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

PICSO-AMI-I trial

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On Behalf of PiCSO-AMI-I Investigators

Disclosure of Relevant Financial Relationships

Within the prior 24 months, I have had a relevant financial relationship(s) with an ineligible company(ies) listed below.

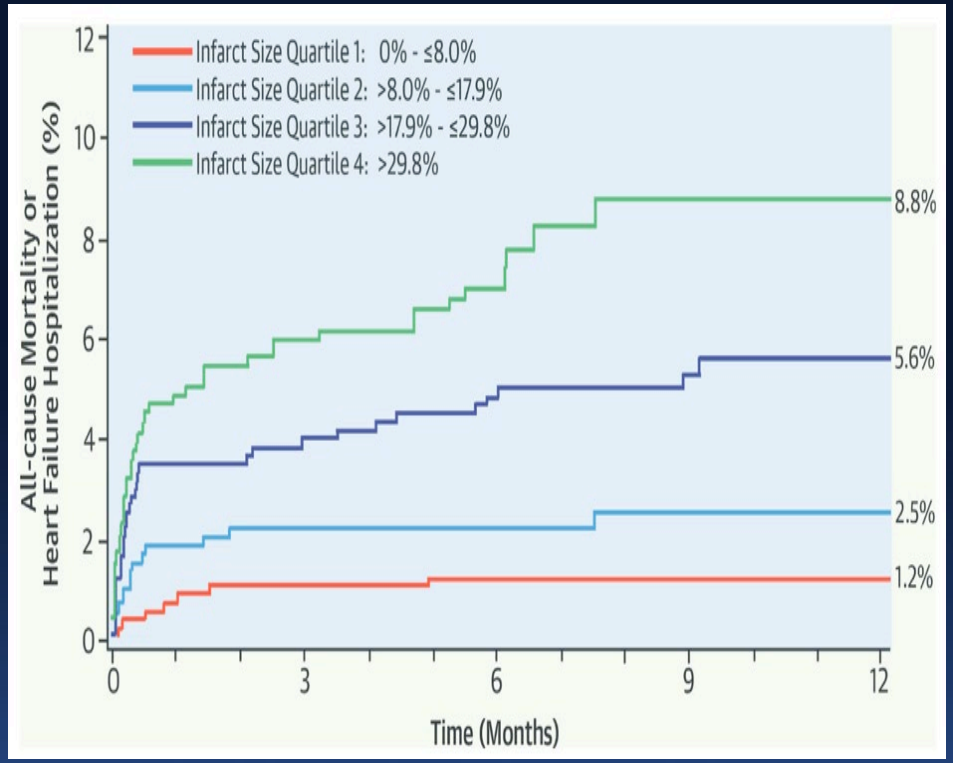
Nature of Financial Relationship	Ineligible Company
Grant/Research Support	Abbott, Medtronic, Terumo, Philips, Opsens, Miracor Medical SA
Consultant Fees/Honoraria	Miracor Medical SA, CorFlow
Individual Stock(s)/Stock Options	None
Royalties/Patent Beneficiary	None
Executive Role/Ownership Interest	None
Other Financial Benefit	None

All Relevant Financial Relationships have been mitigated.

BACKGROUND

- Improved prognosis with primary PCI in STEMI[1]
- Long-term mortality has plateaued over the last decade *(8 -12% @1 year)* [2-5]
- ~ 1:4 /1:5 of heart failure in STEMI survivors[6]
- Infarct Related Artery Patency ≠ Optimal Myocardial Reperfusion

1. Weaver WD et al JAMA 1997; 278: 2093 – 2098
2. Yamashita Y et al Circ Cardiovasc Qual Outcomes 2017; 10: e002790
3. Kristensen SD et al Eur Heart J 2014; 35: 1957 -1970
4. Menees DS et al N Engl J Med 2013; 369:901-909
5. Thrane PG et al J Am Coll Cardiol. 2023 Sep, 82 (10) 999–1010
6. Cahill TJ et al World J Cardiol 2017; 9: 407 - 415



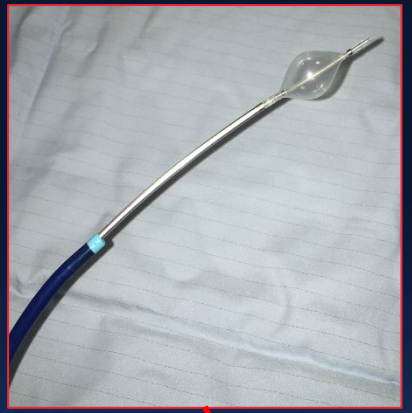
Stone GW et al JACC 2016

Every 5% increase in Infarct Size = ⇑ 20 - 25% Mortality and HF at 1 year

Pressure Controlled Intermittent Coronary Sinus Occlusion (PiCSO)

PiCSO Impulse Catheter

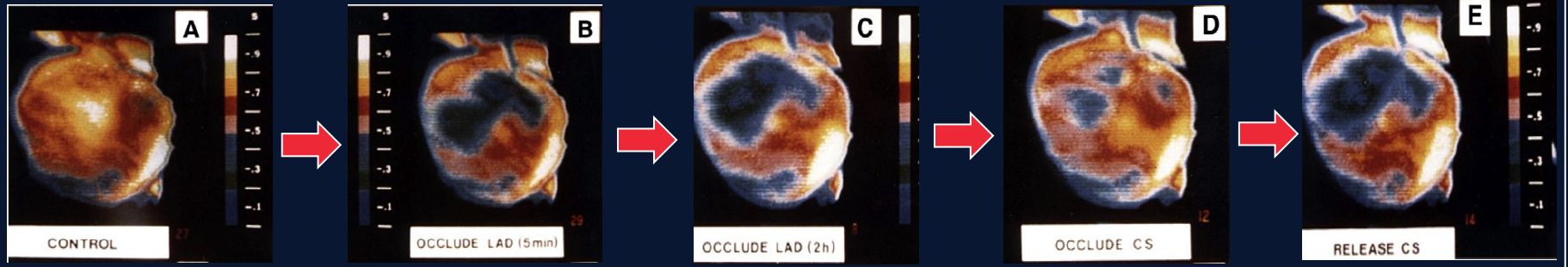
- 8Fr Balloon Tipped Catheter
- 16 x 25 mm Balloon
- Transfemoral Venous Access
- Coronary Sinus Positioning via 10Fr Steerable Guidesheath



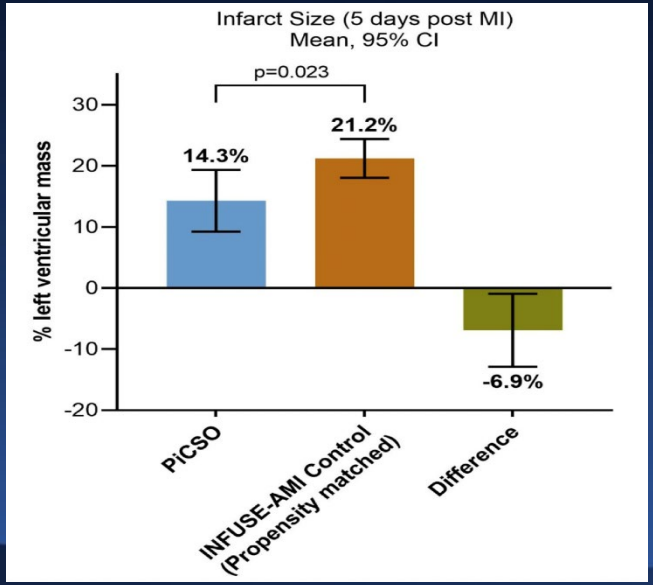
PiCSO Impulse Console

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

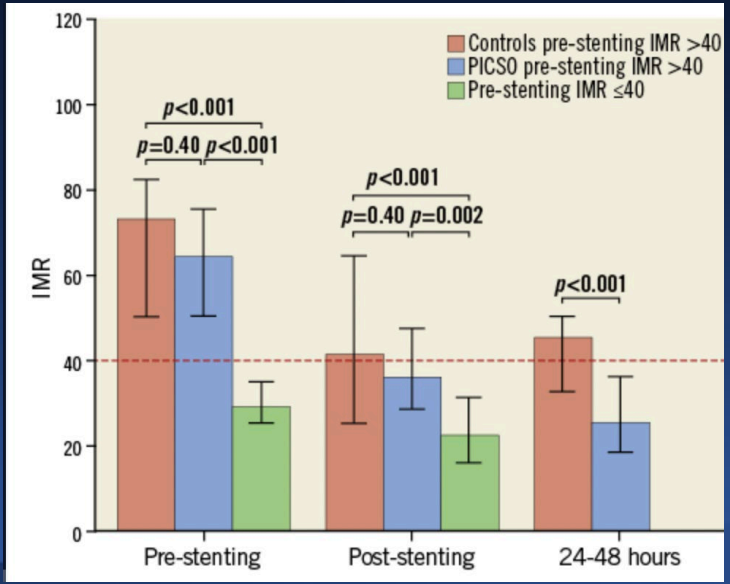
CRF TCT



Mohl W et al Cardiovasc Revasc Med 2015



Egred M L et al IJC Heart & Vasculature 2020



De Maria GL et al EuroIntervention 2018

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

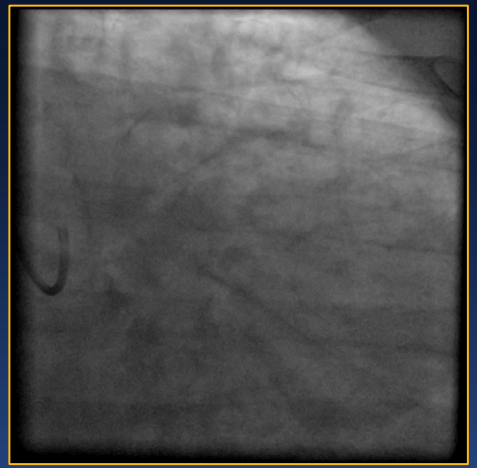
1. Age ≥18 years old with **anterior STEMI**
2. Culprit lesion in proximal or mid LAD
3. Pre-PCI **TIMI flow 0 or 1**
4. Symptoms onset **time ≤ 12 h**
5. Patient deemed eligible for primary PCI
6. Consent per approved national ethical committee specific requirements prior to the procedure.

Exclusion Criteria

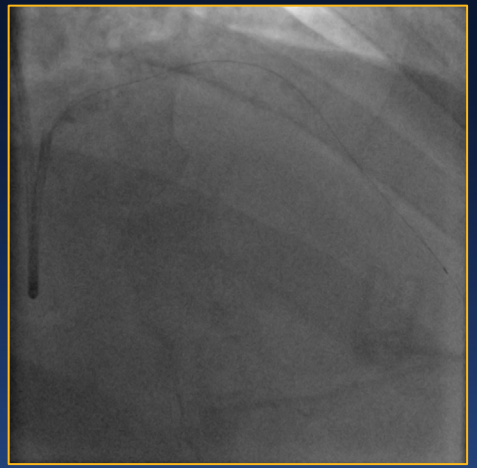
1. Implants or foreign bodies in the coronary sinus
2. Known allergy to polyurethanes, PET or stainless steel
3. Known pregnancy or breastfeeding
4. Pericardial effusion (cardiac tamponade)
5. Central hemodynamically relevant left/right shunt
6. Previous MI or CABG
7. History of stroke, TIA within last 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

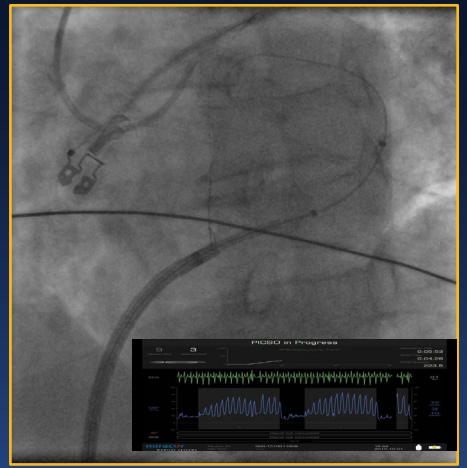
PiCSO Assisted pPCI



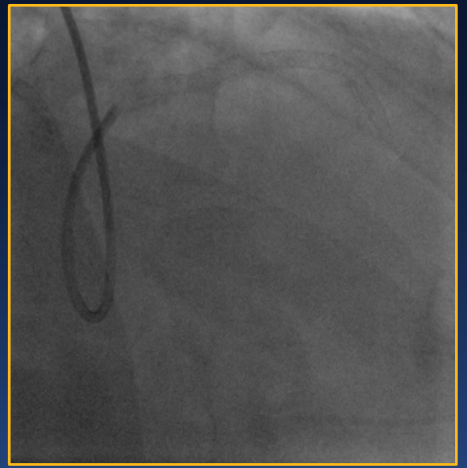
Baseline



IRA flow restoration



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



Stenting

PiCSO-AMI-I trial

Oxford University Hospitals, NHS Foundation Trust, Oxford
Leeds Teaching Hospital NHS Trust, Leeds
Freeman Hospital and Newcastle University, Newcastle
Edinburgh Heart Centre, Edinburgh
Golden Jubilee National Hospital, Glasgow
Royal Brompton and Harefield Hospitals, London
Barts Heart Centre, London
Liverpool Heart Centre and Chest Hospital, Liverpool

CHU Rangueil, Toulouse
Hospital Cardiologique du Haut Leveque, Bordeaux
Institut Coeur-Poumon, Centre Hospitalier Regional, Lille

Aarhus University Hospital, Aarhus
Odense University Hospital, Odense

Istituto Cardiocentreo Ticino, Lugano
Inselspital Bern, Bern

Pauls Stradins Clinical University Hospital, Riga

PiCSO-AMI-I trial

CMR Core lab

CRF Cardiovascular Research Foundation led by Akiko Maehara (New York, USA)

ECG and Angio Core lab, DSMB and CEC management

CERC European Cardiovascular Research Center led by Marie-Claude Maurice and Peter Smith (Paris, France)

Clinical Event Adjudication Committee

George Dangas, CEC Chair (The Mount Sinai Hospital, New York, USA)

Felix Mahfoud (Saarland University Hospital, Homburg, Germany)

Helene Routledge (Worcestershire Royal Hospital, Worcester, UK)

Solene Molin (Hospital Maison Blanche, Reims, France)

Independent Data Safety Monitoring Board

Robert Henderson, DSMB Chair (Nottingham University Hospital, Nottingham, UK)

Olivier Varenne (Hospital Cochin, Paris France)

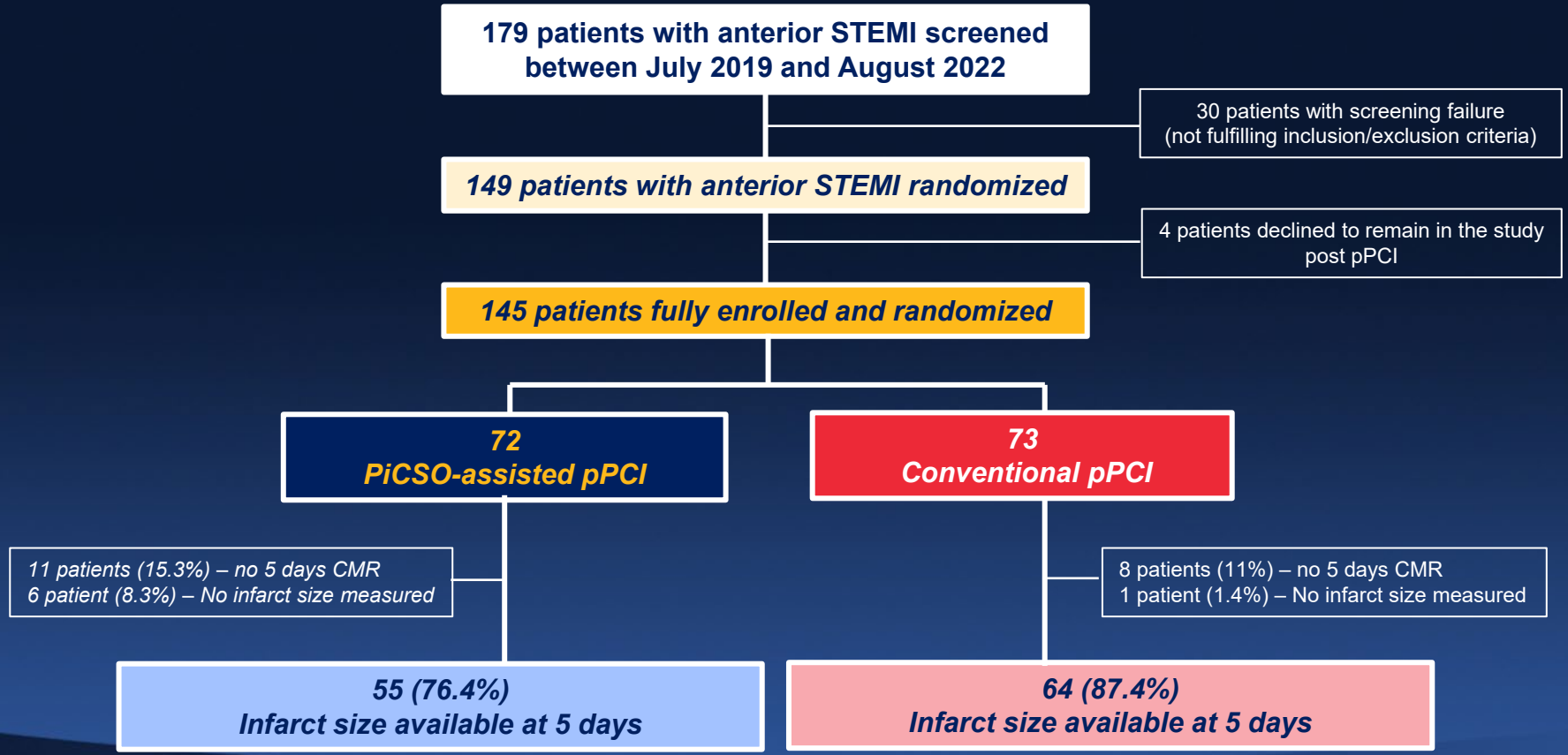
Christian Spaulding (Hospital Europeen Georges Pompidou, Paris, France)

Data Management: AMS Advanced Medical Services: Silke Zimmermann (Mannheim, Germany)

Statistical Analysis: AMS Advanced Medical Services led Nina Teletzky (Mannheim, Germany)
Miracor Medical led by Jozef Tanczos (Awans, Belgium)

Sponsor & Funding : Miracor Medical

PiCSO-AMI-I trial



PiCSO-AMI-I trial

Baseline Characteristics	Overall (n=145)	PiCSO (n= 72)	Control (n= 73)
Male	115 (79.3)	60 (83.3)	55 (75.3)
Age	61.0 (54.0 -70.0)	60.0 (52.5 – 67.5)	65.0 (57.0 – 73.0)
BMI	27.2 (24.5 – 30.4)	27.5 (24.2 – 31.8)	27.1 (24.9 – 29.4)
Smoker	43 (29.9)	26 (36.1)	17 (23.6)
Hypertension	48 (33.1)	23 (31.9)	25 (34.2)
Diabetes	22 (15.2)	10 (13.9)	12 (16.4)
Hyperlipidemia	31 (21.4)	12 (16.7)	19 (26.0)
Previous MI	0 (0.0)	0 (0.0)	0 (0.0)
Previous Coronary Stenting	2 (1.4)	0 (0.00)	2 (2.7)
Peripheral Vascular Disease	3 (2.1)	1 (1.4)	2 (2.7)
Previous stroke/TIA	5 (3.4)	1 (1.4)	4 (5.5)
Creatinine clearance (ml/min)	99.89 (75.8 – 120.5)	104.8 (68.3 – 120.5)	95.4 (77.2 – 116.6)
COPD	3 (2.1)	2 (2.8)	1 (1.4)
Previous COVID-19 infection	13 (12.1)	8 (14.8)	5 (9.4)
Cardiac Arrest pre pPCI	7 (4.8)	3 (4.2)	4 (5.5)

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

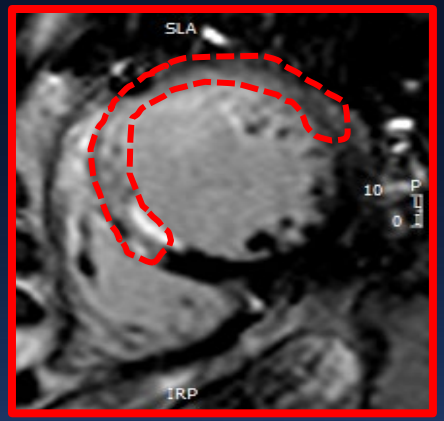
Procedural Characteristics	Overall (n=145)	PiCSO (n= 72)	Control (n= 73)	p
Radial Arterial Access	138 (95.2)	69 (95.8)	69 (94.5)	1.00
Thrombus Aspiration	21 (14.4)	10 (13.9)	11 (15.1)	0.84
Glycoprotein IIb/IIIa inhibitor	8 (5.5)	3 (4.2)	5 (6.8)	0.50
IRA re-occlusion after flow restoration	27 (18.6)	16 (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

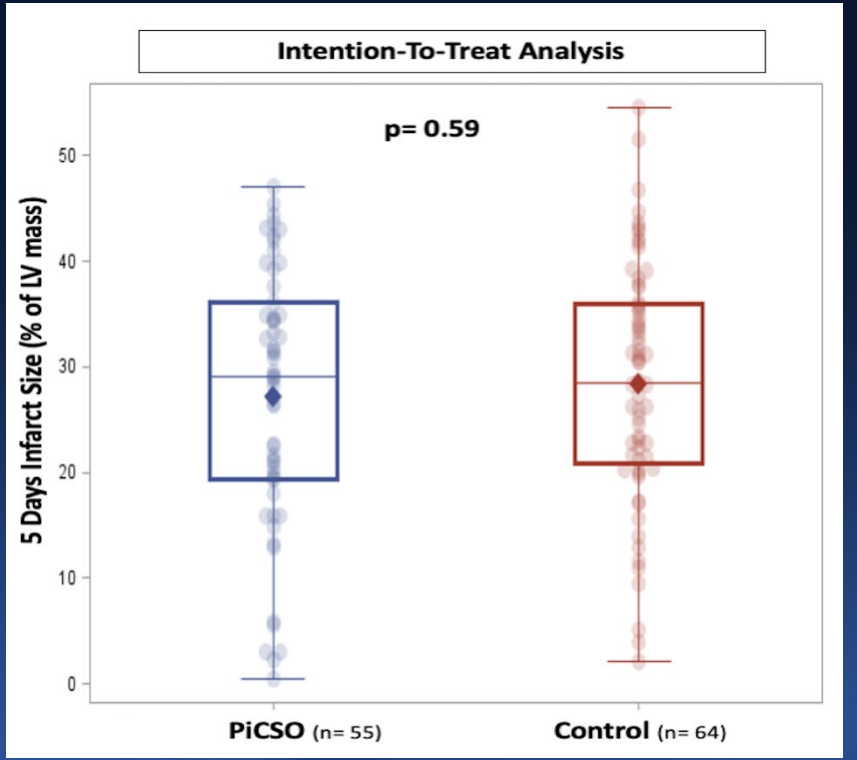
6 months Safety	PiCSO (n= 72)	Control (n= 73)	p
MACE	7 (9.7)	6 (8.2)	0.78
All-cause death	1 (1.4)	2 (2.7)	1.00
Hospitalization for HF	4 (5.6)	2 (2.7)	0.44
New/worsening HF	5 (6.9)	2 (2.7)	0.27
Reinfarction	0 (0.0)	0 (0.0)	1.00
Stroke	0 (0.0)	3 (4.1)	0.25
TVR	0 (0.0)	0 (0.0)	1.00
Stent thrombosis	0 (0.0)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

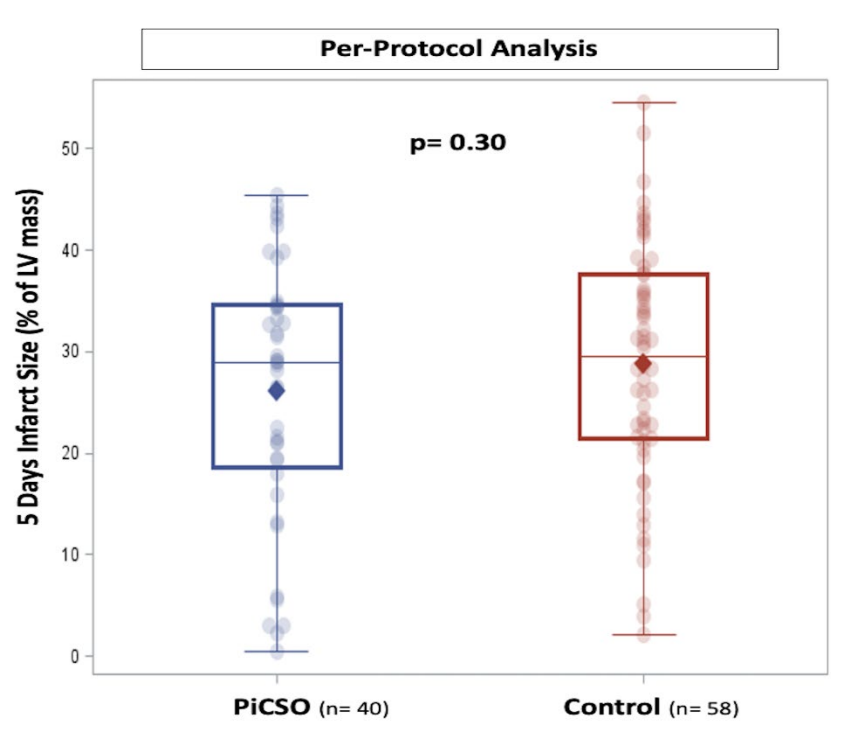


CRF TCT

PiCSO-AMI-I trial

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

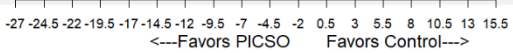
	PiCSO (n= 40)		Control (n= 58)	
	N=72	%	N=73	%
Did not receive treatment per randomization	1	1.4%	1	1.4%
5-day CMR not done	11	15.3%	8	11.0%
5-day CMR not in the time window	4	5.6%	5	6.8%
Infarct size not evaluable on the 5-day CMR	6	8.3%	1	1.4%
Final TIMI flow post PCI <2 by core lab	4	5.6%	1	1.4%
CS 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%**



CRF TCT

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



CRF TCT

PiCSO-AMI-I trial

SECONDARY ENDPOINTS	PiCSO (n= 72)	Control(n= 73)	p
60-90 min Complete ST resolution(>70%)	28 (12.9)	27 (16.4)	0.79
@ 5 days CMR	**PiCSO (n= 55)**	**Control(n= 64)**	**p**
LV end-systolic volume (ml/m^2)	52.8 ± 12.9	54.7 ± 15.1	0.52
LV end-diastolic volume (ml/m^2)	93.6 ± 16.3	96.1 ± 19.9	0.52
LV ejection fraction (%)	44.1 ± 6.5	43.5 ± 7.4	0.69
Microvascular obstruction, any n (%)	37 (67.2)	41 (64.6)	0.85
Microvascular obstruction extent (%LV)	0.30 (0.0-2.05)	0.42 (0.00-2.31)	0.93
Intramyocadial haemorrhage, any	31 (55.7)	38 (60)	0.72
Intramyocardial haemorrhage extent (%LV)	0.00 (0.0-1.27)	0.00 (0.00-2.32)	0.21
Myocardial salvage index (%LV)	41.5 ± 22.5	40.1 ± 19.8	0.84
@ 6 months CMR	**PiCSO (n= 48)**	**Control(n= 51)**	**p**
Infarct size (%LV)	19.2 ± 10.1	18.8 ± 7.7	0.83
LV end-systolic volume (ml/m^2)	53.6 ± 20.0	52.0 ± 15.61	0.67
LV end-diastolic volume (ml/m^2)	95.5 ± 22.9	100.5 ± 21.4	0.67
LV ejection fraction (%)	47.0 ± 9.0	48.7 ±7.5	0.65

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

PiCSO AMI I trial

Investigators

Adrian P. Banning, *Oxford*
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Didier Carrié, *Toulouse*
Pierre Coste, *Bordeaux*
Marco Valgimigli, *Lugano*
Miles Behan, *Edinburgh*
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Andrejs Erglis, *Riga*
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Ajay K Jain, *London*
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Cathlab Teams, Research Fellows and Research Nurse Teams

Keith Channon (Oxford), Jeremy Langrish (Oxford), Rajesh Kharbanda (Oxford), Federico Marian (Oxford) Rafail Kotronias (Oxford) Bernadette Moresby (Oxford), Deborah Barker (Oxford), Abdul Mozid (Leeds), Jonathan Blaxill (Leeds), Stephen Wheatcroft (Leeds), Murugapathy Veerasamy (Leeds), Jennifer Rossington (Leeds), Mohammad Alkhalil (Newcastle), Mohaned Egred (Newcastle), Robert McDade (Glasgow), Alex Tewkesbury (Glasgow), Louise McIlchere (Glasgow), Ruth McLaren (Glasgow), Margaret McEntegart (Glasgow), Keith Robertson (Glasgow), Anna O'Donnell (Glasgow), Richard Brogan (Glasgow), Damian Collison (Glasgow), Vanessa Orchard (Glasgow), Shona MacArthur (Glasgow), Dr Stuart Watkins (Glasgow), Paul Rocchiccioli (Glasgow) Christine Brockway (Glasgow), Fiona Howarth (Glasgow) Pamela Gildea (Glasgow) Maria Petty (Glasgow), Flavien Vincent (Lille) Samy Aghezaff (Lille) Francois Pontana (Lille), Tom Denimal (Lille), Alessandro Cosenza (Lille) Cedric Delhaye (Lille), Guillaume Schurtz (Lille) Augustin Coisne (Lille), David Montaigne (Lille) Thibault Pamart (Lille), Sina Porouchani (Lille) Nicolaj Brejnholt Støttrup (Aarhus) Lars Jakobsen (Aarhus), Karsten tange Veien (Aarhus) Lisette Okkels Jensen (Odense), Julia Ellert-Gregersen (Odense) Anders Junker (Odense) Karsten Tange Veien (Odense)

Sponsor and Funder

Miracor Medical

Patients participating to the PiCSO AMI I trial