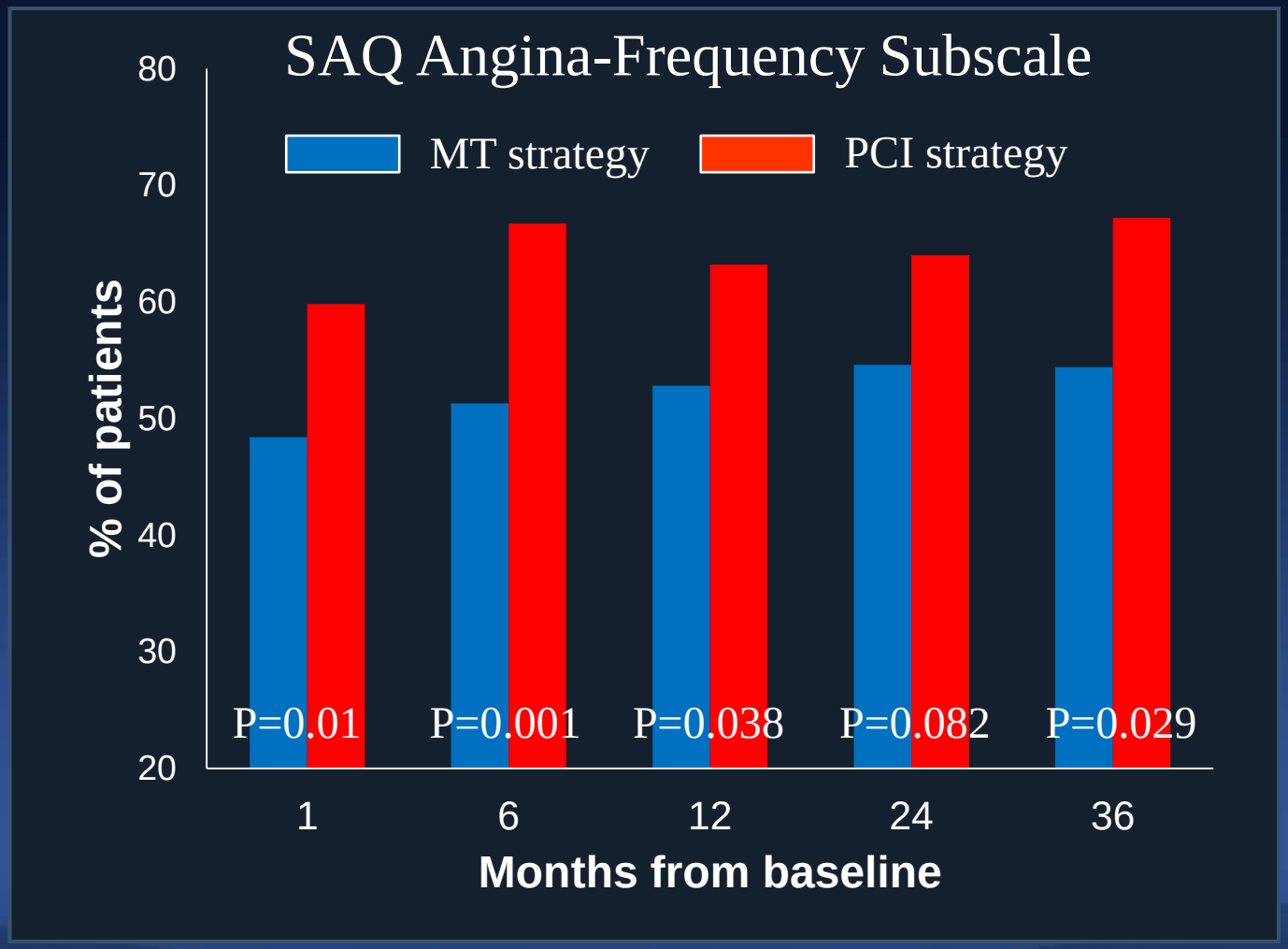
Between group differences over time

	PCI strategy	MT strategy	Difference between PCI and MT strategy (95% CI)*	P value
SAQ physical limitation				
1 mo	90.00 ± 15.66	88.38 ± 17.11	-3.354 (-5.605 − -1.104)	0.004
6 mo	92.22 ± 13.61	91.80 ± 14.32	-1.813 (-4.089 − 0.464)	0.118
12 mo	93.06 ± 11.96	91.77 ± 15.12	-2.309 (-4.710 − 0.092)	0.059
24 mo	94.84 ± 12.72	93.69 ± 12.74	-1.920 (-4.301 − 0.462)	0.114
36 mo	94.52 ± 12.86	93.54 ± 14.98	-1.813 (-4.827 − 1.201)	0.237
SAQ angina frequency				
1 mo	94.63 ± 10.54	93.31 ± 13.78	-2.635 (-4.604 − 0.665)	0.009
6 mo	96.00 ± 10.13	95.44 ± 9.98	-1.037 (-2.911 − 0.837)	0.277
12 mo	94.55 ± 11.18	95.33 ± 10.19	-0.154 (-2.163 − 1.855)	0.880
24 mo	97.31 ± 7.13	97.18 ± 7.65	-0.427 (-1.978 − 1.125)	0.589
36 mo	98.21 ± 5.32	97.38 ± 7.20	-0.981 (-2.480 − 0.518)	0.199
SAQ quality of life				
1 mo	66.16 ± 19.87	64.26 ± 19.65	-3.075 (-6.135 − -0.016)	0.049
6 mo	72.08 ± 17.54	69.74 ± 17.48	-3.336 (-6.444 − -0.227)	0.036
12 mo	72.19 ± 19.06	71.89 ± 16.6	-1.458 (-4.745 − 1.829)	0.384
24 mo	77.37 ± 17.43	75.91 ± 17.77	-2.136 (-5.738 − 1.465)	0.244
36 mo	78.26 ± 17.39	77.53 ± 16.69	-1.213 (5.004 − 2.577)	0.529

*The difference between the PCI and MT strategy groups was adjusted for baseline values.
Negative values indicate better outcomes with PCI strategy.

Substantial Improvement (%) of Angina over Time

Increase from baseline score of 10 points or more



Conclusion

- The DECISION-CTO trial is the largest randomized clinical trial to compare medical strategy alone with PCI strategy in patients with coronary CTO in conjunction with non-CTO intervention in both group.
- Our results showed that medical treatment as an initial strategy was statistically not different compared to PCI strategy in terms of the composite of death, MI, stroke, or any revascularization at 3 years.
- The measures of health-related quality of life in the MT and the PCI strategy were improved compared to baseline in both group and comparable during follow-up periods

Conclusion

- However, SAQ angina frequency subscale is much better in terms of improvement more than 10 points in PCI arm, which suggest PCI strategy is more beneficial effect in angina control in CTO patients.

- However, despite statistical no difference, we did not provide firm conclusion for role of medical treatment strategy in the CTO patients due to early termination and lower enrolment than anticipated.

- There is a signal for role of medical treatment, but further randomized clinical trials are necessary.

Thank You !!

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