AVOID Study

Air Versus Oxygen In ST-elevation MyocarDial Infarction

Dr Dion Stub **MBBS PhD FRACP**
Baker IDI Heart & Diabetes Institute, Melbourne Australia
St Paul's Hospital Vancouver, Canada

On behalf of Karen Smith, Stephen Bernard, Ziad Nehme, Michael Stephenson, Janet E. Bray, Peter Cameron, Bill Barger, Andris H. Ellims, Andrew J. Taylor, Ian T. Meredith, David M. Kaye for the AVOID Investigators.

Background

- For over a century oxygen therapy has been used in the initial treatment of patients with suspected myocardial infarction.

- In patients without hypoxia, there is limited evidence suggesting oxygen therapy is beneficial*

- Supplemental oxygen may reduce coronary blood flow, increase coronary vascular resistance and contribute to reperfusion injury through increased formation of reactive oxygen species.

*Cabello etal. *Cochrane Review* 2010

Objective

We performed an investigator initiated multicenter randomized controlled trial to compare supplemental oxygen therapy with no oxygen therapy in normoxic patients with STEMI to determine its effect on myocardial infarct size.

Trial Design

Paramedics Assess Patient
Symptoms of STEMI <12 hours, O_2 Sats ≥ 94%
ST-elevation ≥2 contiguous ECG leads
Intended for primary PCI

Exclusion Criteria
Oxygen saturation <94% on pulse oximeter
Oxygen administration prior to randomization
Altered conscious state
Planned transport to a non-participating hospital

Randomize 1:1

Oxygen
8L/minute via face mask

No Oxygen
Unless O_2 falls below 94% than minimum titrated O2 via mask

Pre-Hospital

Physician confirms STEMI

In-Hospital

Primary PCI
O_2 (8L/min) in Cath Lab

Primary PCI
No O_2 in Cath Lab
unless O_2 falls below 94%

Cardiac Enzymes for 72 hours
Cardiac MRI and clinical follow up 6 months

Stub et al. *AHJ* 2012;163;3;339-345
Clinicaltrials.gov NCT01272713

Primary and Secondary Endpoints

Primary Endpoint

- Myocardial infarct size on cardiac enzymes
- Mean Peak Creatine Kinase
- Mean Peak Troponin I
- Area under curve of Creatine Kinase and Troponin I

Pre-specified Clinical Secondary Endpoints

- ST-segment resolution (12 lead ECG)
- Survival to hospital discharge
- MACCE: Death, MI, Revascularisation, Stroke at 6 months
- Myocardial infarct size on CMR at 6 months

Trial Conduct

Ethics: The study conformed to the Australian National Health and Medical Research Council framework for the conduct of clinical trials in the emergency setting and was approved by all participating ethics committees

Coordinating Center: Ambulance Victoria

Funding: Alfred Hospital Foundation, FALCK foundation, Paramedics Australia

Primary Investigators: Stephen Bernard and Karen Smith

Steering Committee: Dion Stub, Ziad Nehme, Michael Stephenson, Janet Bray, Bill Barger, Peter Cameron, Ian Meredith, David Kaye.

External Academic Statistical support: Steve Vander Hoorn Melbourne University

Data Safety Monitoring Board: Christopher Reid, Richard Harper, David Garner

Study Sites and Principal Investigators:

Alfred Hospital, Melbourne AUS: Anthony Dart

Austin Hospital, Melbourne AUS: Omar Farouque

Box Hill Hospital, Melbourne AUS: Gishel New and Melanie Freeman

Frankston Hospital, Frankston AUS: Geoff Toogood and Robert Lew

Monash Medical Centre, Melbourne AUS: Ian Meredith

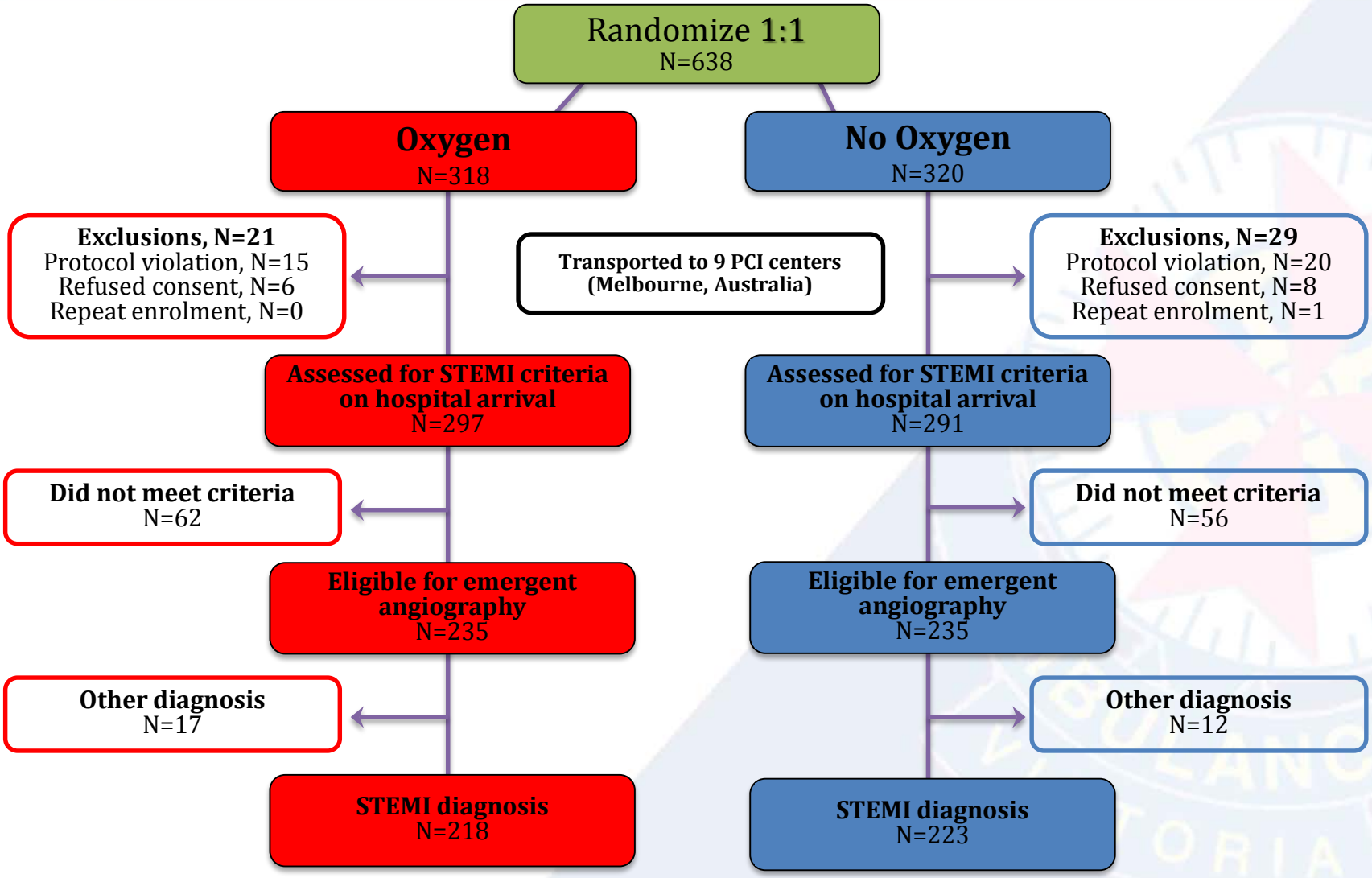
Peninsula Private, Melbourne AUS: Greg Szto

Royal Melbourne Hospital, Melbourne AUS: Leeanne Grigg

St Vincent's Hospital, Melbourne AUS: Robert Whitbourn

Western Hospital, Melbourne AUS: Nicholas Cox and Salvatore Rametta

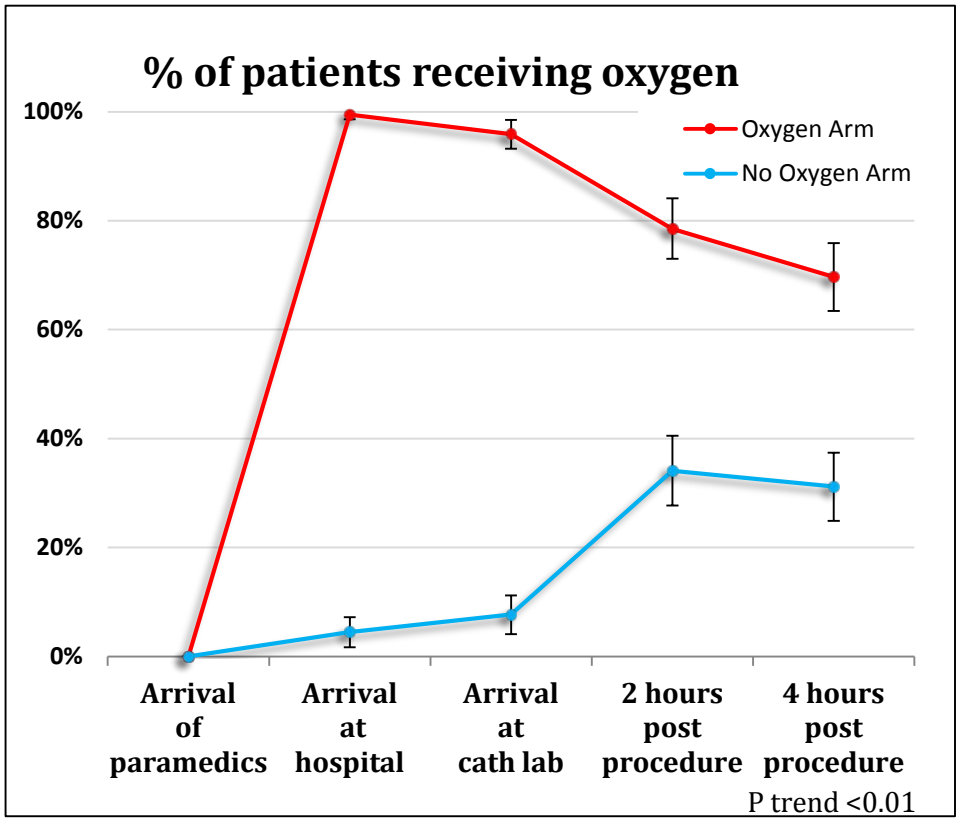
Patient Flow

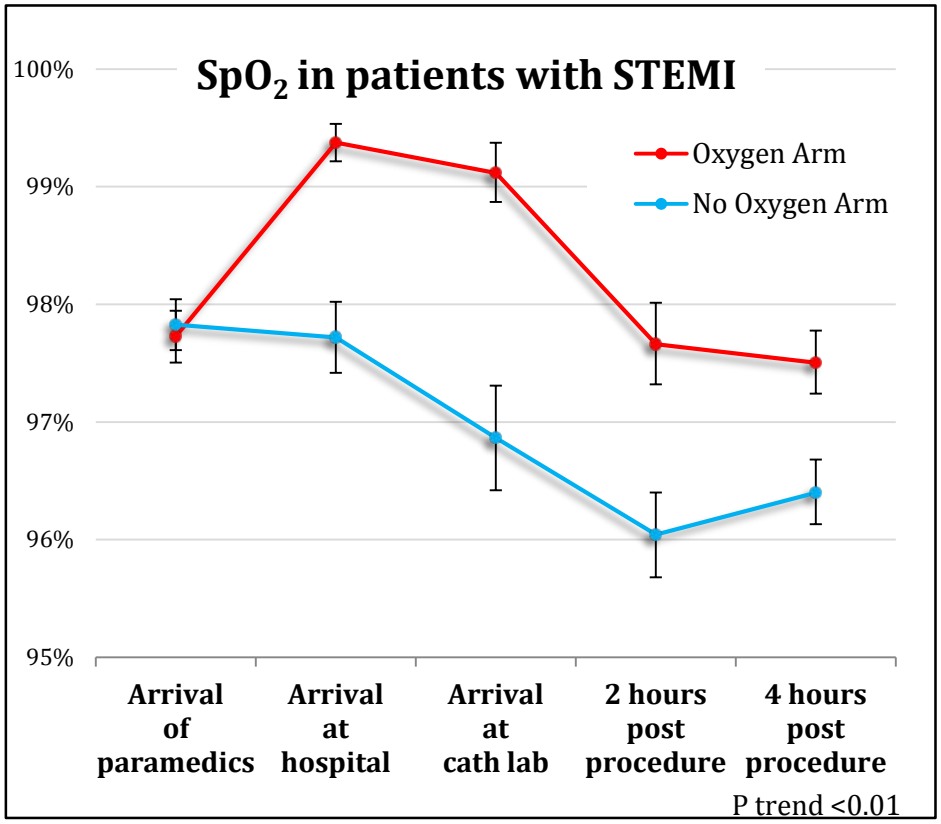


Baseline Characteristics in STEMI

Characteristic	Oxygen Arm N=218	No Oxygen Arm N=223
Age in years, mean +/- SD	63.0 +/- 11.9	62.6 +/- 13.0
Males, %	79.8	78.0
Diabetes mellitus, %	17.0	18.4
Hypertension, %	59.6	55.2
Dyslipidemia, %	55.5	52.9
Status on arrival of paramedics		
Heart rate, median (IQR)	74.0 (61.0, 84.0)	72.0 (60.0, 80.3)
Systolic blood pressure, median (IQR)	130.0 (105.0, 150.0)	130.0 (110.0, 150.0)
Oxygen saturation, median (IQR)	98.0 (97.0, 99.0)	98.0 (97.0, 99.0)
Killip Class I, %	88.9	87.3
Anterior Infarct (ECG), %	38.0	33.8

Characteristic	Oxygen Arm N=218	No Oxygen Arm N=223
Status on arrival at the catheterization laboratory		
Pain score, median (IQR)	2.0 (0.0-4.0)	2.0 (0.5-3.5)
Time from Paramedic on scene to hospital arrival, median (IQR)	55.0 (46.0, 69.0)	56.5 (48.0, 68.8)
Cardiac arrest, %	4.6	3.6
Cardiogenic Shock, %	5.0	5.4



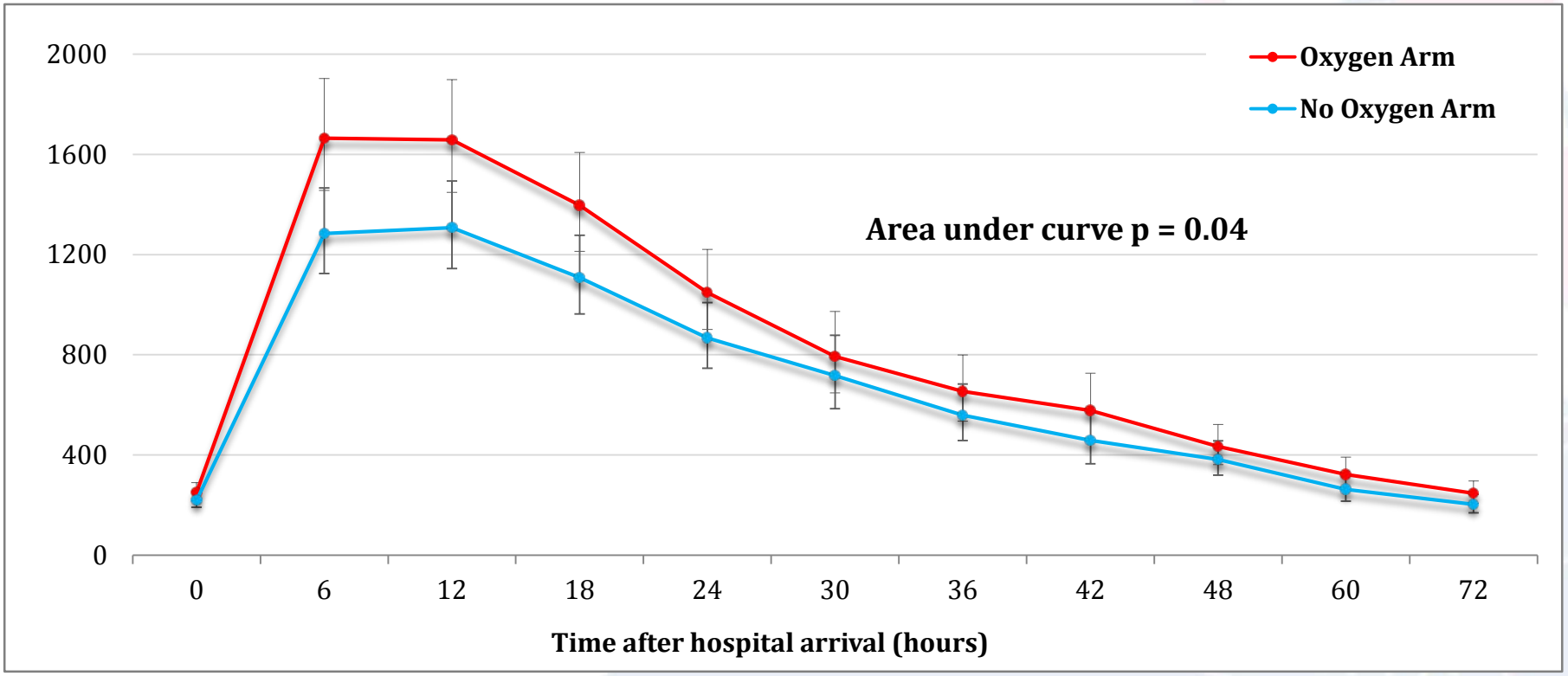


Procedural Details

Values are %	Oxygen Arm N=218	No Oxygen Arm N=223
Radial access	33.2	33.3
Stent implanted	92.7	90.1
Drug-eluting stent	51.4	51.1
Glycoprotein IIb/IIIa inhibitor	44.5	40.4
Thrombus aspiration	49.1	47.1
Intra-aortic balloon pump	3.2	5.4
CABG	2.3	4.0
No revascularisation	5.0	5.9
Symptom to intervention time, median (IQR), minutes	150.5 (125.0, 213.8)	162.0 (130.0, 240.0)
Door to intervention time, median (IQR), minutes	54.0 (39.0, 66.3)	56.0 (42.0, 70.8)

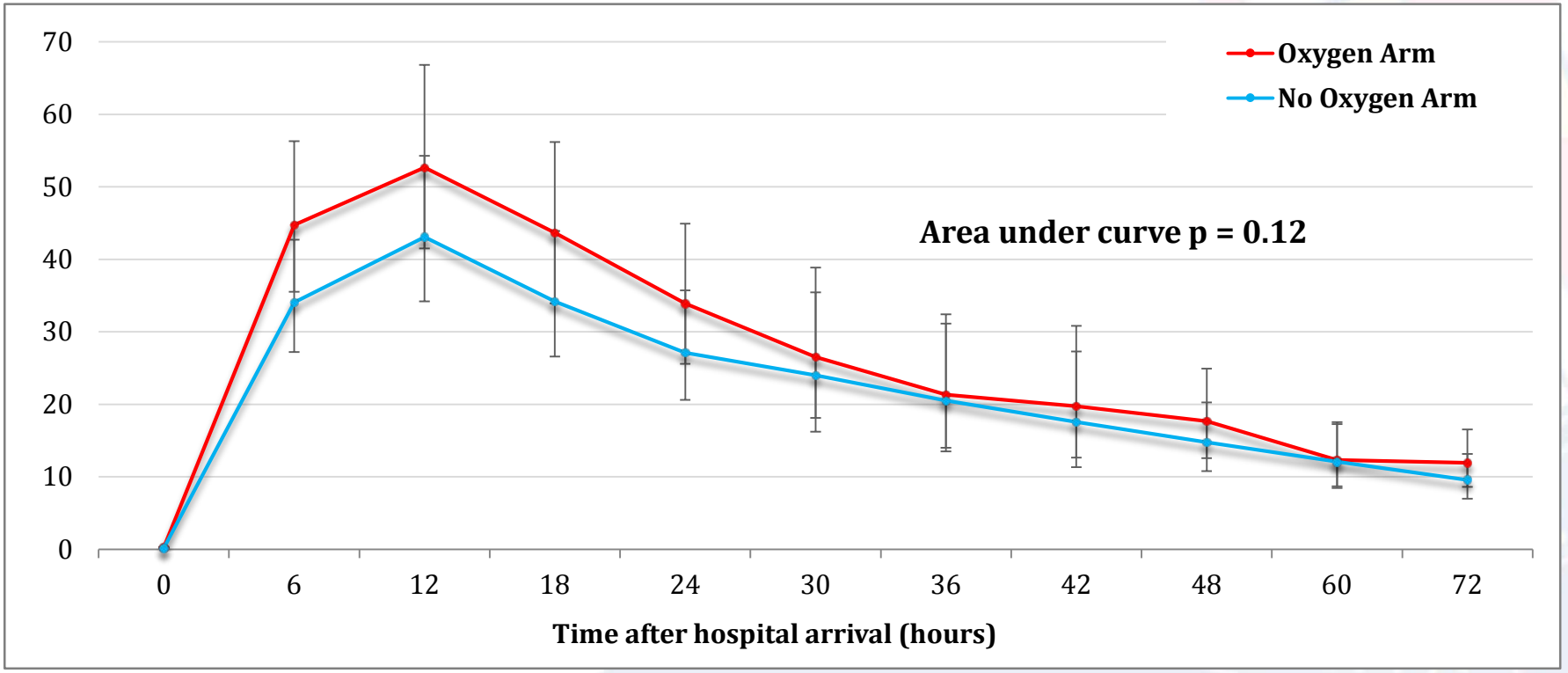
Primary Endpoint Infarct Size

Creatine kinase, U/L	Oxygen Arm N=217	No Oxygen Arm N=222	Ratio of means (Oxygen/No Oxygen)	P-value
Geometric Mean Peak (95% CI)	1948 (1721 – 2205)	1543 (1341 – 1776)	1.26 (1.05 – 1.52)	0.01
Median Peak (IQR)	2073 (1065, 3753)	1727 (737, 3598)		0.04



Primary Endpoint Infarct Size

Troponin I, mcg/L	Oxygen Arm N=200	No Oxygen Arm N=205	Ratio of means (Oxygen/No Oxygen)	P-value
Geometric Mean Peak (95% CI)	57.4 (48.0 – 68.6)	48.0 (39.6 – 58.1)	1.20 (0.92 – 1.55)	0.18
Median Peak (IQR)	65.7 (30.1, 145.1)	62.1 (19.2, 144.0)		0.17



Secondary Endpoint
CMR Infarct Size at 6 months

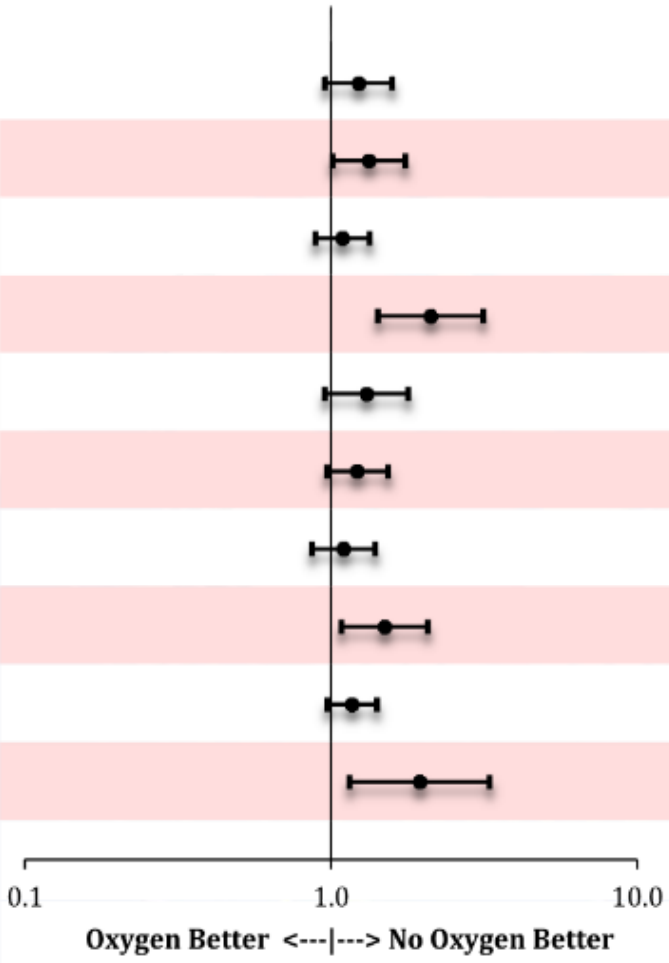
CMR Infarct Size	Oxygen Arm N=65	No Oxygen Arm N=74	Ratio of means (Oxygen/No Oxygen)	P-value
Median (IQR), grams	20.3 (9.6, 29.6)	13.1 (5.2, 23.6)		0.04
Geometric Mean (95% CI), grams	14.6 (11.3 – 18.8)	10.2 (7.7 – 13.4)	1.43 (0.99 – 2.07)	0.06
Median (IQR) proportion of LV mass	12.6 (6.7, 19.2)	9.0 (4.1, 16.3)		0.08
Geometric Mean(95% CI)proportion of LV mass	10.0 (8.1 – 12.5)	7.3 (5.7 – 9.3)	1.38 (0.99 – 1.92)	0.06

Clinical Endpoints

Values are %	Oxygen Arm N=218	No Oxygen Arm N=223	P-Value
At Hospital Discharge			
Mortality	1.8	4.5	0.11
Recurrent myocardial infarction	5.5	0.9	<0.01
Stroke	1.4	0.4	0.30
Major bleeding	4.1	2.7	0.41
Significant arrhythmia	40.4	31.4	0.05
ECG ST-segment resolution > 70%	62.0	69.6	0.10
At 6 months follow up			
Mortality	3.8	5.9	0.32
Recurrent myocardial infarction	7.6	3.6	0.07
Stroke	2.4	1.4	0.43
Repeat revascularization	11.0	7.2	0.17
MACCE	21.9	15.4	0.08

Myocardial Infarct Size on Cardiac Enzymes (CK) by patient characteristics

Sub-group	Ratio of means (Oxygen/No Oxygen)	P-Value
Age < 65 years	1.23 (0.95 – 1.58)	0.11
Age ≥ 65 years	1.33 (1.01 – 1.75)	0.04
Male	1.09 (0.89 – 1.34)	0.42
Female	2.11 (1.42 – 3.14)	<0.001
Culprit LAD	1.30 (0.95 – 1.78)	0.10
Non-LAD	1.22 (0.97 – 1.53)	0.09
Symptom-to-intervention time ≤ 180	1.10 (0.87 – 1.39)	0.44
Symptom-to-intervention time > 180	1.49 (1.08 – 2.07)	0.02
Pre-intervention TIMI flow 0 or 1	1.17 (0.97 – 1.41)	0.10
Pre- intervention TIMI flow 2 or 3	1.94 (1.15 – 3.30)	0.02



Conclusion

Supplemental oxygen therapy in patients with STEMI but without hypoxia increased myocardial injury, recurrent myocardial infarction and major cardiac arrhythmia, and was associated with larger myocardial infarct size assessed at six months.