The Evaluating Xience and left ventricular function in PCI on occlusiOns afteR STEMI (EXPLORE) trial

The impact of PCI for concurrent CTO on left ventricular function in STEMI patients

A randomised multicenter trial

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship

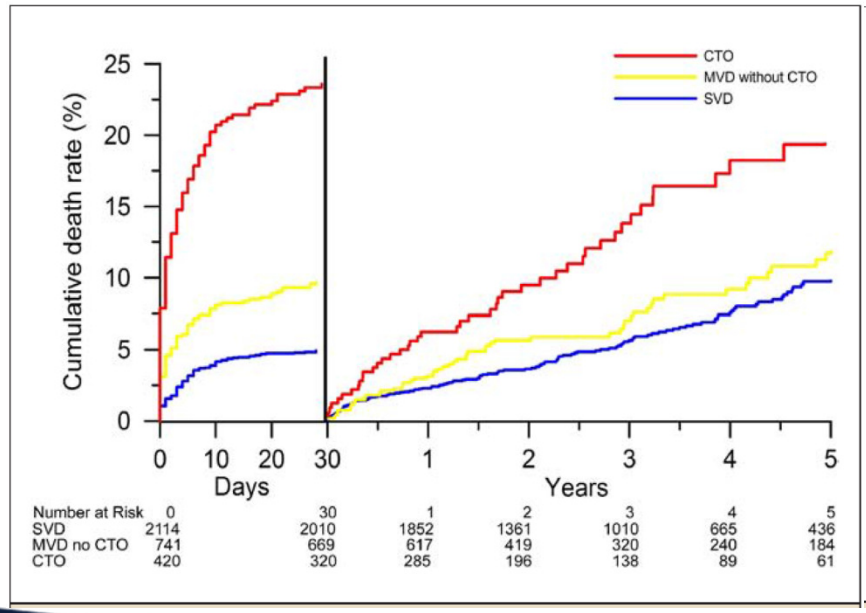
- Grant/Research Support

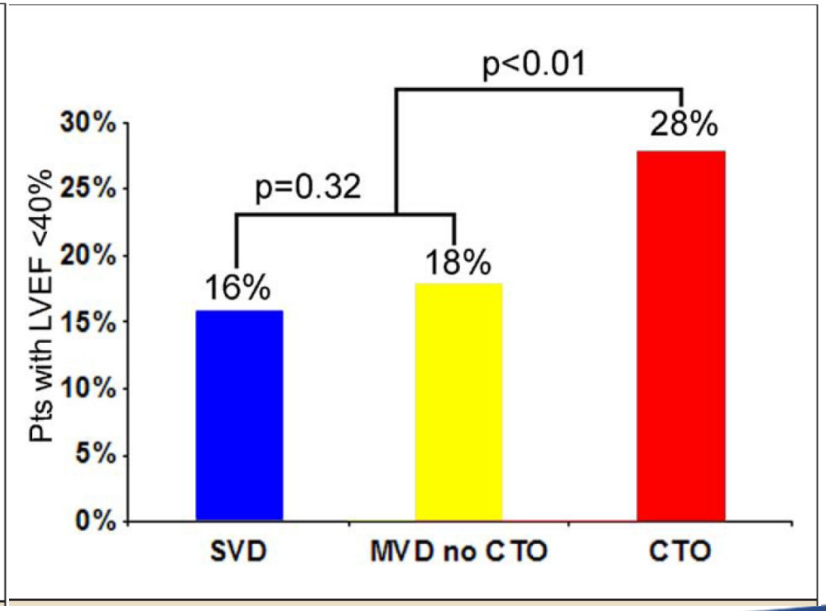
Company

- Abbott Vascular
- Abiomed Inc
- Biotronik
- BBraun

Background (1)

- CTO in non-IRA in 10% of STEMI patients
- Excess mortality in MVD patients mainly driven by presence of CTO
- Reduced LV function in MVD patients mainly driven by presence of CTO





Van der Schaaf et al, *Heart*, 2006
Claessen et al. *JACC: Cardiovascular Interventions*, 2009

Background (2)

- No randomised data on effect of CTO PCI
- Observational studies:
  - Succesful vs not succesful recanalisation in stable CAD
    - improvement LV function
    - reduced need for CABG
    - lower mortality
  - No control group.

EXPLORE

First RCT on the impact of PCI of CTO on LV function (LVEF and LVEDV) and clinical outcome in STEMI patients

Explore Trial Design

- **Patients**

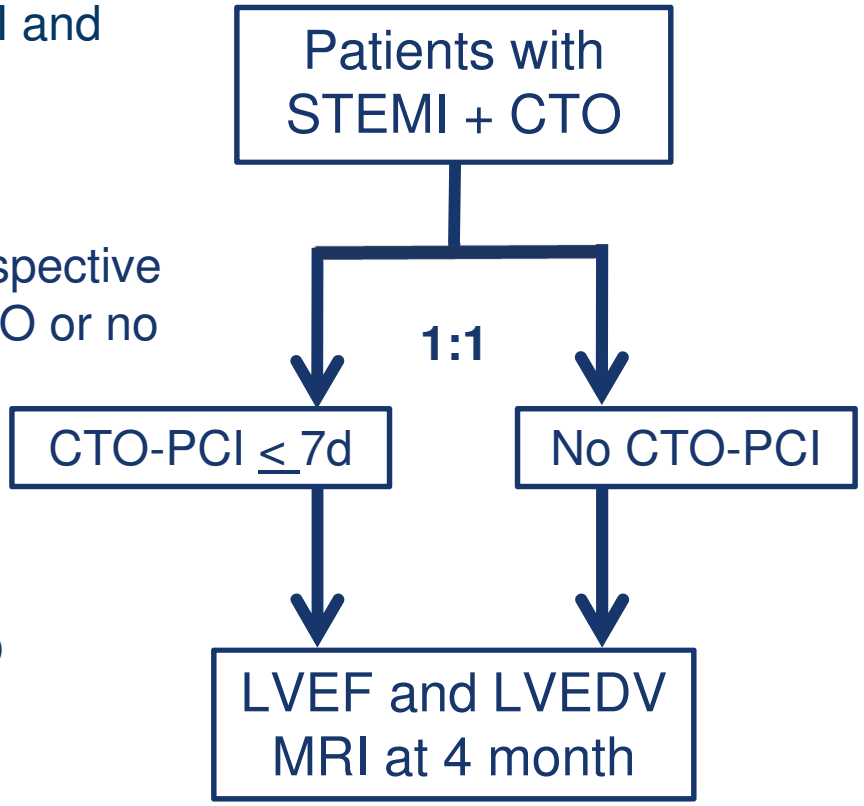
  Patients with STEMI treated with pPCI and with a non-infarct related CTO.

- **Design**

  Global, multi-center, randomized, prospective two-arm trial with either PCI of the CTO or no CTO intervention after STEMI.
  Blinded evaluation of endpoints.

- **Objective**

  To determine whether PCI of the CTO within 7 days after STEMI results in a higher LVEF and a lower LVEDV assessed by MRI at 4 months



Statistical Plan

INTENTION TO TREAT ANALYSIS of CTO-PCI vs No-CTO PCI

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%

Trial organisation

Steering Committee
Jose PS Henriques, Principal investigator, AMC, Amsterdam, The Netherlands

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And all international investigators

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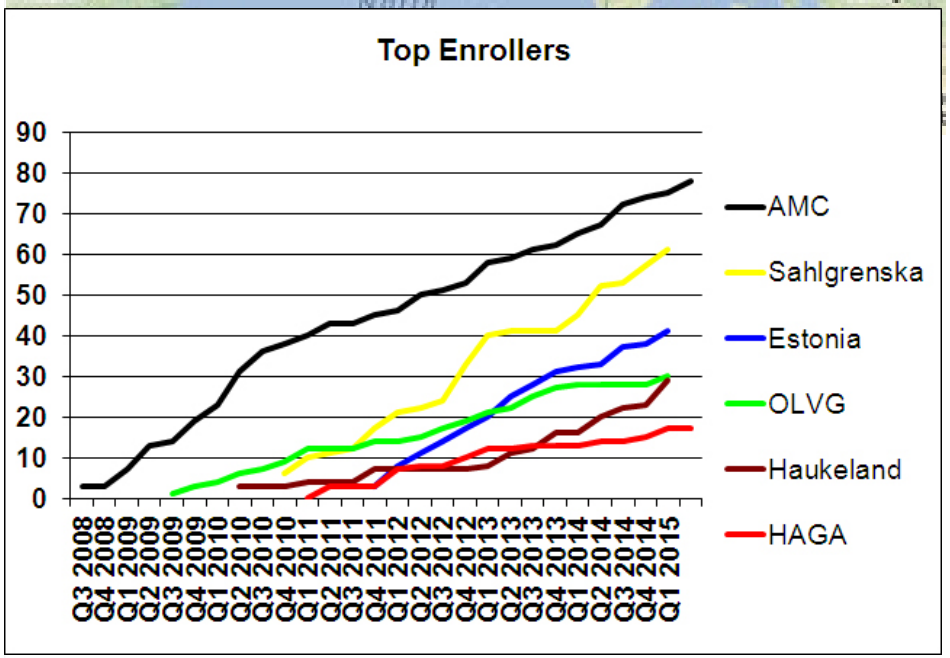
Participating sites & Top enrolling sites



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Flowchart

304 patients randomly assigned

150 randomized to CTO-PCI

154 randomized to No CTO-PCI

2 withdrew consent

0 withdrew consent

148 CTO-PCI
(1 refusal of CTO-PCI)

154 No CTO-PCI

148 with clinical follow-up

154 with clinical follow-up

12 primary imaging endpoints not available
6 poor imaging quality
6 Imaging not available

10 primary imaging endpoints not available
5 with poor imaging quality
5 imaging not available

136 analyzed for primary imaging endpoints

144 analyzed for primary imaging endpoints

Patient characteristics

	CTO-PCI (n=148)		No CTO-PCI (n=154)	
Age (years, mean, SD)	60	(±10)	60	(±10)
Men	131	(89%)	126	(82%)
Diabetes Mellitus	22	(15%)	25	(26%)
Triple vessel disease (>70% stenosis)	62	(42%)	67	(44%)
Patients with multiple CTOs	13	(9%)	22	(14%)
MI Syntax Score I (pre-pPCI) (mean, SD)	29	(±8)	29	(±10)
Infarct size - Peak CK-MB (median, IQR)	130	(39-272)	111	(43-256)
LVEF prior to randomization (mean, SD)	41	(±11)	42	(±12)

CTO characteristics during pPCI

CTO characteristics (adjudicated)	CTO-PCI (n=148)		No CTO-PCI (n=154)	
CTO in RCA	64	(43%)	78	(51%)
in LCX	48	(32%)	37	(24%)
in LAD	36	(24%)	39	(25%)
TIMI flow 0	132	(89%)	139	(90%)
TIMI flow 1	15	(10%)	14	(9%)
TIMI flow 2	1	(1%)	1	(1%)
Total J-CTO score (mean, SD)	2	(±1)	2	(±1)
Previously failed lesion	2	(1%)	4	(3%)
Blunt stump	33	(22%)	45	(29%)
Bending	98	(66%)	108	(70%)
Calcification	115	(78%)	132	(86%)
Occlusion length ≥20mm	60	(41%)	68	(44%)

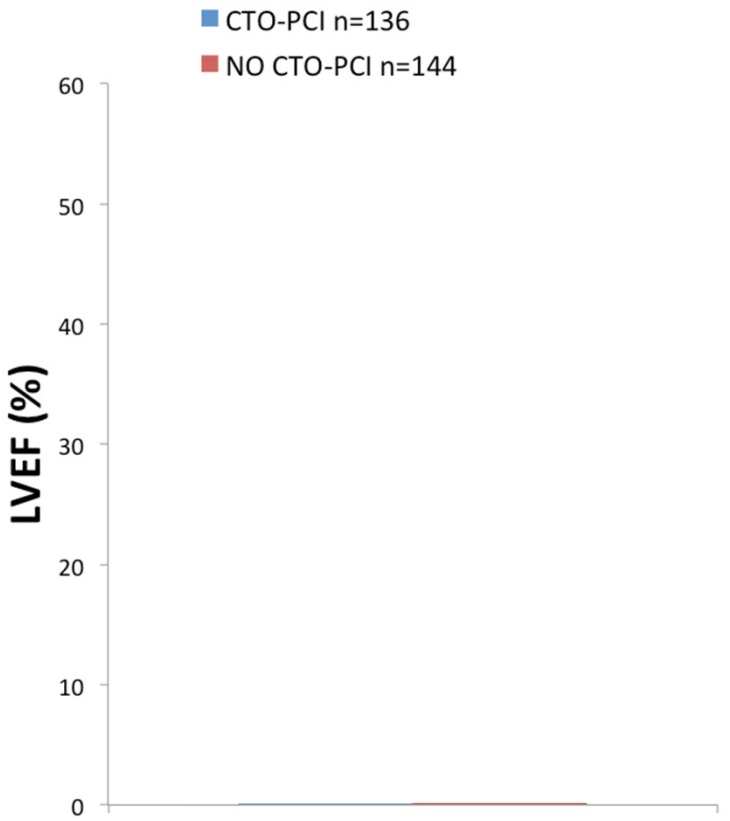
CTO-PCI treatment arm

		CTO-PCI (n=147)	
Number of days from primary PCI to CTO PCI (mean, SD)		5	(±2)
Number of days from randomization to CTO PCI (mean, SD)		2	(±2)
Multiple CTO arteries treated		6	(4%)
Technique CTO procedure	Antegrade only	124	(84%)
	Retrograde	23	(16%)
	Crossboss/ Stingray	5	(3%)
PCI successful, self-reported		***117***	***(80%)***
PCI successful, corelab adjudicated		***106***	***(72%)***
Everolimus eluting stent		95	(90%)
Number of stents used (median, IQR)		2	(1-3)

Periprocedural complications

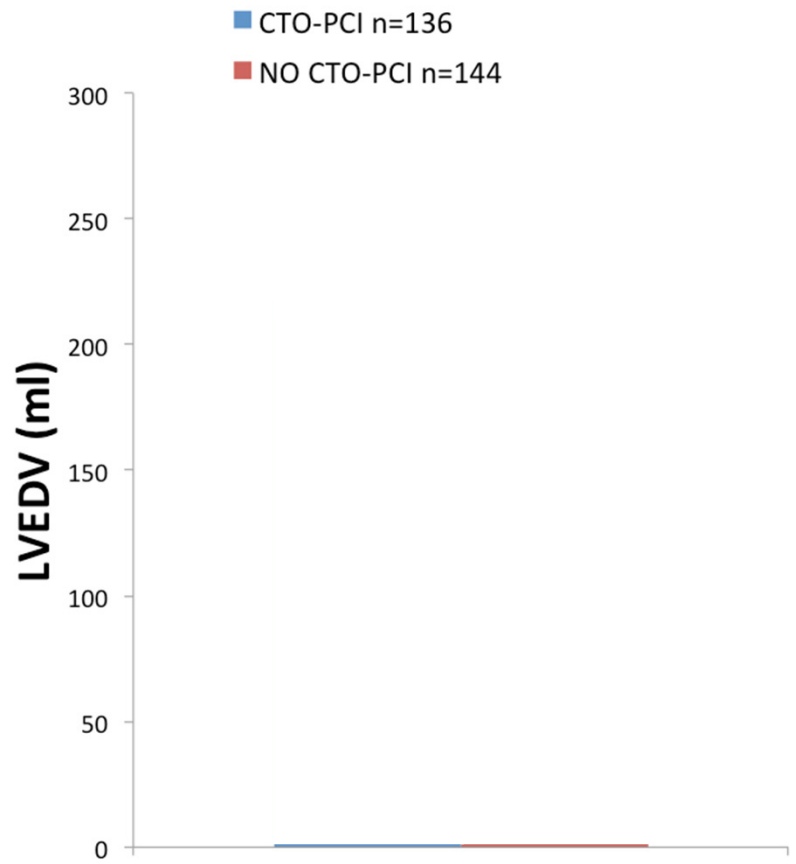
Periprocedural adverse events	CTO Vessel	Donor Artery
Dissection	12	1
Occlusion side branch	2	0
Thrombus	1	0
Tamponade	1	0
Major arrhythmia	2	
Resuscitation	4	
Myocardial infarction (Third Universal)	4	
Emergency CABG/Stroke/Death	0	

Primary Endpoint #1 (LVEF @ 4m)



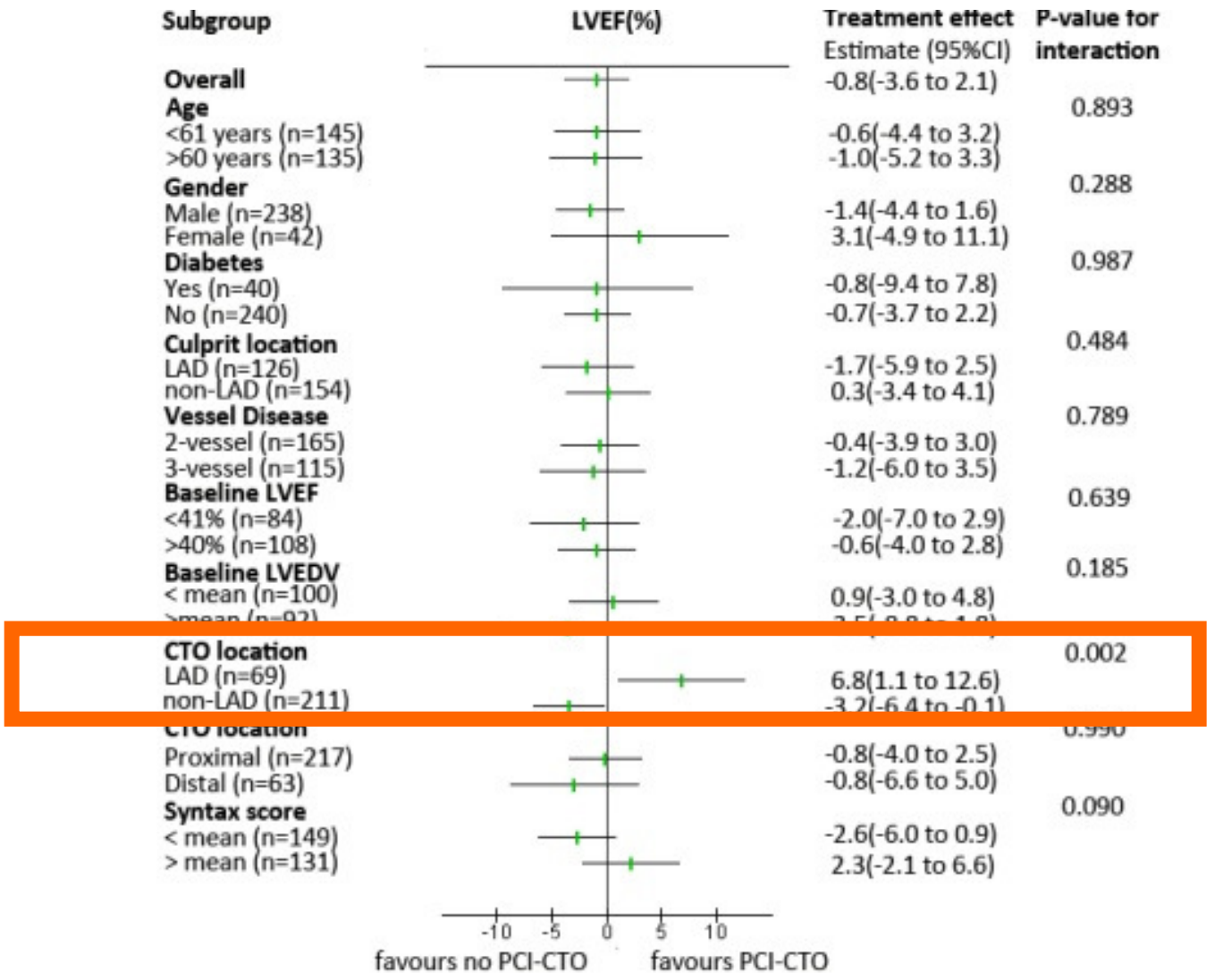
	CTO-PCI (n=136)		No CTO-PCI (n=144)		Difference (95%CI)		p
LVEF (%)	44·1	(12·2)	44·8	(11·9)	-0·8	(-3·6 to 2·1)	0·597

Primary Endpoint #2 (LVEDV @ 4m)

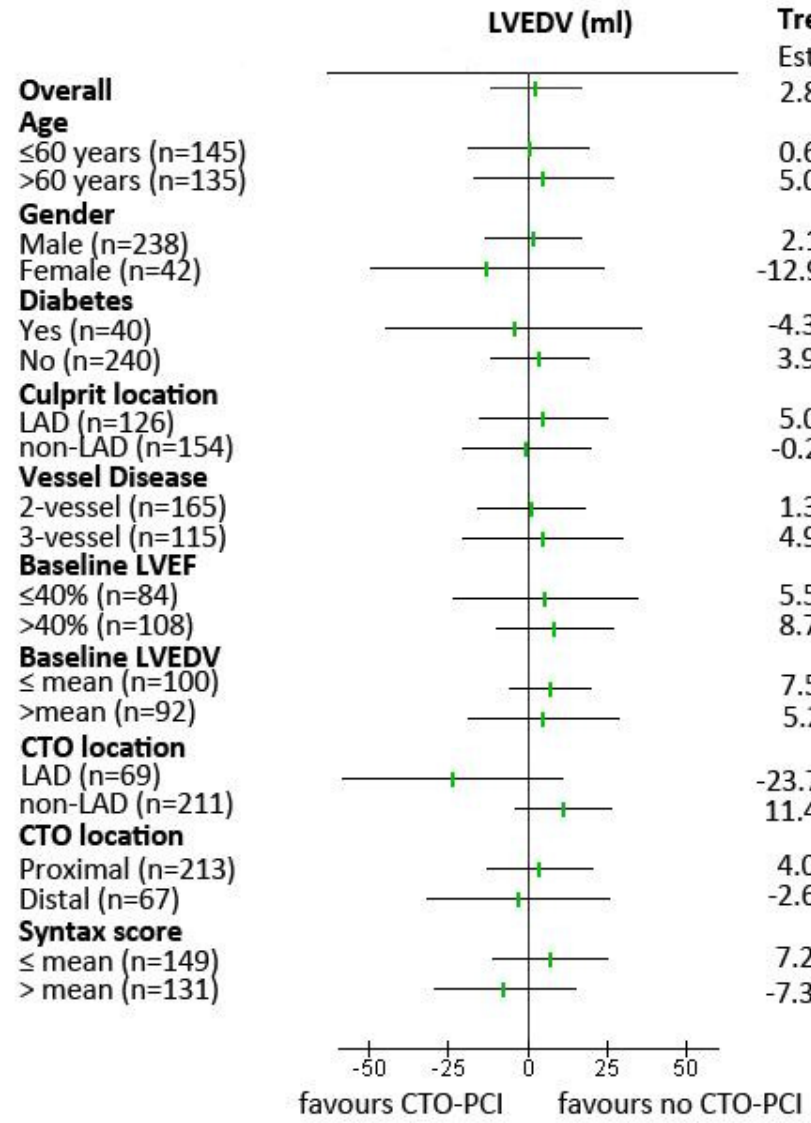


	CTO-PCI (n=136)		No CTO-PCI (n=144)		Difference (95%CI)		p
LVEDV (mL)	215·6	(62·5)	212·8	(60·3)	2·8	(-11·6 to 17·2)	0·703

LVEF – Subgroup analyses



LVEDV – Subgroup analyses

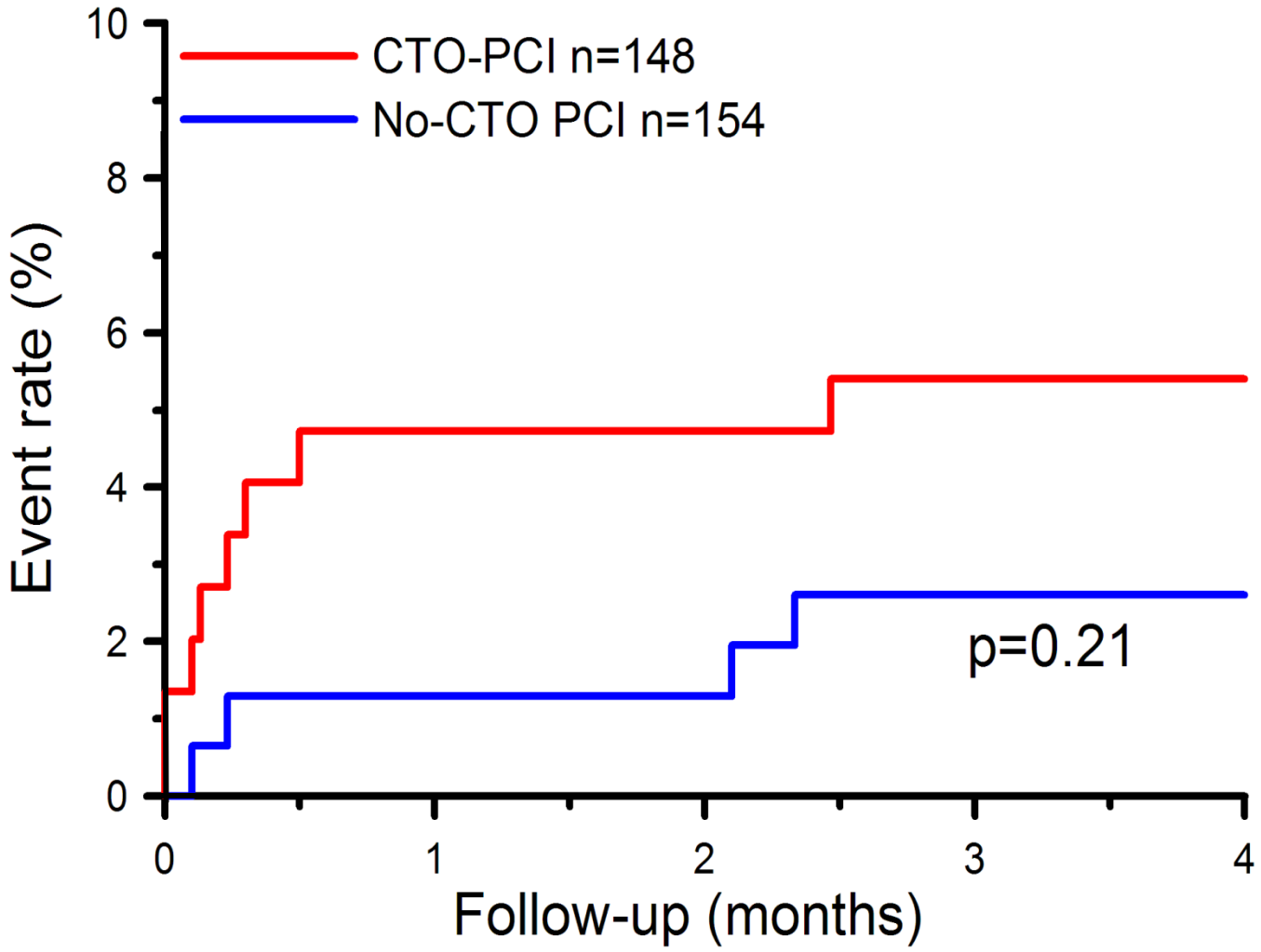


	Treatment effect Estimate (95%CI)	P-value for interaction
Overall	2.8(-11.6 to 17.2)	
Age		0.769
≤60 years (n=145)	0.6(-18.3 to 19.6)	
>60 years (n=135)	5.0(-17.0 to 26.9)	
Gender		0.474
Male (n=238)	2.1(-13.0 to 17.2)	
Female (n=42)	-12.9(-49.7 to 23.9)	
Diabetes		0.698
Yes (n=40)	-4.3(-44.7 to 36.1)	
No (n=240)	3.9(-11.6 to 19.3)	
Culprit location		0.723
LAD (n=126)	5.0(-15.4 to 25.4)	
non-LAD (n=154)	-0.2(-20.5 to 20.1)	
Vessel Disease		0.809
2-vessel (n=165)	1.3(-15.7 to 18.3)	
3-vessel (n=115)	4.9(-20.3 to 30.2)	
Baseline LVEF		0.850
≤40% (n=84)	5.5(-23.6 to 34.7)	
>40% (n=108)	8.7(-9.8 to 27.2)	
Baseline LVEDV		0.864
≤ mean (n=100)	7.5(-5.4 to 20.3)	
>mean (n=92)	5.2(-18.5 to 28.8)	
CTO location		0.039
LAD (n=69)	-23.7(-58.4 to 11.0)	
non-LAD (n=211)	11.4(-3.9 to 26.7)	
CTO location		0.636
Proximal (n=213)	4.0(-12.5 to 20.5)	
Distal (n=67)	-2.6(-31.6 to 26.4)	
Syntax score		0.316
≤ mean (n=149)	7.2(-11.0 to 25.4)	
> mean (n=131)	-7.3(-29.5 to 14.9)	

MACE @ 4 months

Major Adverse Cardiac Events (MACE)	CTO-PCI		No CTO-PCI		p
Cardiac death	4	(2·7%)	0	(0%)	0·056
Myocardial infarction (Third Universal definition)	5	(3·4%)	3	(1·9%)	0·494
Periprocedural	4	(2·7%)	1	(0·6%)	0·207
Spontaneous/Recurrent	2	(1·4%)	2	(1·3%)	1·000
CABG surgery	0	-	1	(0·6%)	1·000
MACE	8	(5·4%)	4	(2·6%)	0·212

MACE @ 4 months



Conclusions

- CTO-PCI within one week after pPCI is feasible and safe

- Early CTO-PCI :
  - not associated with higher LVEF @ 4 months
  - not associated with lower LVEDV @ 4 months

- In the subgroup analysis CTO-PCI of the LAD
  - associated with significantly higher LVEF @ 4 months

Additional PCI of a CTO located in the LAD may improve LVEF and potentially improved clinical outcome during follow up.

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