

# Supplementary Appendix

## *Air Versus Oxygen In ST-Elevation Myocardial Infarction*

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**Table S1. Definitions of outcomes used in the AVOID study.**

<b>Death</b>	Deaths were classified as cardiac or non-cardiac. Examples of cardiac death included myocardial infarction, cardiogenic shock, arrhythmia, or dissection. A non-cardiac cause of death was the result of sepsis, pneumonia, cancer or non-cardiac haemorrhaging. Non-cardiac causes of death which occurred after the index admission were classified as non-cardiac deaths. Causes of death were verified through medical records and autopsy findings (if necessary). Deaths occurring after the index admission were verified through telephone follow-up with the patient's next-of-kin.
<b>Recurrent myocardial infarction</b>	<p>The diagnosis of recurrent myocardial infarction was made using the following criteria:</p> <ol style="list-style-type: none"> <li>1. Occurred after the index admission; <b>AND</b></li> <li>2. Recurrence of ischemic chest discomfort and/or new ST segment elevation, in at least two contiguous limbs leads (<math>\geq 1</math> mm) or chest leads (<math>\geq 2</math>mm), or new left bundle branch block (LBBB) pattern; <b>AND</b></li> <li>3. A 50% increase in the serum cardiac enzyme level in a patient with a previously established peak value, and where the result is greater than <math>3 \times 99</math>th percentile Upper Reference Limit (URL) <b>OR</b></li> <li>4. Angiographic evidence of new thrombus, or either complete or partial vessel occlusion.</li> </ol>
<b>Stroke or transient ischemic attack</b>	Neurological deficits classified by a clinician as stroke or transient ischaemic attack. Strokes were classified as haemorrhagic or ischaemic on the basis of brain imaging.
<b>Major adverse cardiac event</b>	A major adverse cardiac event was defined as death from any cause, recurrent myocardial infarction, recurrent revascularisation, and stroke.
<b>Cardiogenic shock</b>	Evidence of inadequate tissue perfusion in the setting of adequate intravascular volume, characterised by persistent hypotension (systolic blood pressure $\leq 90$ mm Hg), with or without altered mental status and peripheral hypoperfusion, requiring either pharmacologic or mechanical circulatory support.
<b>Major bleeding</b>	<p>Clinically overt bleeding associated with either one of the following:</p> <ol style="list-style-type: none"> <li>1. A drop in haemoglobin of <math>&gt; 3</math> g/dL;</li> <li>2. Haemodynamic compromise;</li> <li>3. Requires blood transfusion;</li> <li>4. Intracranial haemorrhage.</li> </ol> <p>Bleeding occurring after the index admission was classified as major bleeding when associated with death, hospital admission, blood transfusion, or intracranial haemorrhage.</p>
<b>Repeat revascularization</b>	Any subsequent revascularisation (i.e. percutaneous coronary intervention or coronary artery bypass grafting) of any lesion which occurs after the index admission and verified at 6 months follow-up.
<b>Target vessel revascularization</b>	Any subsequent revascularisation (i.e. percutaneous coronary intervention or coronary artery bypass grafting) which occurs after the index admission, and involves the target lesion treated at the index admission.
<b>Readmissions</b>	Re-hospitalisations occurring for any reason after the index admission.
<b>ST segment resolution at 1 day after admission</b>	The reduction in ST-segment elevation one day after the admission as a proportion of the initial pre-procedural ECG.
<b>Major Cardiac Arrhythmia</b>	Defined as sustained and non-sustained ventricular and atrial tachyarrhythmia requiring medical intervention

**Table S2. Sensitivity analyses of area under the curve estimation for cTnI and CK release in patients with confirmed STEMI.**

	Oxygen Arm	No Oxygen Arm	Ratio of Means (Oxygen/No Oxygen)	P-Value
<b>Geometric Mean AUC<sub>72</sub> (95% CI) cTnI, mcg/L</b>				
Primary analysis*	2000.4 (1692.8 – 2363.9)	1647.9 (1380.1 – 1967.6)	1.21 (0.95 – 1.55)	0.12
Sensitivity analysis 1†	1978.3 (1683.6-2324.6)	1620.2 (1354.2-1938.5)	1.22 (0.96 – 1.55)	0.10
Sensitivity analysis 2‡	NA	NA	1.28 (1.04 – 1.56)	0.02
Sensitivity analysis 3§	2164.4 (1824.8 – 2567.2)	1820.4 (1518.1 – 2183)	1.19 (0.93 – 1.53)	0.17
<b>Geometric Mean AUC<sub>72</sub> (95% CI) CK, U/L</b>				
Primary model*	60395 (54185 - 67316)	50726 (44861 - 57358)	1.19 (1.01 – 1.40)	0.04
Sensitivity analysis 1†	60749 (5414 - 67699)	51168 (45232 - 57883)	1.19 (1.01 – 1.40)	0.04
Sensitivity analysis 2‡	NA	NA	1.20 (1.05 – 1.38)	0.007
Sensitivity analysis 3§	69937 (62494 – 78266)	58760 (51891 – 66538)	1.19 (1.01 – 1.41)	0.04

NA denotes not applicable.

\* Trapezoidal integration was used for the estimation of AUC<sub>72</sub>. Data for patients with one or more missing biomarker assays were replaced by multiple imputation using the Markov Chain Monte Carlo (MCMC) method. Analyses were conducted on the log-transformed data, with comparisons obtained by back-transformation.

† Trapezoidal integration was used for the estimation of AUC<sub>72</sub>, as per the primary analysis. For this sensitivity analysis, the imputation model included additional baseline covariates were associated with cTnI/CK release and missingness of data. The imputation model considered additional covariates as follows: age, gender, TIMI flow pre procedure, LAD culprit artery, symptom to intervention time and procedural success.

‡ A repeated measures analysis was used to estimate the overall profile of cTnI/CK release over the 72 hour window. All available biomarker data were analyzed using linear mixed-effects (LMM) regression with patient as a random effect together with treatment group, time of assay, and an interaction term between treatment group and time of assay included as fixed effects. For this analysis, the non-significant interaction term between treatment group and time of assay was removed from the model.

§ Trapezoidal integration was used for the estimation of AUC<sub>72</sub>, as per the primary analysis. Patients with one or more missing biomarker assays were replaced by linear interpolation and extrapolation.

**Table S3. Spearman's rank correlation coefficient between derived endpoints\***

	Peak CK	AUC <sub>72</sub> CK	Peak cTnI	AUC <sub>72</sub> cTnI
AUC <sub>72</sub> CK	0.95	-	-	-
Peak cTnI	0.87	0.81	-	-
AUC <sub>72</sub> cTnI	0.89	0.86	0.97	-
CMRI Infarct size	0.65	0.59	0.68	0.70

\* All correlations are significant ( $p < 0.001$ ).

**Table S4. Baseline characteristics of all randomized patients.\***

Characteristic	Oxygen Arm N=312	No Oxygen Arm N=312	P-Value
<b>Age in years, median (IQR)</b>	63.5 (54.0, 73.0)	62.0 (53.0, 71.0)	0.28
<b>Males, n (%)</b>	240 (76.9)	242 (77.6)	0.85
<b>Body mass index, median (IQR) †</b>	27.4 (25.0, 31.0)	27.5 (24.7, 30.1)	0.80
<b>Status on arrival of paramedics</b>			
Heart rate, median (IQR)	76.0 (64.0, 88.0)	72.0 (62.0, 84.0)	0.28
Systolic blood pressure (mmHg), median (IQR)	130.0 (108.0, 150.0)	130.0 (110.0, 150.0)	0.57
Oxygen saturation (%), median (IQR)	98.0 (97.0, 99.0)	98.0 (97.0, 99.0)	0.50
Pain score, median (IQR)	6.0 (4.8, 8.0)	6.0 (4.0, 8.0)	0.17
<b>Status on arrival at hospital</b>			
Heart rate, median (IQR)	75.0 (64.0, 84.5)	74.0 (63.0, 84.0)	0.48
Systolic blood pressure (mmHg), median (IQR)	130.0 (118.3, 148.8)	130.0 (115.0, 145.0)	0.13
Oxygen saturation (%), median (IQR)	99.0 (99.0, 100.0)	98.0 (97.0, 99.0)	<0.001
Pain score, median (IQR)	2.0 (0.0, 4.0)	2.0 (0.5, 3.5)	0.77
<b>Hospital diagnosis, n (%) ‡</b>			
ST elevation myocardial infarction	220 (75.1)	227 (78.0)	0.41
Non-ST elevation myocardial infarction	11 (3.8)	13 (4.5)	0.66
Unstable angina	4 (1.4)	3 (1.0)	0.71
Pericarditis	9 (3.1)	6 (2.1)	0.44
Apical ballooning	4 (1.4)	8 (2.7)	0.24
Chest pain, non-specific	20 (6.8)	13 (4.5)	0.22
Arrhythmia	4 (1.4)	5 (1.7)	0.73
Syncope	6 (2.0)	7 (2.4)	0.77
Other	15 (5.1)	9 (3.1)	0.22
<b>All-cause mortality during hospital admission, n (%)</b>	5 (1.6)	11 (3.5)	0.13

IQR denotes interquartile range.

\* Excludes 14 of 638 patients who did not consent for participation in the trial.

† Available in 302 of 624 patients.

‡ Available in 584 of 624 patients.

**Table S5. Baseline characteristics of randomized patients by enrolment criteria.\***

Characteristic	All randomized patients N=624	Assessed for STEMI criteria on hospital arrival N=588	Confirmed STEMI on emergent coronary angiogram N=441
<b>Age in years, median (IQR)</b>	63.0 (54.0, 72.0)	63.0 (54.0, 72.0)	63.0 (54.0, 71.0)
<b>Males, n (%)</b>	482 (77.2)	457 (77.7)	348 (78.9)
<b>Body mass index, median (IQR) †</b>	27.4 (24.9, 30.8)	27.4 (24.9, 30.8)	27.5 (24.9, 30.9)
<b>Status on arrival of paramedics</b>			
Heart rate, median (IQR)	74.0 (62.5, 84.0)	74.0 (62.0, 84.5)	72.0 (60.0, 84.0)
Systolic blood pressure (mmHg), median (IQR)	130.0 (110.0, 150.0)	130.0 (110.0, 150.0)	130.0 (110.0, 150.0)
Oxygen saturation (%), median (IQR)	98.0 (97.0, 99.0)	98.0 (97.0, 99.0)	98.0 (97.0, 99.0)
Pain score, median (IQR)	6.0 (4.0, 8.0)	6.0 (5.0, 8.0)	7.0 (5.0, 8.0)
<b>Status on arrival at hospital</b>			
Heart rate, median (IQR)	74.0 (64.0, 84.0)	74.0 (64.0, 84.0)	72.5 (64.0, 84.0)
Systolic blood pressure (mmHg), median (IQR)	130.0 (115.8, 146.0)	130.0 (116.3, 145.8)	130.0 (120.0, 148.0)
Oxygen saturation (%), median (IQR)	99.0 (99.0, 100.0)	99.0 (98.0, 100.0)	99.0 (98.0, 100.0)
Pain score, median (IQR)	2.0 (0.0, 4.0)	2.0 (0.0, 4.0)	2.0 (1.0, 4.0)
<b>Hospital diagnosis, n (%) ‡</b>			
ST elevation myocardial infarction	447 (76.5)	443 (76.4)	441 (100.0)
Non-ST elevation myocardial infarction	24 (4.1)	24 (4.1)	0
Unstable angina	7 (1.2)	7 (1.2)	0
Pericarditis	15 (2.6)	15 (2.6)	0
Apical ballooning	12 (2.1)	12 (2.1)	0
Chest pain, non-specific	33 (5.7)	33 (5.7)	0
Arrhythmia	9 (1.5)	9 (1.6)	0
Syncope	13 (2.2)	13 (2.2)	0
Other	24 (4.1)	24 (4.1)	0
<b>All-cause mortality during hospital admission, n (%)</b>	16 (2.6)	15 (2.6)	14 (3.2)

IQR denotes interquartile range.

\* Excludes 14 of 638 patients who did not consent for participation in the trial.

† Available in 302 of 624 patients.

‡ Available in 584 of 624 patients.

**Table S6. Baseline characteristics of patients included in the primary endpoint analysis and those excluded after randomization.\***

Characteristic	Confirmed STEMI on emergent coronary angiogram N=441	Excluded after randomization N=183	P-Value
Age in years, median (IQR)	63.0 (54.0, 71.0)	63.0 (50.0, 73.0)	0.86
Males, n (%)	348 (78.9)	134 (73.2)	0.12
Body mass index, median (IQR) †	27.5 (24.9, 30.9)	26.8 (24.4, 29.4)	0.30
<b>Status on arrival of paramedics</b>			
Heart rate, median (IQR)	72.0 (60.0, 84.0)	77.0 (66.0, 89.3)	0.003
Systolic blood pressure (mmHg), median (IQR)	130.0 (110.0, 150.0)	130.0 (110.0, 150.0)	0.36
Oxygen saturation (%), median (IQR)	98.0 (97.0, 99.0)	98.0 (97.0, 99.0)	0.60
Pain score, median (IQR)	7.0 (5.0, 8.0)	5.0 (1.0, 8.0)	<0.001
<b>Status on arrival at hospital</b>			
Heart rate, median (IQR)	72.5 (64.0, 84.0)	76.0 (64.0, 84.0)	0.41
Systolic blood pressure (mmHg), median (IQR)	130.0 (120.0, 148.0)	125.0 (111.3, 145.0)	0.06
Oxygen saturation (%), median (IQR)	99.0 (98.0, 100.0)	99.0 (98.0, 100.0)	0.61
Pain score, median (IQR)	2.0 (1.0, 4.0)	1.0 (0.0, 2.0)	<0.001
<b>Hospital diagnosis, n (%) ‡</b>			
ST elevation myocardial infarction	441 (100.0)	6 (4.2)	<0.001
Non-ST elevation myocardial infarction	0	24 (16.8)	<0.001
Unstable angina	0	7 (4.9)	<0.001
Pericarditis	0	15 (10.5)	<0.001
Apical ballooning	0	12 (8.4)	<0.001
Chest pain, non-specific	0	33 (23.1)	<0.001
Arrhythmia	0	9 (6.3)	<0.001
Syncope	0	13 (9.1)	<0.001
Other	0	24 (16.8)	<0.001
<b>All-cause mortality during hospital admission, n (%)</b>	14 (3.2)	2 (1.1)	0.13

SD denotes standard deviation; IQR, interquartile range.

\* Excludes 14 of 638 patients who did not consent for participation in the trial.

† Available in 302 of 624 patients.

‡ Available in 584 of 624 patients.



**Table S7. Baseline characteristics and procedural details of patients with confirmed STEMI with and without CMRI data at six months follow-up.**

Characteristic	Patients without MRI data N=302	Patients with MRI data N=139	P-Value
Age in years, median (IQR)	64.0 (55.0, 74.0)	60.0 (53.0, 65.0)	<0.001
Males, n (%)	231 (76.5)	117 (84.2)	0.07
Body mass index, median (IQR)*	27.4 (24.7, 31.1)	27.7 (25.9, 30.7)	0.60
Previous IHD, n (%)	54 (17.9)	24 (17.3)	0.88
Diabetes mellitus, n (%)	59 (19.5)	19 (13.7)	0.13
Current or ex-smoker, n (%)	209 (69.9)	97 (69.8)	0.98
<b>Status on arrival of paramedics</b>			
Heart rate, median (IQR)	72.0 (60.0, 84.0)	72.0 (60.0, 84.0)	0.90
Systolic blood pressure, median (IQR)	130.0 (108.5, 150.0)	135.0 (110.0, 154.0)	0.51
Oxygen saturation, median (IQR)	98.0 (97.0, 99.0)	98.0 (97.0, 99.0)	0.11
Pain score, median (IQR)	7.0 (5.0, 8.0)	7.0 (5.0, 8.0)	0.59
<b>Procedural details, n (%)</b>			
LAD Culprit artery	101 (34.1)	55 (39.6)	0.27
Multi-vessel coronary disease	180 (59.8)	81 (58.3)	0.76
Pre-procedural TIMI flow 0/1	259 (88.7)	123 (88.5)	0.95
Post-procedural TIMI flow 0/1	12 (4.1)	1 (0.7)	0.06
Radial intervention	105 (35.0)	42 (30.2)	0.32
Stent implanted	270 (89.4)	133 (95.7)	0.03
Glycoprotein IIb/IIIa inhibitor	118 (39.1)	69 (49.6)	0.04
Thrombus aspiration	139 (46.0)	73 (52.5)	0.21
Length of stay (days), median (IQR)	4.0 (4.0, 5.0)	4.0 (3.0, 5.0)	0.09
Symptom-to-intervention time in minutes, median (IQR)	158.0 (127.0, 230.0)	156.0 (123.5, 219.8)	0.43
Geometric Mean Peak cTnI (95% CI), mcg/L	53.3 (45.3 – 62.7)	50.5 (40.5 – 62.9)	0.71
Geometric Mean Peak CK (95% CI), U/L	1719 (1530 – 1931)	1760 (1498 – 2066)	0.82

IHD denotes ischemic heart disease, TIMI thrombolysis in myocardial infarction, LAD left anterior descending, IQR interquartile range, CI confidence interval.

\* Available in 280 of 441 patients.

**Table S8. Paramedic treatment of patients with confirmed STEMI.**

	Oxygen Arm N=218	No Oxygen Arm N=223	P-Value
<b>Status on arrival of paramedics</b>			
Heart rate, median (IQR)	74.0 (61.0, 84.0)	72.0 (60.0, 80.3)	0.24
Systolic blood pressure (mmHg), median (IQR)	130.0 (105.0, 150.0)	130.0 (110.0, 150.0)	0.29
Oxygen saturation (%), median (IQR)	98.0 (97.0, 99.0)	98.0 (97.0, 99.0)	0.51
Pain score, median (IQR)	7.0 (5.0, 9.0)	7.0 (5.0, 8.0)	0.08
<b>Status on arrival at hospital</b>			
Heart rate, median (IQR)	75.0 (64.0, 86.0)	72.0 (62.5, 84.0)	0.32
Systolic blood pressure (mmHg), median (IQR)	130.0 (120.0, 148.0)	130.0 (118.0, 147.8)	0.45
Oxygen saturation (%), median (IQR)	100.0 (99.0, 100.0)	98.0 (97.0, 99.0)	<0.001
Pain score, median (IQR)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	0.59
Oxygen being administered, n (%)	215 (99.5)	10 (4.5)	<0.001
Oxygen dose (L/min), median (IQR)	8.0 (8.0, 8.0)	4.0 (2.8, 8.0)	< 0.001
Morphine administered, n (%)	192 (89.3)	204 (91.5)	0.44
Morphine dose total (mg), median (IQR)	12.5 (8.0, 20.0)	11.3 (7.5, 15.0)	0.33
Fentanyl administered, n (%)	20 (9.3)	21 (9.4)	0.97
Fentanyl dose total (mcg), median (IQR)	137.5 (63.8, 218.8)	100.0 (80.0, 150.0)	0.45
Nitrates administered, n (%)	46 (21.3)	54 (24.2)	0.47
Nitrates dose total (mg), median (IQR)	0.6 (0.3, 1.3)	0.6 (0.3, 0.9)	0.44

IQR denotes interquartile range.

**Table S9. Medical therapy at six months follow-up.**

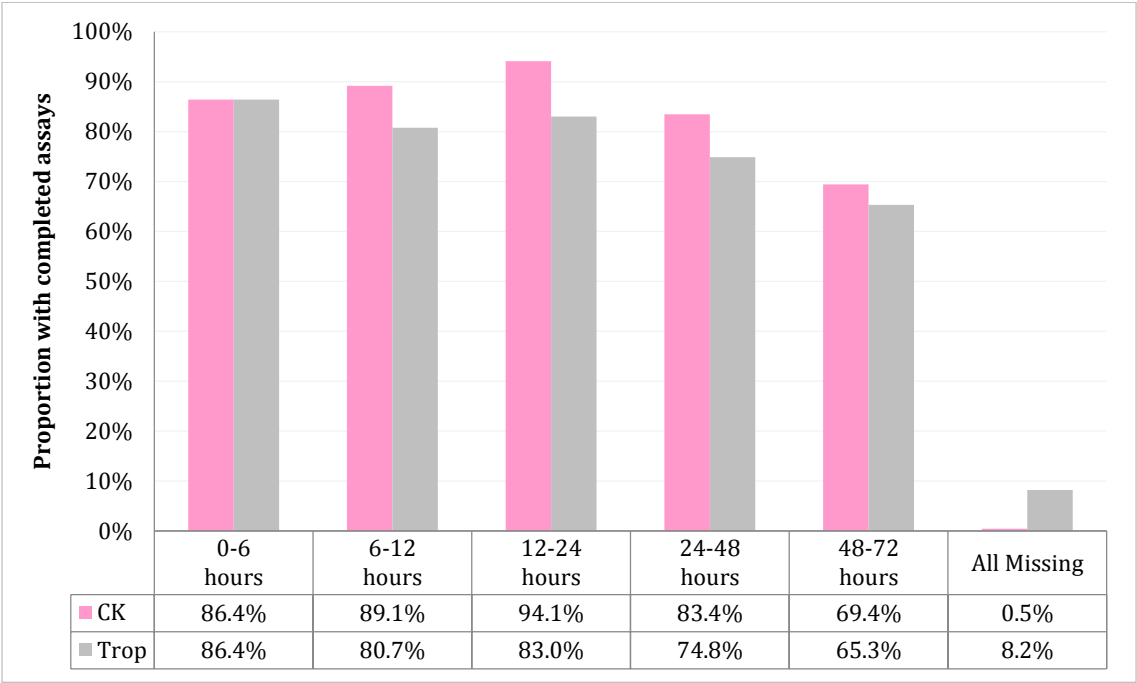
	Oxygen Arm N=218	No Oxygen Arm N=223	P-Value
Aspirin	172 (83.9)	181 (85.8)	0.59
Clopidogrel	84 (41.0)	82 (38.9)	0.66
Prasugrel	39 (19.0)	45 (21.3)	0.56
Ticagrelor	41 (20.0)	44 (20.9)	0.83
Aspirin + (Clopidogrel OR Prasugrel OR Ticagrelor)	151 (73.7)	159 (75.4)	0.69
Beta-blocker	161 (78.5)	171 (81.0)	0.52
Statin	182 (88.8)	182 (86.3)	0.44
ACE/ARB	166 (81.0)	169 (80.1)	0.82
Ca-channel blocker	10 (4.9)	9 (4.3)	0.77
Aldosterone antagonist	1 (0.5)	2 (0.9)	0.58
Diuretic	23 (11.2)	14 (6.6)	0.10
Anticoagulation	9 (4.4)	5 (2.4)	0.25

**Table S10. Baseline characteristics and findings in 139 patients with confirmed STEMI undergoing cardiac magnetic resonance imaging (CMRI) at six months follow-up.**

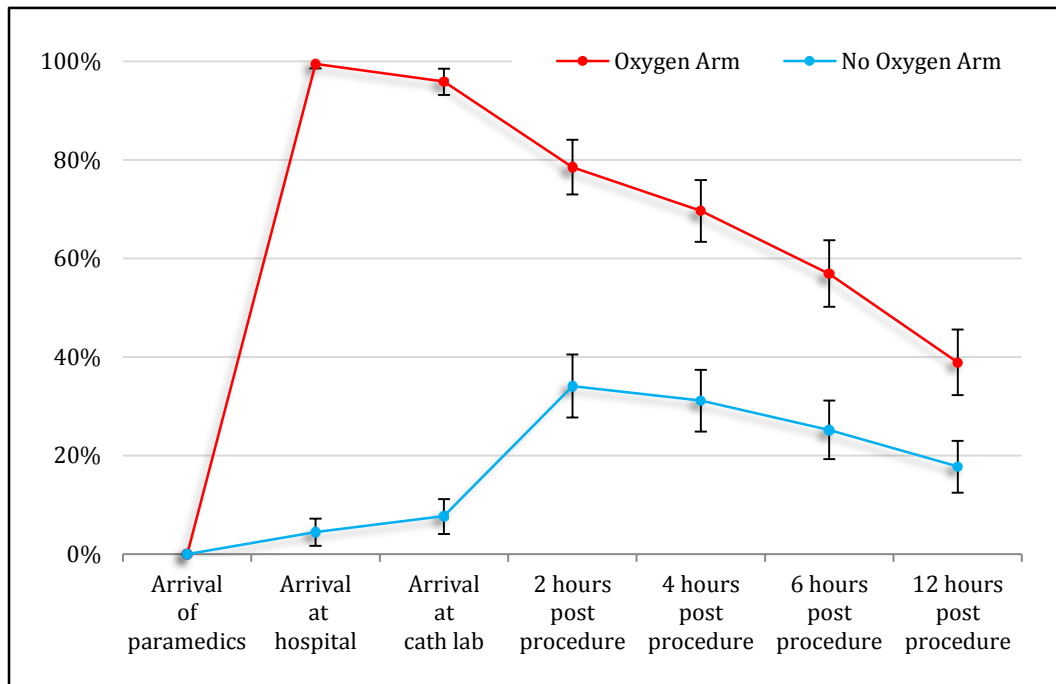
Characteristic/measure	Oxygen Arm N=65	No Oxygen Arm N=74	P-Value
Age in years, mean (SD)	60.0 (10.7)	59.0 (9.9)	0.60
Males, n (%)	55 (84.6)	62 (83.8)	0.89
Body mass index, median (IQR)	26.8 (25.2, 30.8)	27.7 (24.8, 31.0)	0.90
Previous IHD, n (%)	12 (18.5)	12 (16.2)	0.73
LAD culprit artery, n (%)	27 (26.5)	55 (39.6)	0.43
Pre-procedural TIMI flow 0/1, n (%)	58 (89.2)	65 (87.8)	0.80
Post-procedural TIMI flow 0/1, n (%)	0	1 (1.4)	0.35
Symptom-to-intervention time in minutes, median (IQR)	147.0 (119.0, 221.5)	162.0 (129.0, 213.5)	0.32
Recurrent MI, n (%)	4 (6.2)	1 (1.4)	0.13
LV end diastolic volume, mean (SD)	180.4 (43.9)	178.1 (44.1)	0.75
LV end systolic volume, median (IQR)	84.3 (59.8, 108.1)	77.7 (56.9, 100.5)	0.34
LV stroke volume, mean (SD)	96.1 (21.8)	95.3 (20.8)	0.81
LV ejection fraction, mean (SD)	54.4 (9.5)	54.9 (10.0)	0.76
Pre-procedural TIMI flow 0/1	53.9 (9.7)	54.3 (9.8)	0.83
Pre-procedural TIMI flow 2/3	58.9 (6.9)	59.7 (10.9)	0.86
LAD culprit artery	52.7 (9.3)	52.8 (10.9)	0.96
Non-LAD culprit artery	55.8 (9.6)	56.2 (9.4)	0.85
Symptom to intervention ≤180mins	54.5 (9.9)	55.4 (9.3)	0.76
Symptom to intervention >180mins	54.2 (9.0)	55.0 (11.4)	0.80
Infarct size (grams), median (IQR)	20.3 (9.6, 29.6)	13.1 (5.2, 23.6)	0.04
Pre-procedural TIMI flow 0/1	20.7 (10.0, 31.4)	15.2 (6.3, 24.3)	0.06
Pre-procedural TIMI flow 2/3	16.2 (4.2, 25.0)	7.0 (2.3, 24.2)	0.64
LAD culprit artery	20.7 (10.6, 33.3)	20.1 (4.4, 632.3)	0.60
Non-LAD culprit artery	15.2 (7.4, 26.3)	10.6 (5.2, 18.9)	0.05
Symptom to intervention ≤180mins	20.3 (9.9, 29.1)	12.9 (6.2, 22.2)	0.10
Symptom to intervention >180mins	20.8 (8.2, 30.5)	13.1 (3.3, 25.8)	0.15
Infarct size (% of LV mass), median (IQR)	12.6 (6.7, 19.2)	9.0 (4.1, 16.3)	0.08
Pre-procedural TIMI flow 0/1	12.7 (6.9, 19.3)	9.5 (5.5, 16.3)	0.14
Pre-procedural TIMI flow 2/3	9.0 (3.4, 17.0)	5.9 (2.1, 14.1)	0.32
LAD culprit artery	13.5 (8.1, 21.0)	14.8 (3.3, 20.1)	0.64
Non-LAD culprit artery	11.9 (5.8, 17.2)	8.1 (4.1, 15.0)	0.13
Symptom to intervention ≤180mins	11.9 (6.3, 17.6)	9.4 (4.3, 16.2)	0.28
Symptom to intervention >180mins	12.8 (7.4, 20.4)	7.9 (2.5, 16.5)	0.13

LV denotes left ventricular, IHD ischemic heart disease, TIMI thrombolysis in myocardial infarction, LAD left anterior descending, IQR interquartile range, SD standard deviation, MI myocardial infarction.

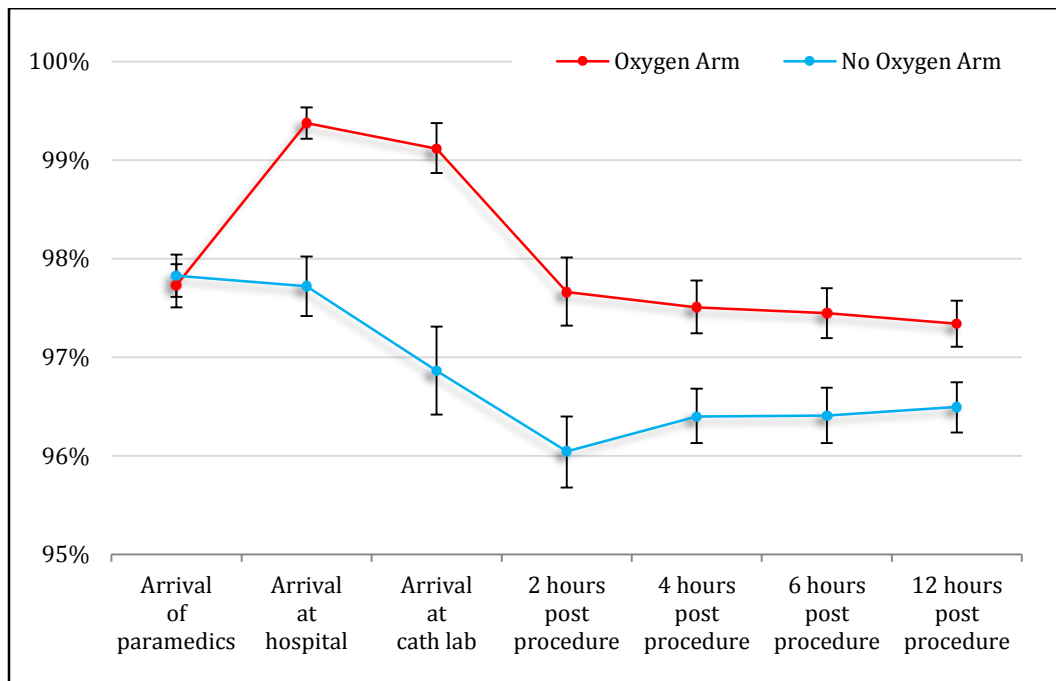
Figure S1: Proportion of patients with completed biomarker assays for each time-point.



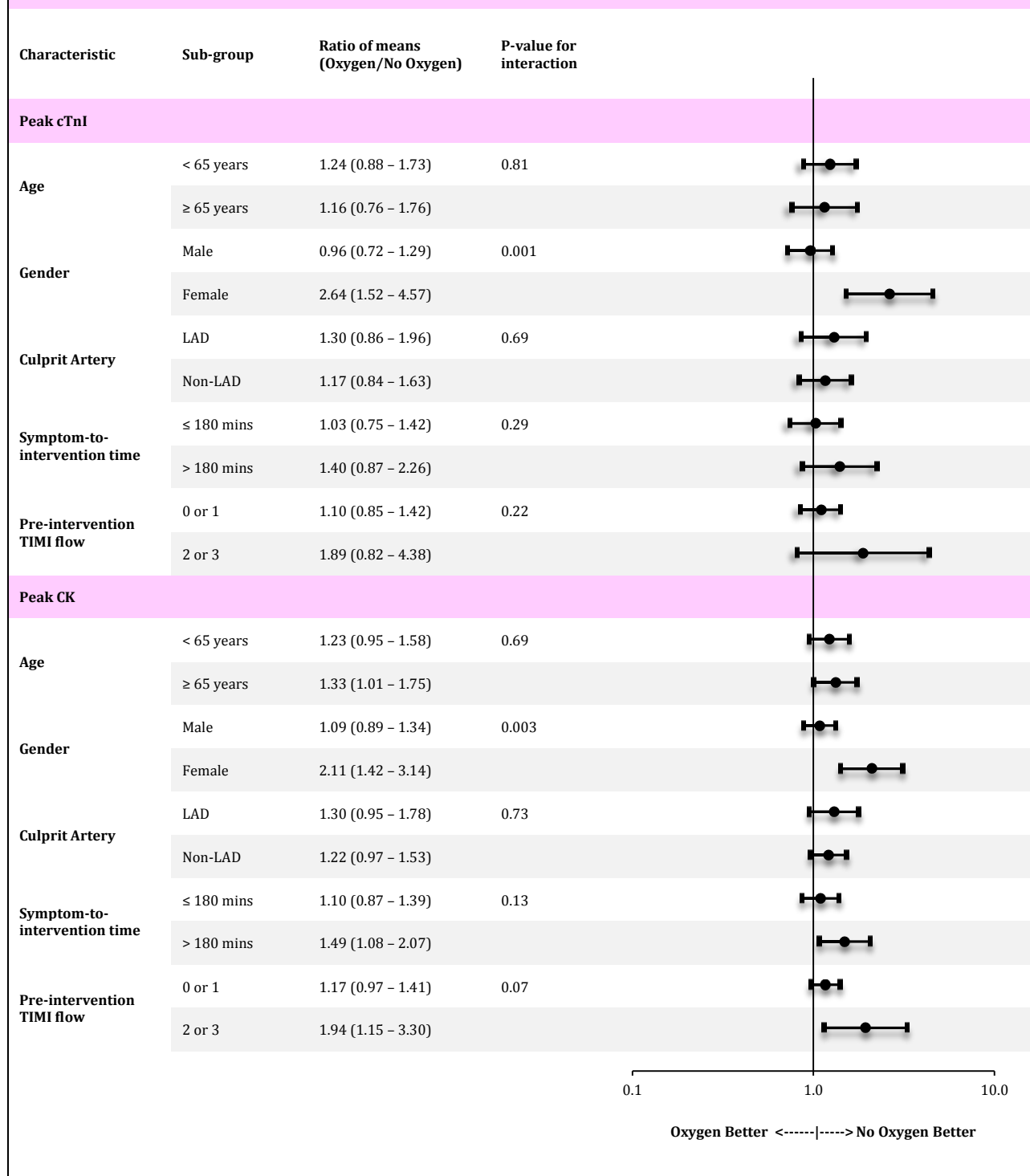
**Figure S2. Proportion of patients receiving supplemental oxygen across study time points and treatment groups in patients with confirmed STEMI.**



**Figure S3. Geometric mean (95% CI) for peripheral blood oxygen saturation (SpO<sub>2</sub>) across time points in patients with confirmed STEMI.**



**Figure S4: Ratio of geometric means (95% CI) for peak cTnI and peak CK release in patients with confirmed STEMI.**



TIMI denotes thrombolysis in myocardial infarction, LAD left anterior descending,