How Can We Further Improve Reperfusion in AMI?:

Revising or Novel Approach

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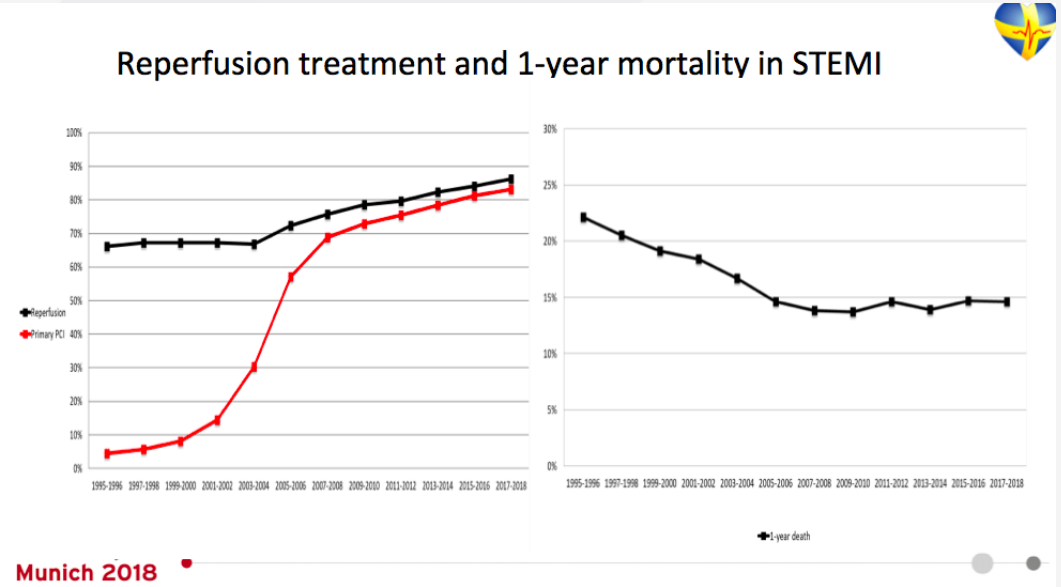
Disclosure

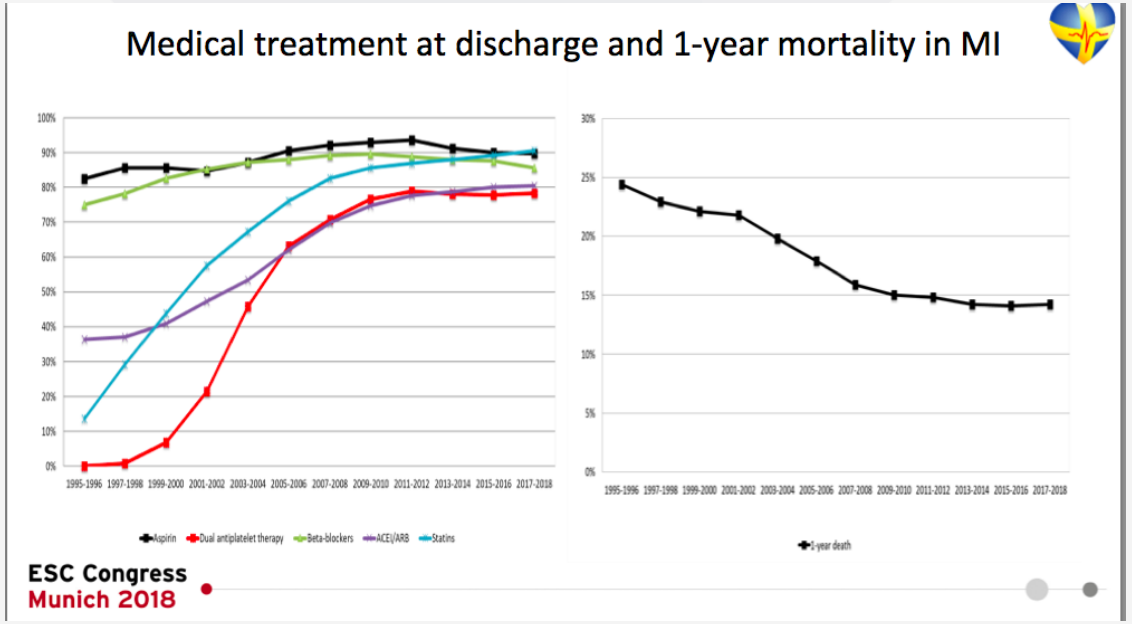
- Potential conflicts of interest
- Unrestricted institutional grant for fellowship from Boston Scientific
- Speaker fees
  - Bosoton, Medtronic, Abbott Vascular, Miracor

Reperfusion in STEMI

- Well its all fine isn’t it since we started primary PCI?
- Outcomes are good: whats the problem?

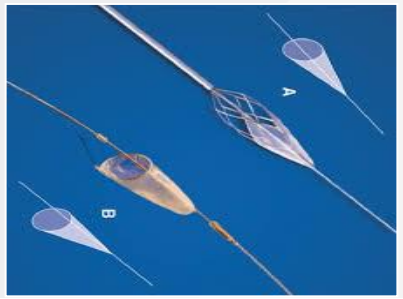
Improvement in the outcomes for STEMI patients have plateaued
But we seem to be doing our best !

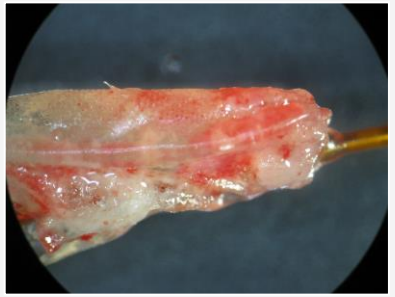


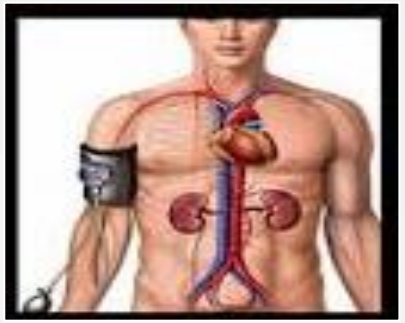


Which treatments have we tried in STEMI … and abandoned

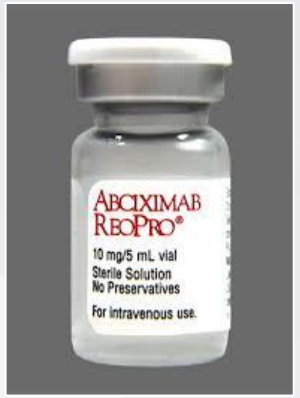
Mechanical

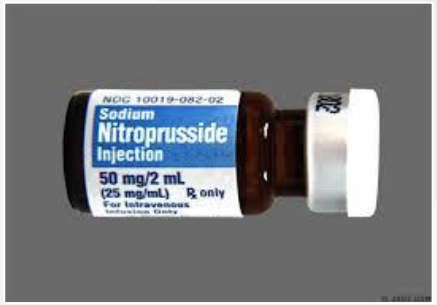






Pharmacological





To improve outcomes for those patients where “standard therapy” isnt enough – we need to know who they are likely to be

“Standard” therapy for STEMI

Anticoagulation, Predilation /aspiration, Stent, DAPT

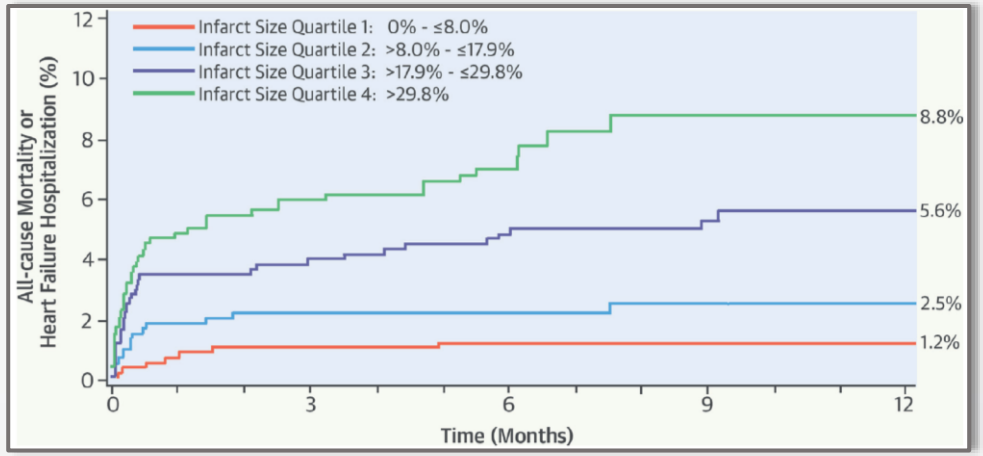
Works well for around 60-70% patients with STEMI

Individual identification would allow triage for additional therapy

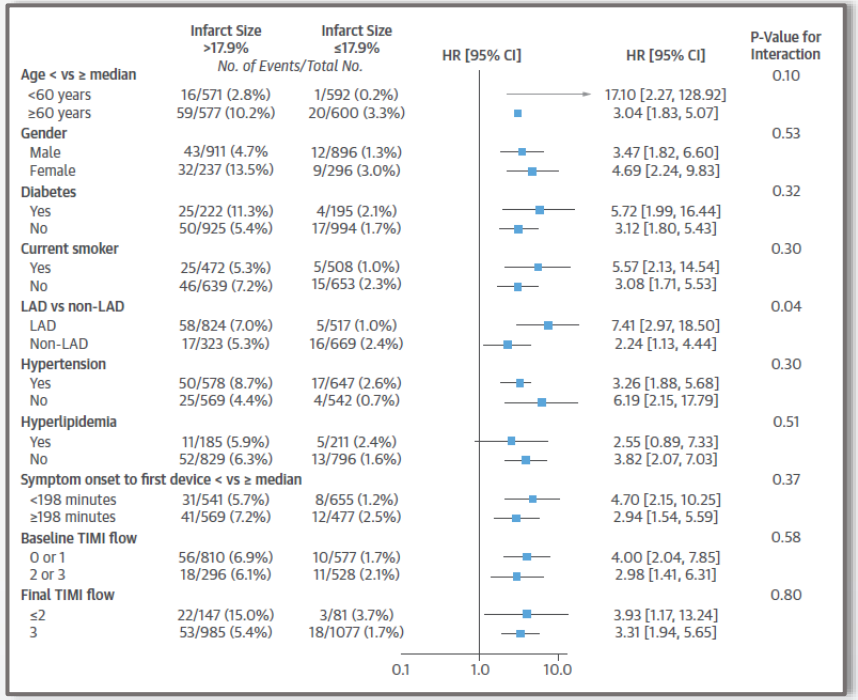
Relationship Between Infarct Size and Clinical Outcomes Following PPCI

- Patient level meta-analysis 10 RCTs PPCI, N = 2362, infarct size assessed within 1 month by CMR or SPECT with clinical FU for >6M
- KM estimated 1 year rates:
  - ❖ All Cause Mortality 2.2%
  - ❖ Reinfarction 2.5%
  - ❖ Heart Failure Hospitalisation 2.6%

Infarct Size and Prognosis After PPCI



Relationship between Infarct Size and the Composite EP of All-Cause Mortality or HF Hospitalisation During 1Y FU

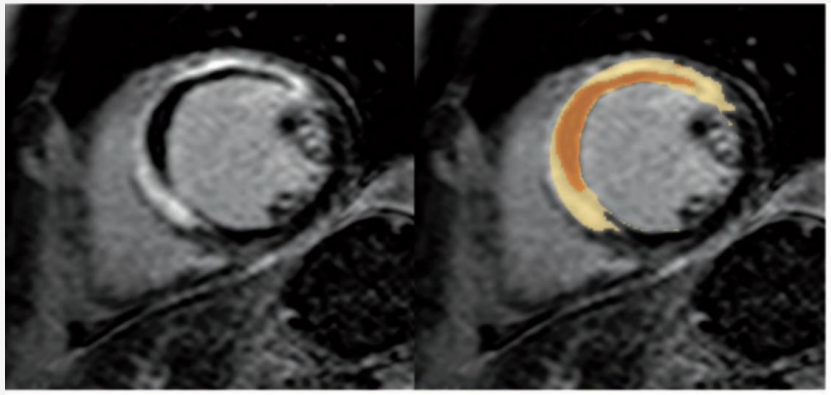


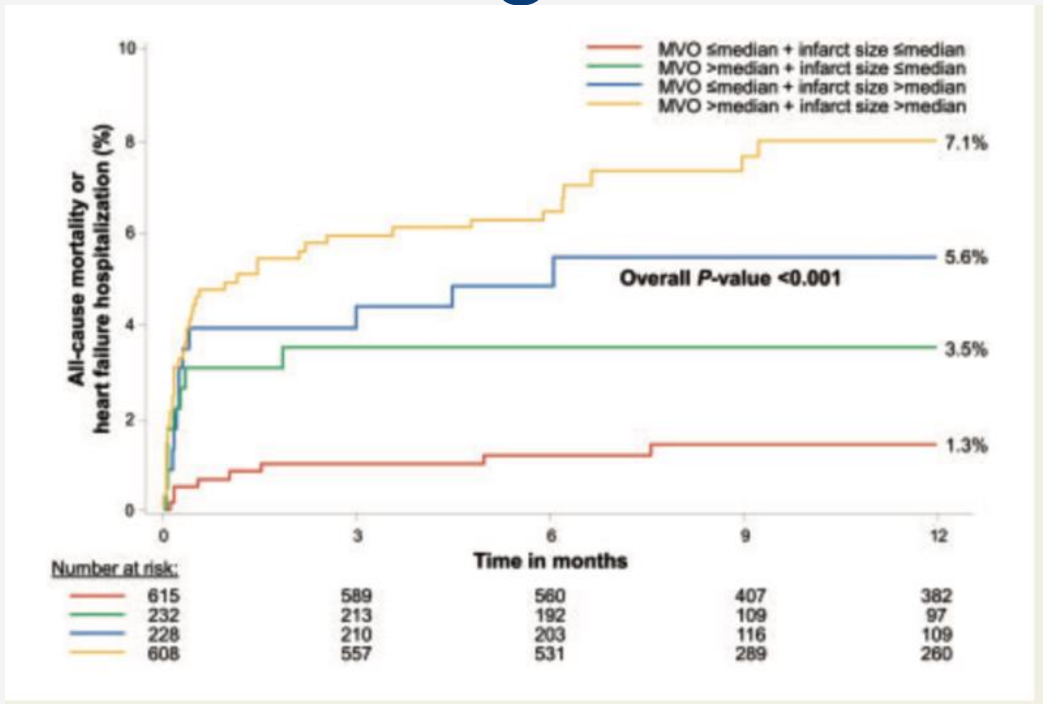
	Infarct Size >17.9%	Infarct Size ≤17.9%	HR [95% CI]	HR [95% CI]	P-Value for Interaction
	No. of Events/Total No.				
Age < vs ≥ median					0.10
<60 years	16/571 (2.8%)	1/592 (0.2%)		17.10 [2.27, 128.92]	
≥60 years	59/577 (10.2%)	20/600 (3.3%)		3.04 [1.83, 5.07]	
Gender					0.53
Male	43/911 (4.7%)	12/896 (1.3%)		3.47 [1.82, 6.60]	
Female	32/237 (13.5%)	9/296 (3.0%)		4.69 [2.24, 9.83]	
Diabetes					0.32
Yes	25/222 (11.3%)	4/195 (2.1%)		5.72 [1.99, 16.44]	
No	50/925 (5.4%)	17/994 (1.7%)		3.12 [1.80, 5.43]	
Current smoker					0.30
Yes	25/472 (5.3%)	5/508 (1.0%)		5.57 [2.13, 14.54]	
No	46/639 (7.2%)	15/653 (2.3%)		3.08 [1.71, 5.53]	
LAD vs non-LAD					0.04
LAD	58/824 (7.0%)	5/517 (1.0%)		7.41 [2.97, 18.50]	
Non-LAD	17/323 (5.3%)	16/669 (2.4%)		2.24 [1.13, 4.44]	
Hypertension					0.30
Yes	50/578 (8.7%)	17/647 (2.6%)		3.26 [1.88, 5.68]	
No	25/569 (4.4%)	4/542 (0.7%)		6.19 [2.15, 17.79]	
Hyperlipidemia					0.51
Yes	11/185 (5.9%)	5/211 (2.4%)		2.55 [0.89, 7.33]	
No	52/829 (6.3%)	13/796 (1.6%)		3.82 [2.07, 7.03]	
Symptom onset to first device < vs ≥ median					0.37
<198 minutes	31/541 (5.7%)	8/655 (1.2%)		4.70 [2.15, 10.25]	
≥198 minutes	41/569 (7.2%)	12/477 (2.5%)		2.94 [1.54, 5.59]	
Baseline TIMI flow					0.58
0 or 1	56/810 (6.9%)	10/577 (1.7%)		4.00 [2.04, 7.85]	
2 or 3	18/296 (6.1%)	11/528 (2.1%)		2.98 [1.41, 6.31]	
Final TIMI flow					0.80
≤2	22/147 (15.0%)	3/81 (3.7%)		3.93 [1.17, 13.24]	
3	53/985 (5.4%)	18/1077 (1.7%)		3.31 [1.94, 5.65]	

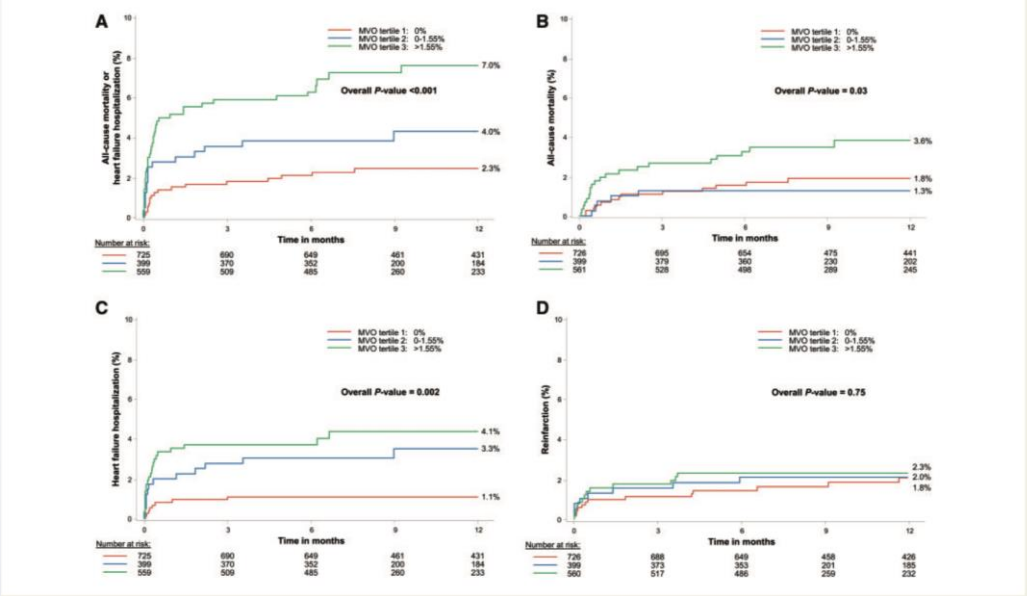
Outcomes were examined in patients with large versus small infarct size (IS) (above or below the median of 17.9%). Interaction p values are for comparison of the hazard ratios in each subgroup. HF = heart failure; LAD = left anterior descending; TIMI = Thrombolysis In Myocardial Infarction.

[1]Stone GW. et al. J Am Coll Cardiol. 2016;67:1674-83;

Added value of detecting MVO

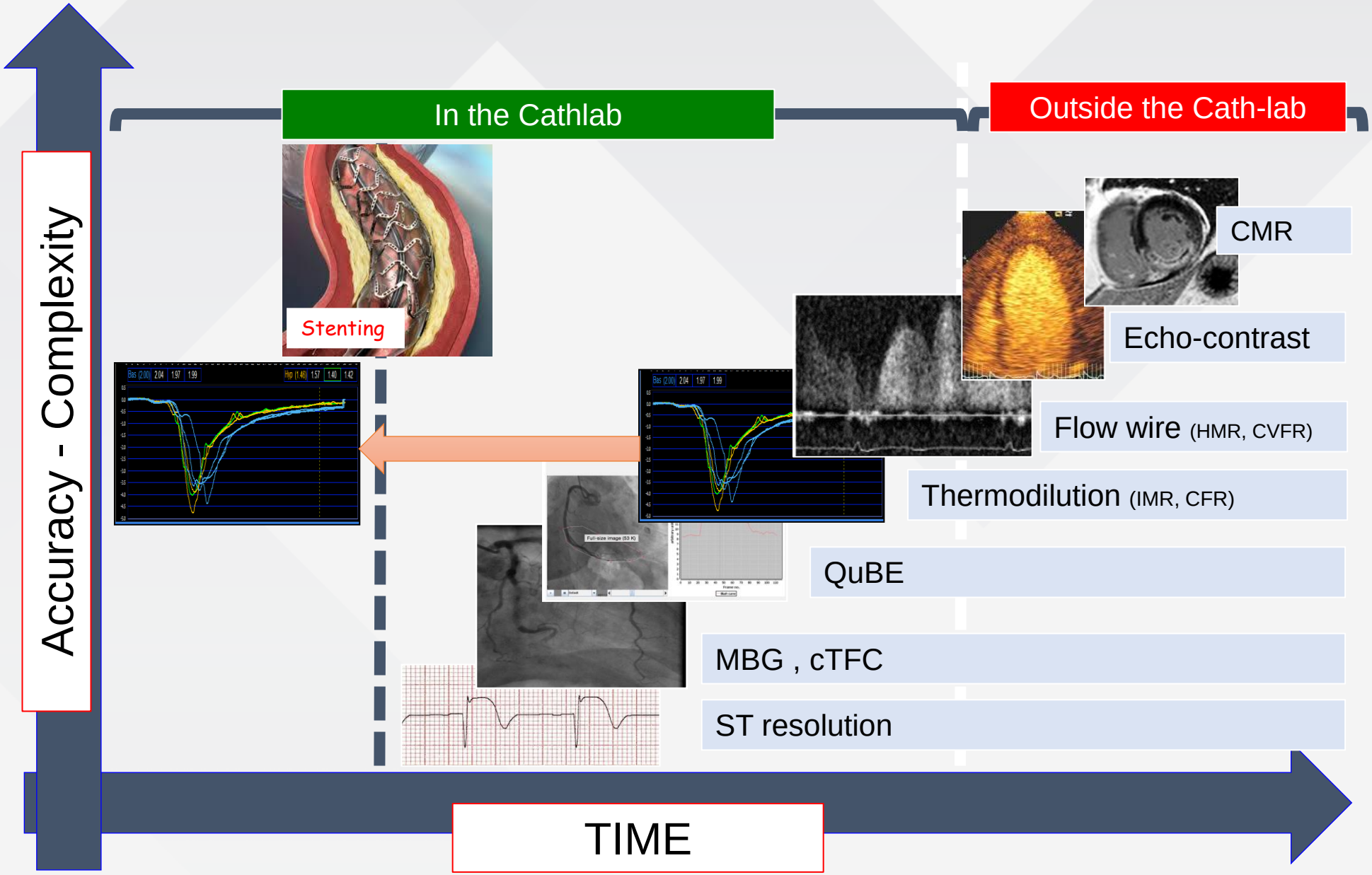






European Heart Journal (2017) **38**, 3502–3510
doi:10.1093/eurheartj/ehx414

How and when can we predict the outcome in STEMI?



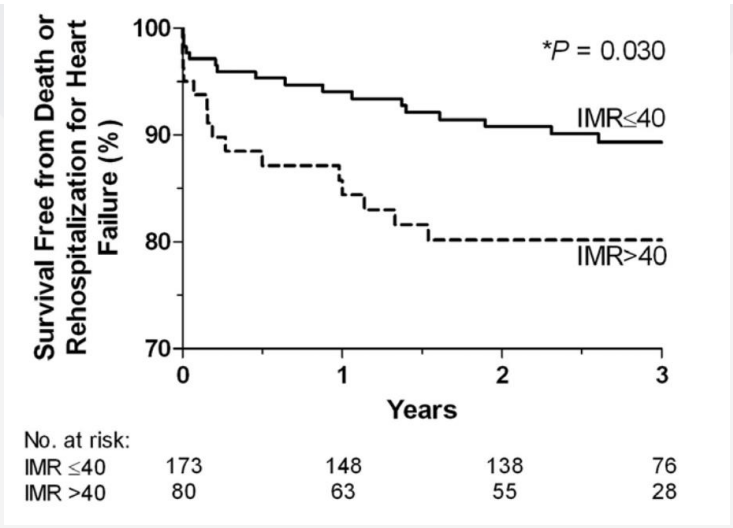
Can we predict the outcome in the lab during STEMI?

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

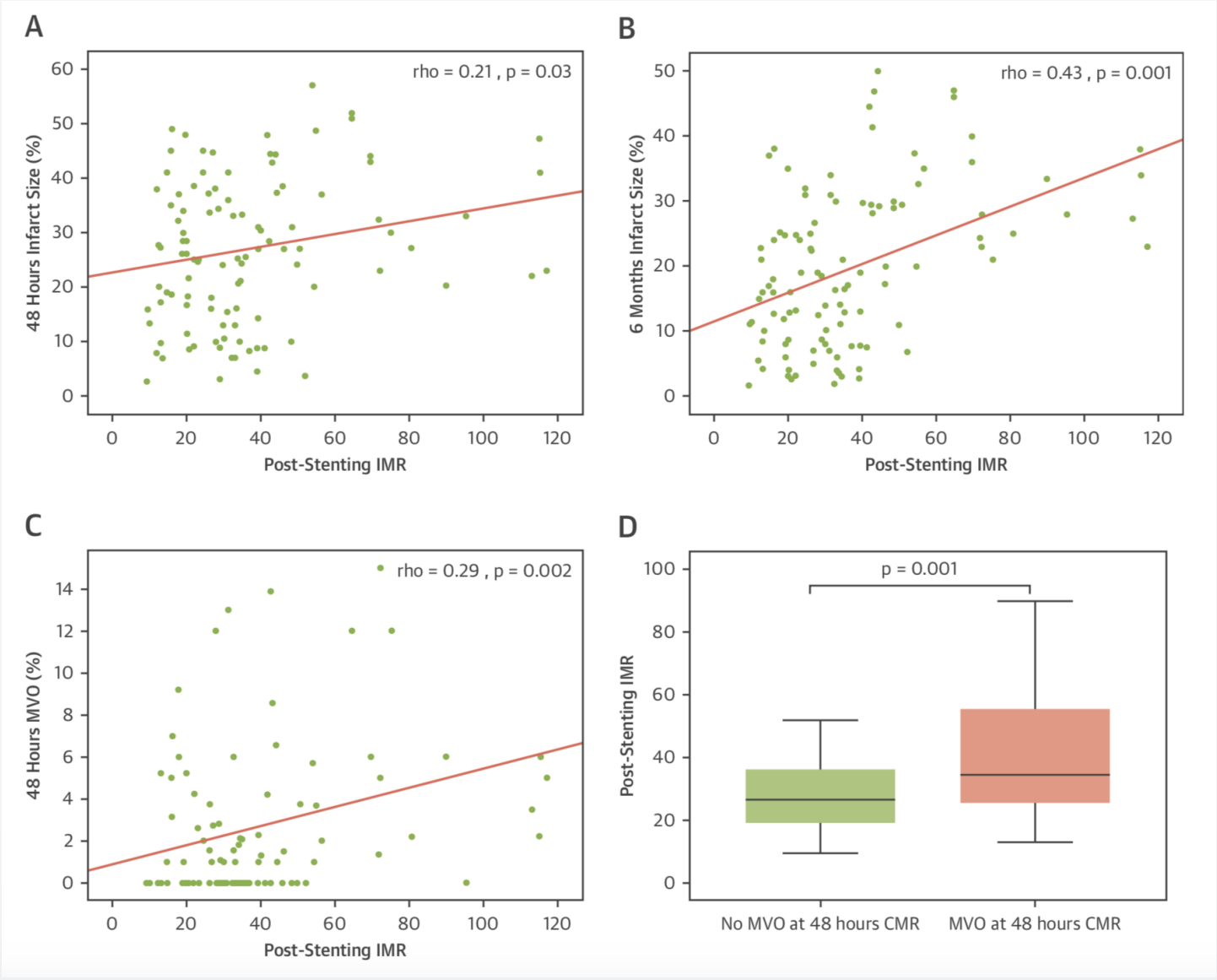
American Heart Association

Prognostic Value of the Index of Microcirculatory Resistance Measured After Primary Percutaneous Coronary Intervention

William F. Fearon, Adrian F. Low, Andy S. Yong, Ross McGeoch, Colin Berry, Maulik G. Shah, Michael Y. Ho, Hyun-Sook Kim, Joshua P. Loh and Keith G. Oldroyd



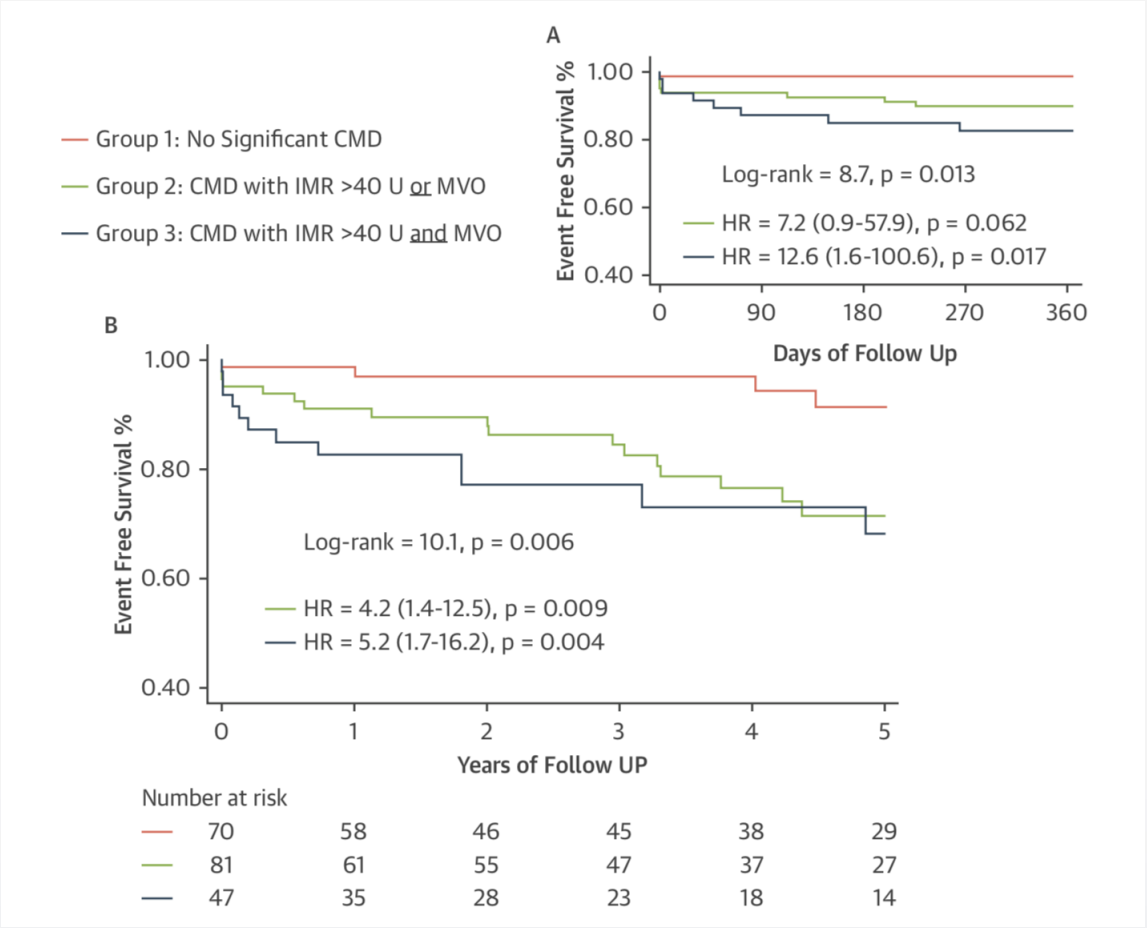
In STEMI an IMR > 40 at the end of the procedure predicts an adverse outcome

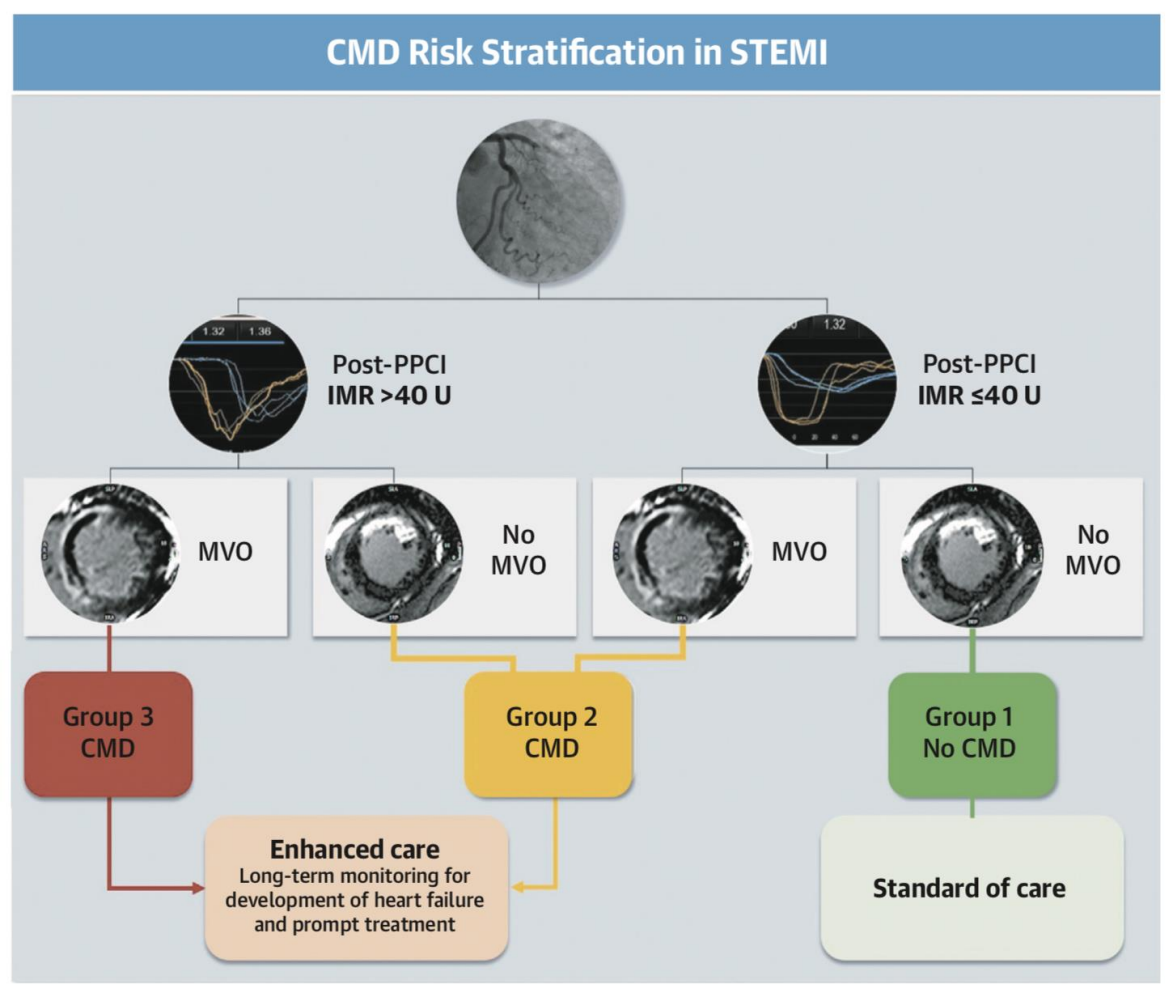


How do IMR & MRI measured infarct size /MVO relate in practice ?

De Maria, Banning A et al. JACC Cardiov Imaging 2019

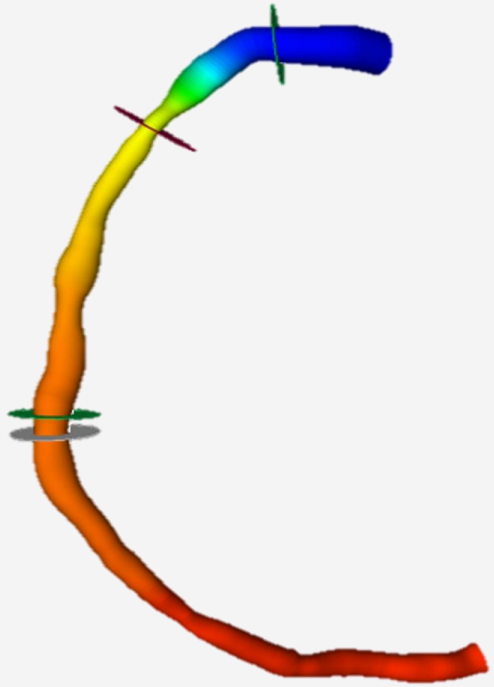
High IMR and/or MVO : impact on prognosis





Scarsini R, Banning A et al. JACC Cardiov Imaging 2021

Can we use a wire free angio-based index of CMD in STEMI?

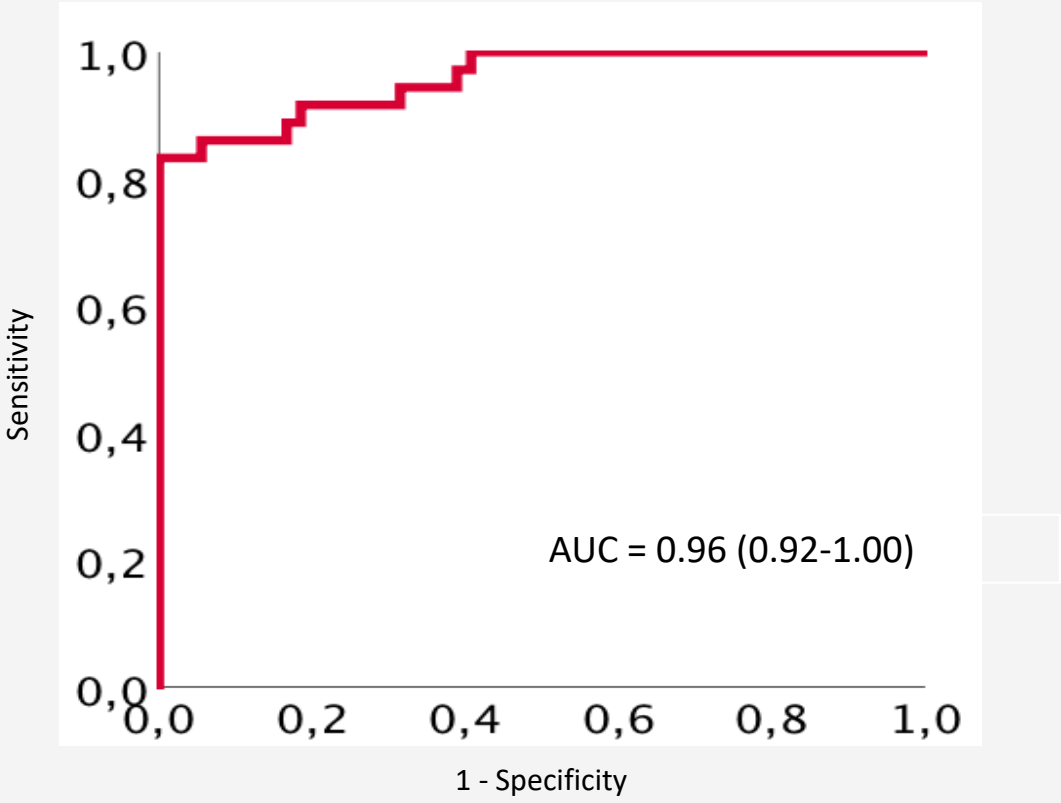


- Application of invasive IMR in practice is limited

- Main limitations of IMR remains:
  - pressure-wire based technique
    - instrumentation of the infarct-related artery
    - extra procedural time
    - technical complexity
    - extra costs
- angio-derived IMR (IMR_{angio}) has been recently developed through application of computational flow dynamic to 3-D vessel modelling

De Maria GL, Banning et al. Int J Cardiov Imaging 2020
De Maria GL, Banning. Eur Heart J Acute Cardiovasc Care 2021

Diagnostic accuracy of IMR_{angio} in STEMI



*IMR_{angio} in predicting IMR>40 U

IMR_{angio} diagnostic performance	
Accuracy	92.4%
Sensitivity	83.0%
Specificity	100%
Negative predictive value	90.2%
Positive predictive value	96.8%

De Maria GL, Banning et al. Int J Cardiov Imaging 2020

Pressure-controlled Intermittent Coronary Sinus Occlusion (PiCSO) in Acute Myocardial Infarction

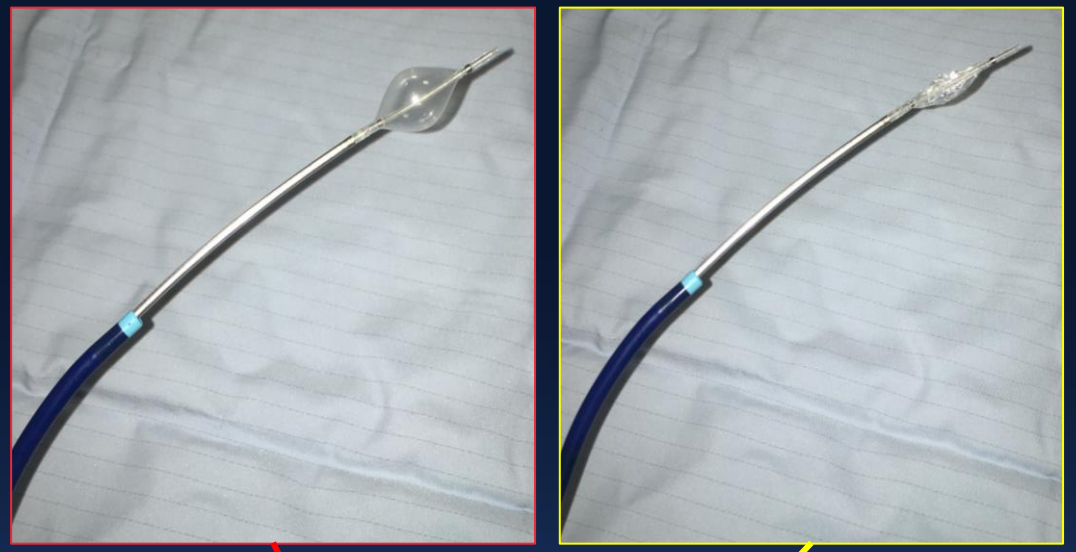
PICSO-AMI-I trial

On Behalf of PiCSO-AMI-I Investigators

Pressure Controlled Intermittent Coronary Sinus Occlusion (PiCSO)

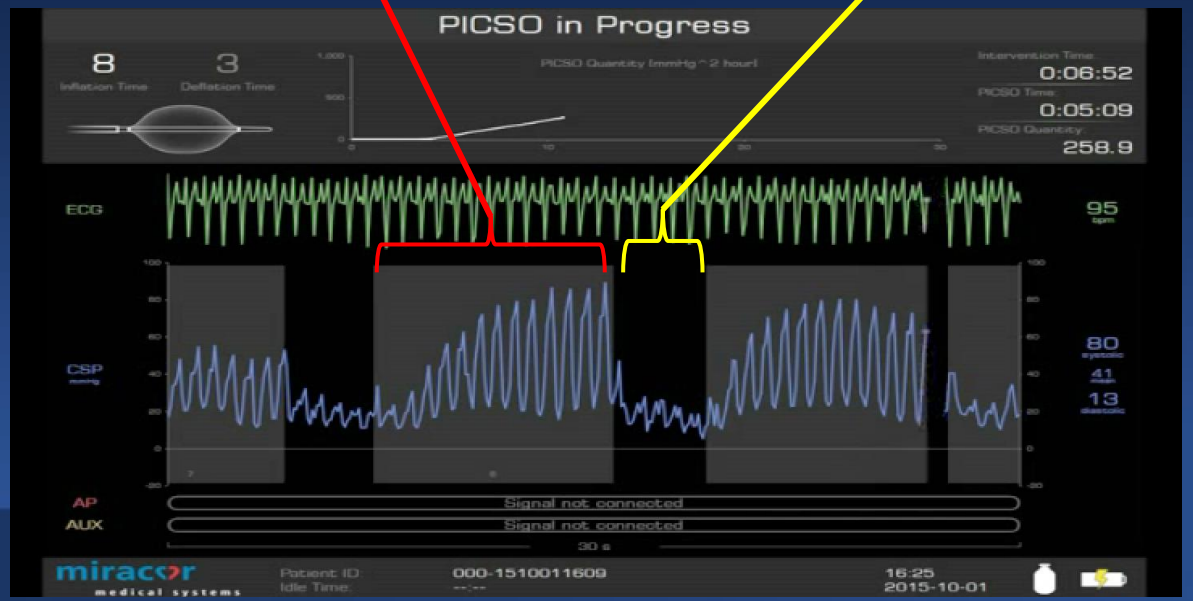
PiCSO Impulse Catheter

- 8Fr Balloon Tipped Catheter
- 16 x 25 mm Balloon
- Transfemoral Venous Access
- Coronary Sinus Positioning via 10Fr Steerable Guidesheath

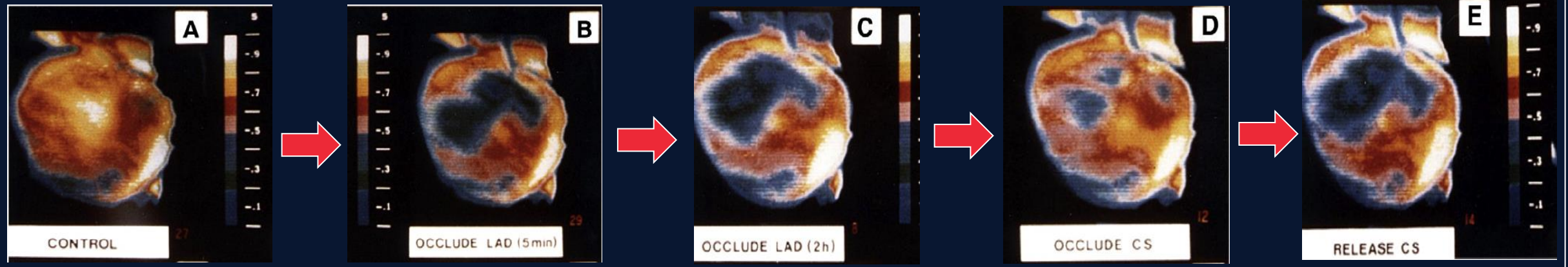


PiCSO Impulse Console

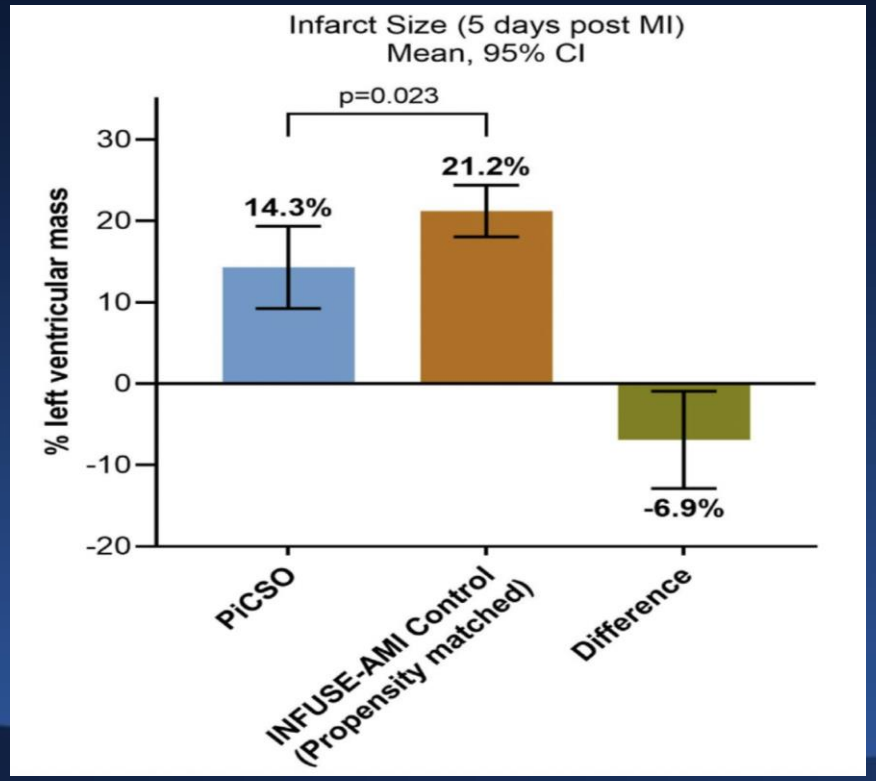
- Proprietary Wien Algorithm
- ECG and Coronary Sinus Pressure monitoring
- Helium shuttled in/out PiCSO Balloon



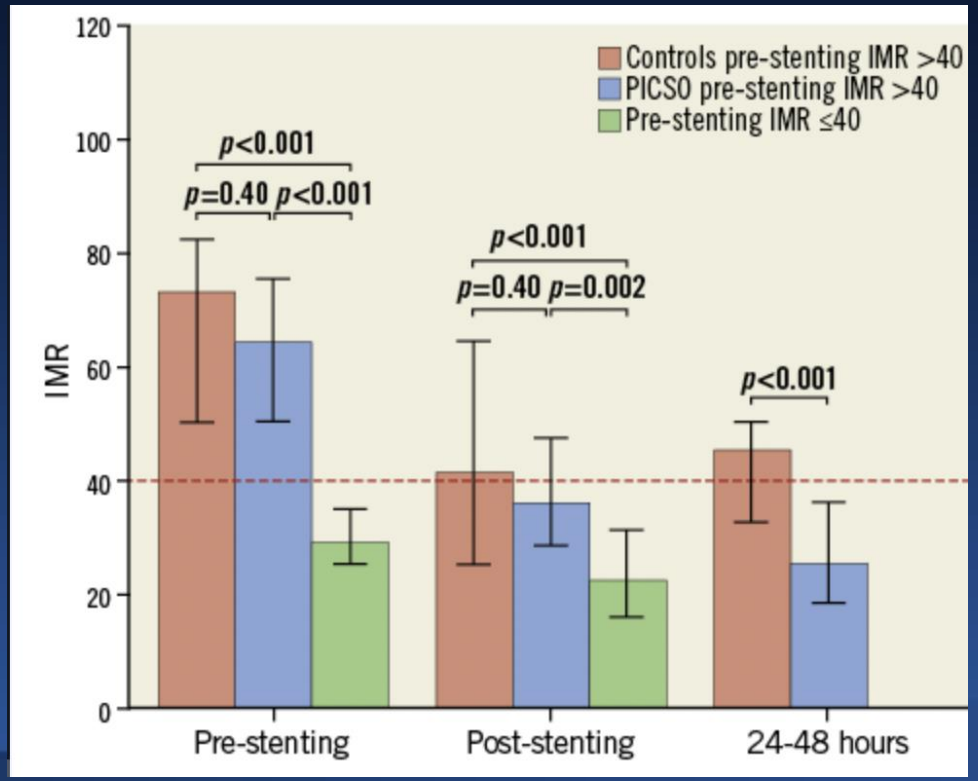
CRF TCT



Mohl W et al Cardiovasc Revasc Med 2015



Egred M L et al IJC Heart & Vasculature 2020



De Maria GL et al EuroIntervention 2018

CRF TCT

PiCSO-AMI-I trial

Design

International
Multicenter
Prospective
Randomized (1:1)
Controlled
Parallel-groups

PiCSO assisted pPCI

vs

Conventional pPCI

*144 sample size
80% power, alpha 0.05
To detect 25% reduction in IS
Assuming IS of 26%±12 in Control group and 20% drop-out rate

Primary Outcome

Infarct Size (%LV) at 5±2 days CMR*

Secondary Outcome

MVO (%LV) at 5±2 days CMR

IMH (%LV) at 5±2 days CMR

Infarct Size (%LV) at 6±1 months CMR

Myocardial Salvage 5 days CMR

Ejection Fraction 5 days /6 months CMR

ST segment resolution 60 – 90 min post flow restored

PiCSO Procedural Success rate

MACE at 6 months

PiCSO-AMI-I trial

Inclusion Criteria

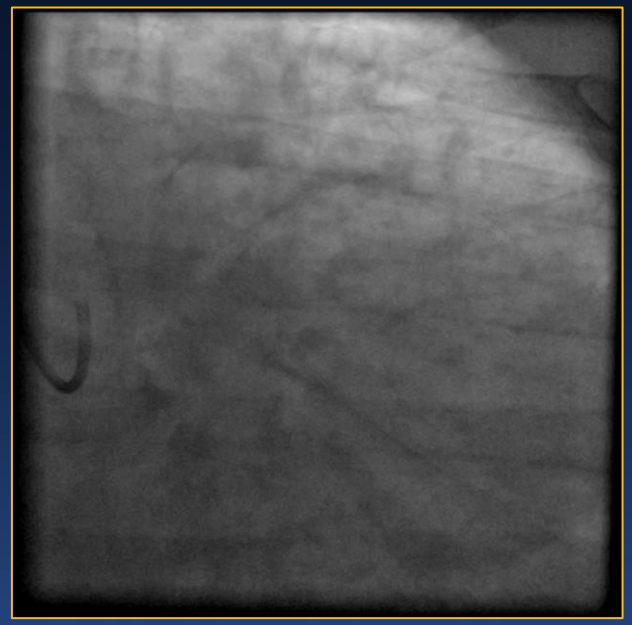
1. Age ≥18 years old with **anterior STEMI**
2. Culprit lesion in proximal or mid LAD
3. Pre-PCI **TIMI flow 0 or 1**
4. Symptoms onset **time ≤ 12 h**
5. Patient deemed eligible for primary PCI
6. Consent per approved national ethical committee specific requirements prior to the procedure.

Exclusion Criteria

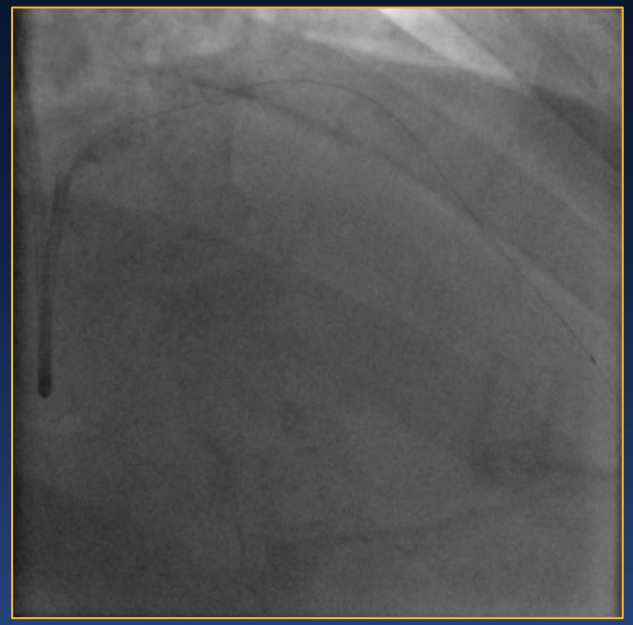
1. Implants or foreign bodies in the coronary sinus
2. Known allergy to polyurethanes, PET or stainless steel
3. Known pregnancy or breastfeeding
4. Pericardial effusion (cardiac tamponade)
5. Central hemodynamically relevant left/right shunt
6. Previous MI or CABG
7. History of stroke, TIA within last 6 months
8. Known Coagulopathy
9. Need for circulatory support or pre-procedural ventilation
10. CPR cardiac arrest for more than 5 min
11. Patient not suitable for femoral vein access
12. Contraindication to cardiac magnetic resonance imaging (CMR),
13. Active participation in another drug or device investigational study
14. Known severe kidney disease or on hemodialysis
15. Unconscious on presentation
16. Patients under judicial protection, legal guardianship or curatorship

PiCSO-AMI-I trial

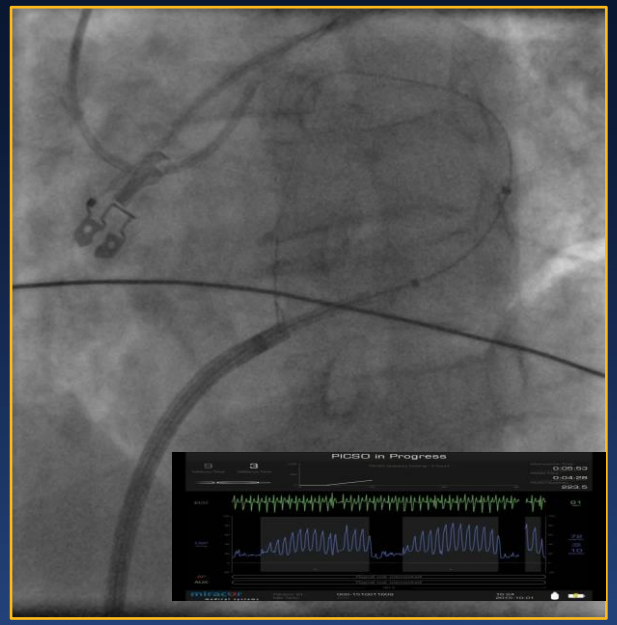
PiCSO Assisted pPCI



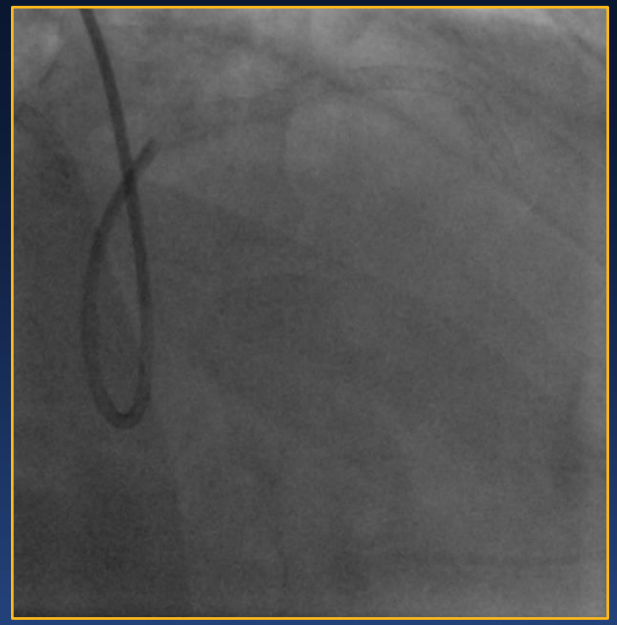
Baseline



IRA flow restoration

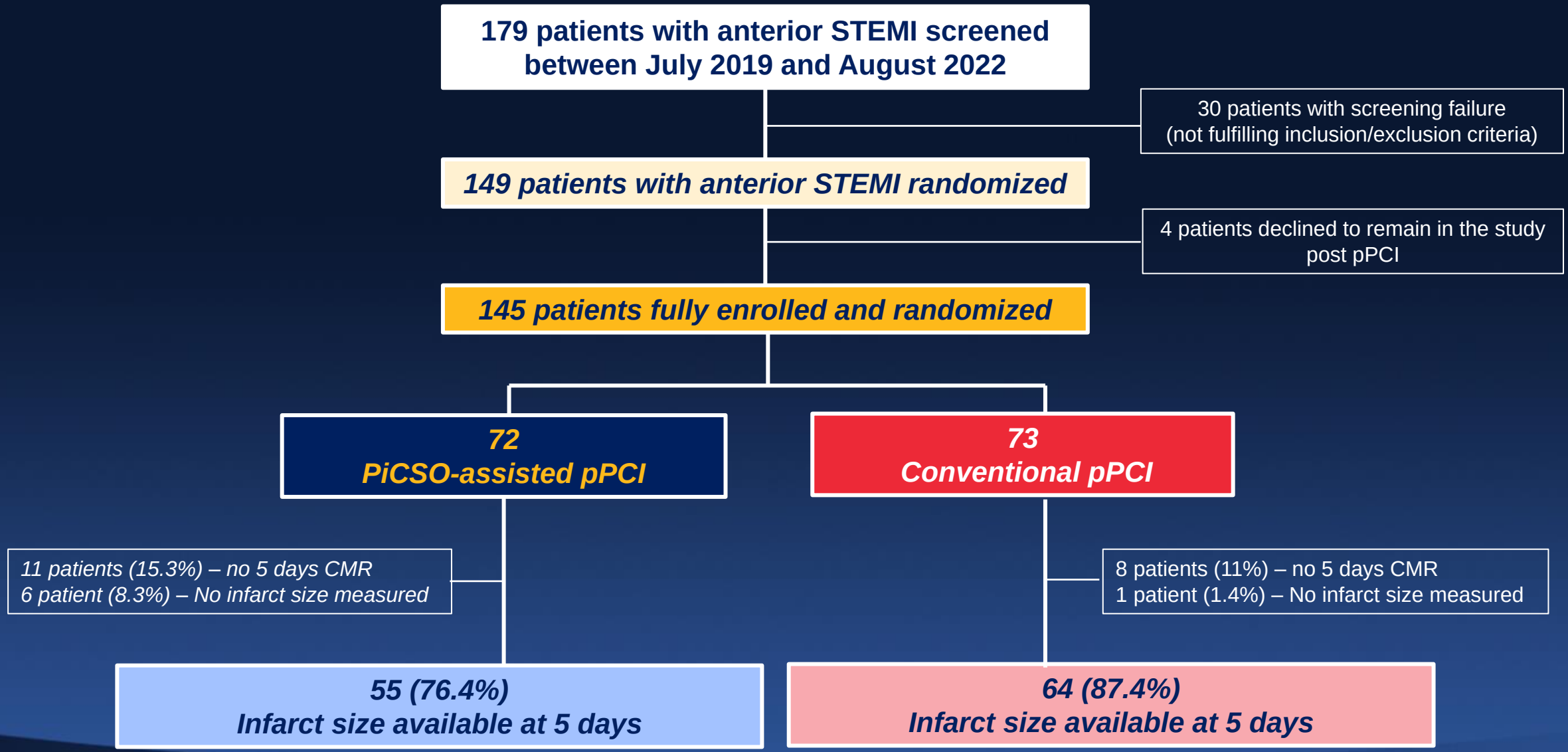


CS cannulation at PiCSO
(aiming at 45±5 min therapy)



Stenting

PiCSO-AMI-I trial



PiCSO-AMI-I trial

Baseline Characteristics	Overall (n=145)	PiCSO (n= 72)	Control (n= 73)
Killip Class			
I	120 (86.3)	59 (85.5)	61 (87.1)
II	17 (12.2)	10 (14.5)	7 (10.0)
III	2 (1.4)	0 (0.0)	2 (2.9)
Culprit Lesion Location			
Proximal LAD	91 (62.8)	45 (62.5)	46 (63.0)
Mid LAD	54 (37.2)	27 (37.5)	27 (37.0)
Number Vessel disease (diameter stenosis > 50%)			
1 vessel disease	76 (52.4)	39 (54.2)	37 (50.7)
2 vessel disease	45 (31.0)	19 (26.4)	25 (35.6)
3 vessel disease	24 (16.6)	14 (19.4)	10 (13.7)
Total Ischaemic time (minutes)	223.0 (134.0 – 310.0)	187.5 (130.0 – 295.0)	228.0 (149.0 – 350.0)
Time from FMC to flow (minutes)	106.0 (84.0 – 141.0)	102.0 (87.0 – 135.0)	112.0 (84.0 – 148.5)
Fibrinolysis prior pPCI	1 (0.7)	0	1 (1.4)
IRA TIMI flow pre pPCI (site reported)			
0	123 (84.8)	59 (81.9)	64 (87.7)
1	22 (15.2)	13 (18.1)	9 (12.3)

PiCSO-AMI-I trial

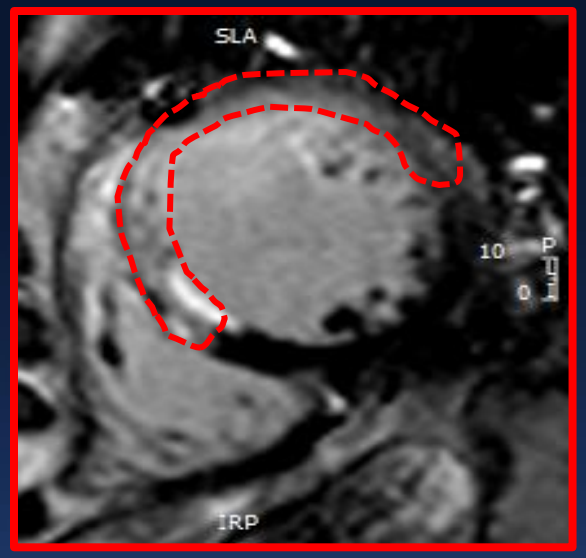
Procedural Characteristics	Overall (n=145)	PiCSO (n= 72)	Control (n= 73)	p
Radial Arterial Access	138 (95.2)	69 (95.8)	69 (94.5)	1.00
Thrombus Aspiration	21 (14.4)	10 (13.9)	11 (15.1)	0.84
Glycoprotein IIb/IIIa inhibitor	8 (5.5)	3 (4.2)	5 (6.8)	0.50
IRA re-occlusion after flow restoration	27 (18.6)	16 (22.2)	11 (15.1)	0.29
Final TIMI flow (site reported)				
2	14 (9.7)	6 (8.3)	8 (11.0)	0.78
3	131 (90.3)	66 (91.7)	65 (89.0)	
pPCI procedural time (minutes)	**68.0 (35.0 -100.0)**	**99.5 (83.0 -118.5)**	**35.0 (29.0 - 45.0)**	**< 0.001**
Fluoroscopy Time (minutes)	**12.0 (9.00 – 21.00)**	**21.0 (13.5 – 30.0)**	**10.0 (7.0 – 12.0)**	**< 0.001**
Dose-area product (Gy*cm^2)	**38.7 (16.9 – 65.7)**	**53.6 (26.6 – 93.1)**	**29.3 (15.7 – 47.5)**	**< 0.001**
Contrast Dye volume (ml)	**212.5 (180.0 – 250.0)**	**190.0 (150.0 – 241.0)**	**160.0 (130.0 – 200.0)**	**< 0.001**
PiCSO Procedural Success (at least 20 min of therapy)	-	**62 (86.1)**	-	-
PiCSO therapy target 45 min	-	**46 (63.9)**	-	-

PiCSO-AMI-I trial

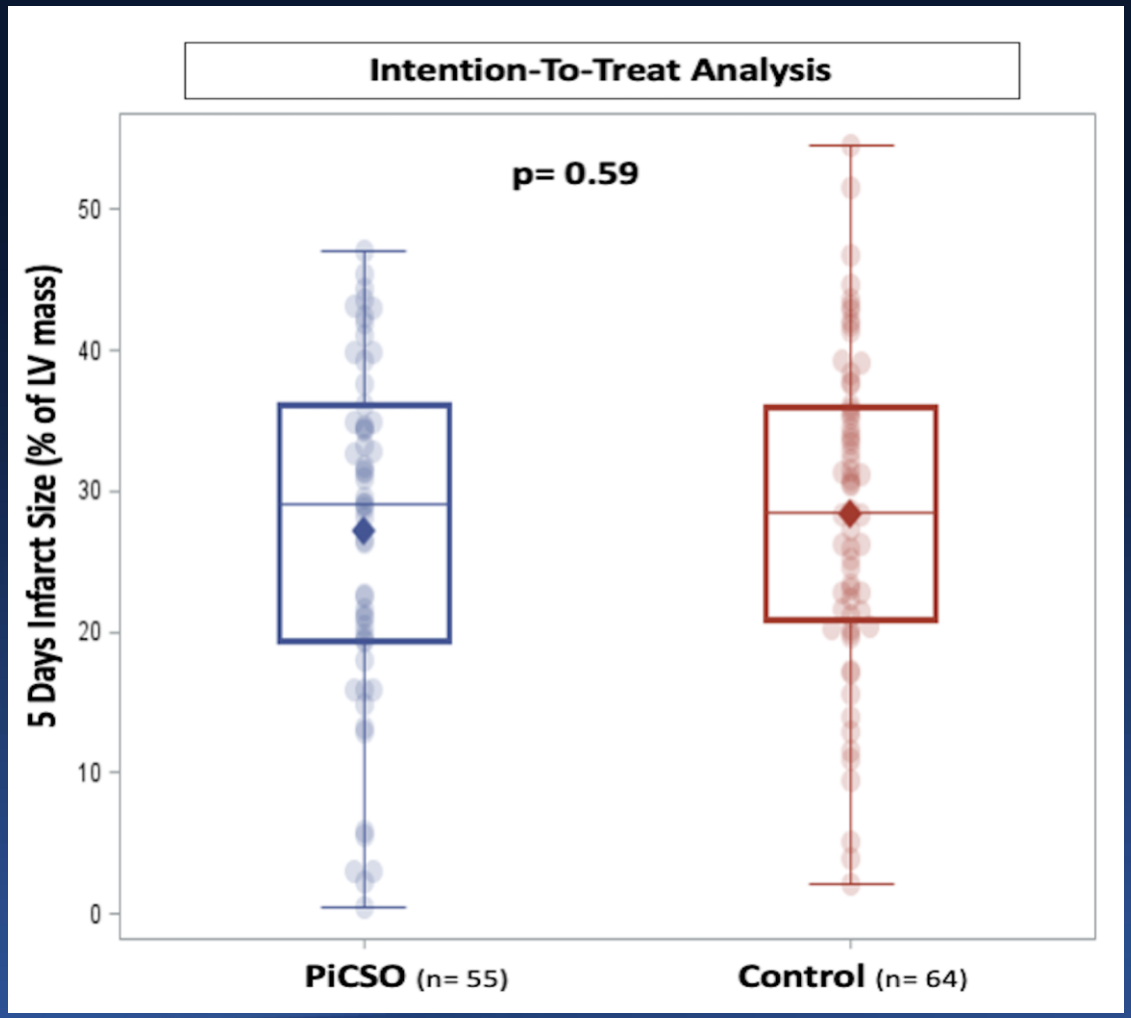
6 months Safety	PiCSO (n= 72)	Control (n= 73)	p
MACE	7 (9.7)	6 (8.2)	0.78
All-cause death	1 (1.4)	2 (2.7)	1.00
Hospitalization for HF	4 (5.6)	2 (2.7)	0.44
New/worsening HF	5 (6.9)	2 (2.7)	0.27
Reinfarction	0 (0.0)	0 (0.0)	1.00
Stroke	0 (0.0)	3 (4.1)	0.25
TVR	0 (0.0)	0 (0.0)	1.00
Stent thrombosis	0 (0.0)	1 (1.4)	1.00
CS damage	0 (0.0)	-	-
Vascular complications	0 (0.0)	0 (0.0)	1.00
BARC 3-5 bleeding	2 (2.8)	0 (0.0)	0.25
Ventricular tachycardia/fibrillation	1 (1.4)	0 (0.0)	0.50

PiCSO-AMI-I trial

PRIMARY ENDPOINT: IS% @5days CMR – Intention to treat Analysis



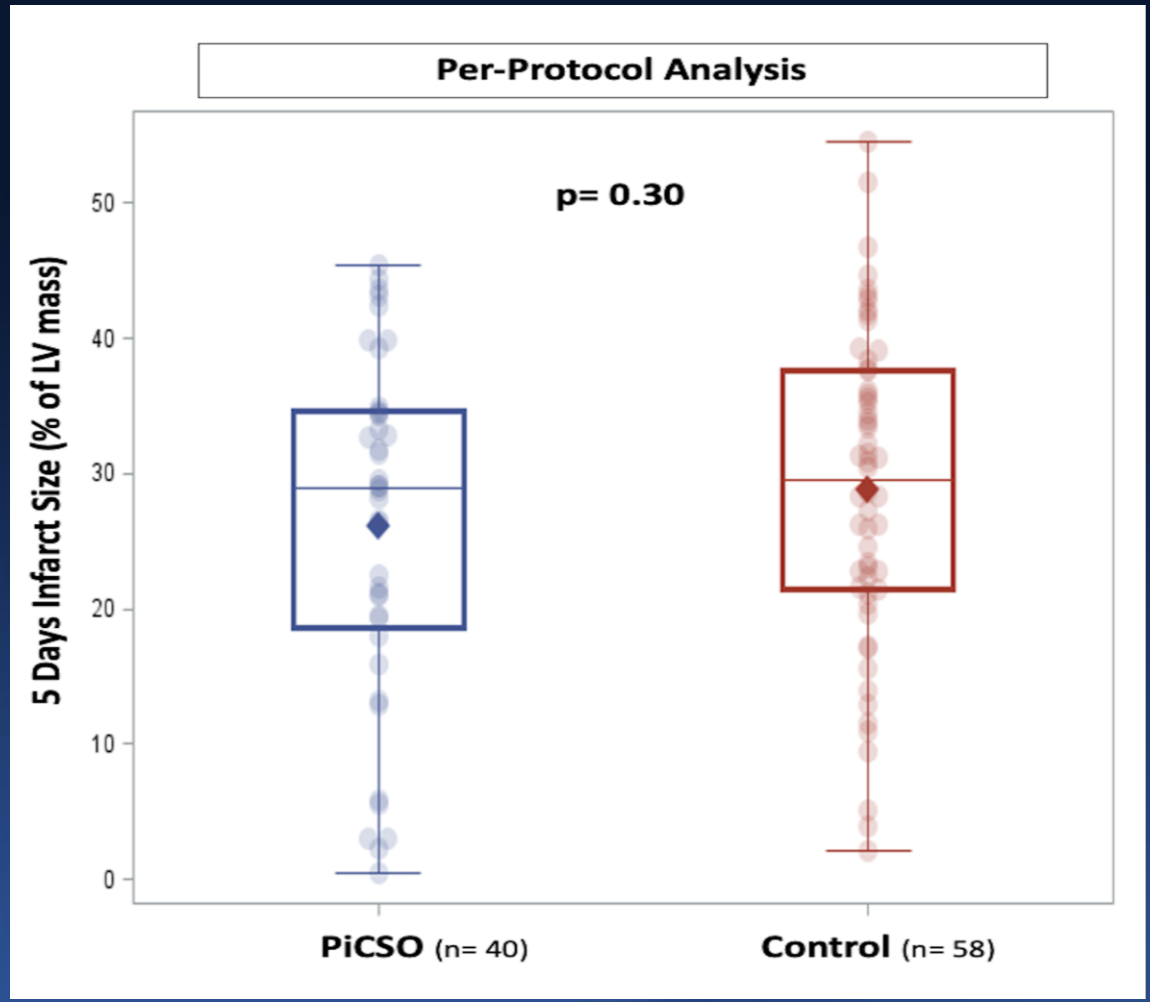
	PiCSO (n = 55)	Control (n= 64)	p
IS 5 days (LV%)	27.2% ± 12.4	28.3% ± 11.45	0.59



PiCSO-AMI-I trial

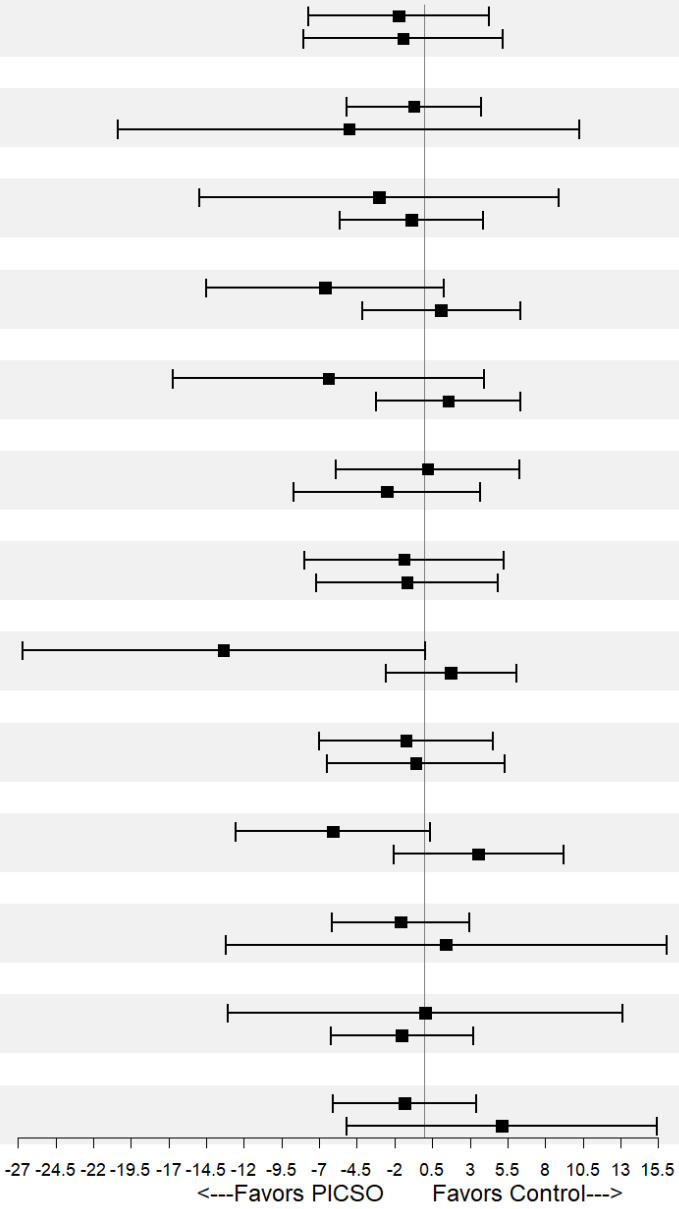
PRIMARY ENDPOINT: IS% @5days CMR – Per Protocol Analysis

	PiCSO (n= 40)		Control (n= 58)	
	N=72	%	N=73	%
Did not receive treatment per randomization	1	1.4%	1	1.4%
5-day CMR not done	11	15.3%	8	11.0%
5-day CMR not in the time window	4	5.6%	5	6.8%
Infarct size not evaluable on the 5-day CMR	6	8.3%	1	1.4%
Final TIMI flow post PCI <2 by core lab	4	5.6%	1	1.4%
CS canulation >30 min	8	11.1%		
Stenting prior to PiCSO start	7	9.7%		
PiCSO treatment <20 min	11	15.3%		
Patients dropping-out for Per-Protocol Analysis	**32**	**44.4%**	**15**	**20.6%**



PiCSO-AMI-I trial

Subgroup	No. of Patients PICSO	No. of Patients Control	Mean difference	Low CI95	High CI95	p-value
Age						
< 62.4	36	31	-1.72	-7.75	4.3	0.6
≥ 62.4	19	33	-1.43	-8.07	5.21	0.67
Sex						
Male	48	52	-0.73	-5.2	3.75	0.75
Female	7	12	-5.03	-20.35	10.27	0.5
Diabetes						
Yes	7	9	-3.04	-14.96	8.87	0.59
No	48	55	-0.87	-5.63	3.88	0.72
Hypertension						
Yes	16	21	-6.6	-14.49	1.29	0.1
No	39	43	1.09	-4.13	6.33	0.68
Active smoker						
Yes	20	15	-6.4	-16.74	3.94	0.22
No	35	48	1.57	-3.24	6.38	0.61
Total Ischaemic Time						
< 223 min	28	32	0.19	-5.91	6.3	0.95
≥ 223 min	27	32	-2.51	-8.73	3.71	0.42
FMC to Balloon Time						
< 106 min	29	32	-1.37	-7.98	5.23	0.7
≥ 106 min	25	31	-1.18	-7.21	4.85	0.7
Enrolment time						
Pre COVID19 pandemic	11	10	-13.36	-26.7	0.03	0.05
Post COVID19 pandemic	44	54	1.74	-2.59	6.07	0.43
Culprit lesion location						
Proximal LAD	32	39	-1.23	-7.03	4.56	0.67
Mid LAD	23	25	-0.59	-6.5	5.32	0.84
Multivessel coronary disease						
Yes	27	29	-6.09	-12.52	0.34	0.06
No	28	35	3.56	-2.08	9.2	0.21
TIMI flow at presentation						
0	45	55	-1.6	-6.13	2.94	0.5
1	10	9	1.41	-13.22	16.04	0.84
IRA re-occlusion after flow restoration						
Yes	11	7	0.02	-13.08	13.13	1
No	44	57	-1.52	-6.25	3.21	0.52
Killip Class at presentation						
I	45	53	-1.34	-6.11	3.42	0.58
> I	7	9	5.11	-5.2	15.42	0.3



PiCSO-AMI-I trial

In patients with anterior STEMI, TIMI 0-1 at presentation and ischaemic time < 12 h

- PiCSO assisted pPCI is feasible though it is associated with
  - *Prolonged procedural time*
  - *Increased contrast dye volume and radiation exposure*
- PiCSO assisted pPCI is not associated with increased rate of adverse events (device and non-device related) @ 6 months follow up
- In the PiCSO –AMI-I trial, PiCSO assisted pPCI did not reduce infarct size measured with CMR @ 5days or @6 months when compared to conventional pPCI

Conclusions

Outcomes for patients presenting with STEMI have plateaued

Surrogate measures of likely clinical outcome following/during STEMI are desirable

- Infarct size cMRI and MVO
- IMR measured with pressure wire (and possibly IMR_{angio})

Both MVO and IMR are predictive and may even be additive

Additional therapies for pts with STEMI are required for a sizeable minority – triaged therapy using IMR may be best approach