

SUPPLEMENTAL MATERIAL

DEFINITIONS

- ST Elevation Myocardial Infarction (STEMI)
 - Defined as the presence of chest pain lasting >20 min associated with electrocardiographic changes meeting criteria for PPCI (ST-segment elevation ≥ 1 mm in at least 2 limb ECG leads or ≥ 2 mm in at least 2 contiguous precordial leads or left bundle branch block of new onset or ST-segment depression ≥ 2 mm in at least 2 contiguous precordial leads (V1-3/4) suggestive of true posterior STEMI). Diagnostic confirmation on coronary angiography was mandated in all patients.

- Cardiovascular Death
 - Defined as unexplained sudden death, death secondary to acute MI, heart failure, or arrhythmia.

- Cerebrovascular accident (CVA)
 - Defined by the sudden onset of loss of neurologic function caused by an ischemic or haemorrhagic event, which is persistent for greater than 24 hours.

- Myocardial infarction (MI)
 - Ischaemic chest pain lasting longer than 20 minutes;
 - With either cardiac enzymes
 - Within 24 hours: not diagnostic
 - Prior to normalisation of cardiac enzymes: 50% increase in troponin T level compared to previous falling level
 - Following normalisation of cardiac enzymes: troponin T levels above upper limit of normal
 - and/or ECG
 - Within 24 hours: new ST elevation

- Otherwise a significant ST-segment change, development of new Q waves in ≥ 2 contiguous ECG leads, or new left branch bundle block pattern
- Repeat revascularisation
 - Revascularisation was defined as any further intervention required on the infarct related vessel due to restenosis or thrombosis during the period of follow up, either percutaneous or surgical.

VARIABLE COLLECTED FOR EACH SUBJECT

Baseline characteristics

- Age (years)
- Sex (male/female)
- Weight (kilograms)
- Height (metres)
- Smoker (current/ex/never) and pack years
- Performance Status (WHO score 0-5) (Table A)
- Family history of ischaemic heart disease
- Past medical history
 - Diabetes mellitus (including length of diagnosis and treatment received)
 - Known diabetic complications
 - Hypertension
 - Hypercholesterolaemia
 - Ischaemic Heart Disease
 - Previous PCI / CABG
 - Heart Failure
 - Cerebrovascular Disease
 - Peripheral Vascular Disease
 - Chronic Kidney Disease (KDOQI (Kidney Disease Outcomes Quality Initiative) stage IV or V)
- Past medication history prior to admission
 - Betablockers
 - ACEi
 - ARB
 - Statin
 - Aspirin
 - Other anti-platelet agent eg clopidogrel
 - Warfarin or other anti-coagulant therapy
 - Glycaemic control

- Metformin / Sulphonylureas / Gliptins / Insulin

Grade	Explanation of activity
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

Table A: WHO Performance status (adapted from Eastern Cooperative Oncology Group (ECOG) score) [1]

Admission and procedural characteristics

Data recording related to the initial event and procedure were documented by the attending primary PCI team as routine care and acquired from procedural notes/nursing records during admission.

- Admission blood pressure (mmHg)
- Admission heart rate (beats per minute)
- Admission oxygen saturations (percentage)
- Inspired oxygen (FiO₂ percentage)
- Symptom to door time (minutes)
- Door to balloon time (minutes)
- Premedication (and timing)
 - Aspirin / Clopidogrel / Ticagrelor / Prasugrel / Heparin (dose)
- Blood glucose (mmol/L) from ambulance sheet or procedural report

- Glycoprotein IIb/IIIa inhibitors (dose and timing)
 - Intravenous / Intracoronary
- Intracoronary nitrate (dose and timing)
- Intracoronary nitroprusside (dose and timing)
- Adenosine (dose and timing)
- Atropine (dose and timing)
- Intravenous fluids (volume and timing)
- Activated clotting time(s) (seconds) (including time of result(s))
- Intra-Aortic Balloon Pump use (pre / post PCI)
- Temporary pacing wire insertion
- Thrombectomy use
- Predilation with balloon (details of size and inflation pressure)
- Stent (details of size(s), type, and inflation pressure)
- Post dilation with balloon (details of size and inflation pressure)
- Screening time (minutes)
- Radiation exposure (dose area product)

In hospital investigation results

Information related to the relevant hospital admission was acquired from patient notes and computerised hospital care records

- Fasting glucose levels (mmol/L) – in subjects with elevated admission blood glucose or known diabetes
- HbA1c (mmol/mol) – in subjects with elevated admission blood glucose or known diabetes
- Time from admission until initiation of hyperglycaemia treatment (as applicable)
- Troponin (ng/ml) (12-24 hours after onset of chest pain)
- Pro BNP(pg/ml) (within 24 hours of admission)
- CRP (mg/L) (initial result)
- Renal function (eGFR/Cr) (initial result)
- Haemoglobin (g/L) (admission result)

- Neutrophil count ($\times 10^9/L$) (initial result)
- Platelet count ($\times 10^9/L$) (initial result)
- Cholesterol (mmol/L)
- 60 minutes post procedure electrocardiogram (to determine presence of $\geq 70\%$ reduction in ST elevation)
- Left ventricular impairment on echocardiography within 24 hours of admission (non/mild/moderate/severe)
- Epicardial adipose tissue (EAT) on echocardiography (cm)
 - EAT is described as the echo free space between the outer myocardial wall and the visceral pericardial layer in the PLAX view. This was measured during end-systole at the midline point (perpendicular to the aortic annulus) on the free wall of the right ventricle and an average of three cycles recorded.
- Aortic valvular sclerosis presence on echocardiography required all three points –
 1. Irregular, non-uniform thickening of portions of the aortic valve leaflets or commissures, or both.
 2. Thickened portions of the valve with an appearance suggesting calcification.
 3. Non-restricted or minimally restricted opening of the aortic cusps; and peak continuous wave velocity across the valve of < 2 m/sec.

Clinical outcomes

In hospital clinical outcomes:

- Worse Killip class (defined table B)
- Red cell transfusion required (number of units)
- Cardiovascular death
- Death
- Myocardial infarction
- Cerebrovascular accident (infarct / haemorrhage)
- Repeat angiography (planned versus un-planned)
- Repeat unplanned revascularisation

Day 30 clinical outcomes:

- Death
- Heart Failure (Killip class)
- Myocardial infarction
- Cerebrovascular accident (infarct / haemorrhage)
- Repeat unplanned angiography
- Repeat unplanned revascularisation

Killip Class I	No clinical signs of heart failure
Killip Class II	Rales or crackles in the lungs, a third heart sound and elevated jugular venous pressure
Killip Class III	Frank pulmonary oedema
Killip Class IV	Cardiogenic shock (systolic blood pressure <90mmHg) and evidence of peripheral vasoconstriction (oliguria, cyanosis or sweating)

Table B: Killip class definitions [2]

Coronary angiography characteristics

The angiographic procedure was analysed in detail. PPCI operators were instructed to acquire images of the non-culprit vessel first and perform initial/final runs of long enough duration for venous filling to be evident. Following re-establishment of flow, a single lesion defining image was required. Final images were mandated at 30 frames/second in prespecified views (left coronary system: left lateral view; right coronary artery: right anterior oblique [3]) for assessment of myocardial blush grade. If at the end of the procedure TIMI flow < III at least ten minutes delay, following appropriate clinician led therapy administration, was requested before acquiring the final images.

Angiography review:

- Initial TIMI flow (0-III) (see table C for definitions)
- Evidence of intra/post procedural no reflow phenomenon (see earlier definition)
- End procedure TIMI flow (0-III)

- End procedure myocardial blush grade (0-III) (see table C for definitions)
- Thrombus classification (0-5) (Table D)
- Culprit vessel (LAD/RCA/LCx/other)
- Multi-vessel flow limiting disease (number of vessels diseased (LAD, RCA, LCx, LMS or side branch diameter >2mm))
- Lesion characteristics
 - Classification (American College of Cardiology/American Heart Association type A/B1/B2/C) (Table E)
 - Ostial
 - Bifurcation
 - Collateralisation (Rentrop Score 0-III) (Table F)
 - Reference vessel diameter mm (Quantitative Coronary Angiographic System (QCA))
 - Lesion severity % (QCA system if patency or 100% in occluded)
 - Lesion length mm following re-established flow (QCA system)
 - Post PCI minimal luminal diameter (QCA system)

QCA calibration was performed using the guiding catheter, with measurement of the reference diameter performed close to the lesion. Preference was placed on proximal measurement, if ostial or at site of bifurcation distal measurement was accepted. Maximal stenosis if vessel was occluded was documented as 100%, if not a minimal luminal area percentage was recorded. Lesion length was recorded in millimetres following re-establishment of flow. The post PCI minimal luminal diameter (mm) was recorded as the mean of two orthogonal measurements.

TIMI score		Blush Grade	
0	No flow	0	No blush
I	Flow at a standstill	I	Blush but no clearance
II	Flow but sluggish	II	Blush but sluggish clearance
III	Normal flow	III	Blush and cleared within 3 cardiac cycles

Table C: Thrombolysis in Myocardial Infarction Flow and Blush Grade definitions

Grade	Definition
0	No cine angiographic characteristics of thrombus present
1	Possible thrombus is present, with such angiography characteristics as reduced contrast density, haziness, irregular lesion contour, or a smooth convex “meniscus” at the site of total occlusion suggestive but not diagnostic of thrombus
2	There is definite thrombus (small size), with greatest dimensions $\leq 1/2$ the vessel diameter
3	There is definite thrombus (moderate size), but with greatest linear dimension $> 1/2$ but < 2 vessel diameters
4	There is definite thrombus (large size), as grade 3, but with the largest diameter ≥ 2 vessel diameters
5	Total occlusion

Table D: Thrombus classification [4]

Type A Lesions (requires all characteristics)	Type B Lesions B1 has 1 characteristic B2 has ≥ 2 characteristics	Type C Lesions (requires any characteristic)
Discreteness (< 10 mm)	Tubular shape (10-20 mm)	Diffuseness (> 20 mm)

Concentricity	Eccentricity	Excessive tortuosity of proximal segments
Ready accessibility	Accessibility influenced by moderate tortuosity of proximal segment	Location in an extremely angulated segment (>90°)
Location in a non angulated segment (<45°)	Location in a moderately angulated segment (>45°, <90°)	Total occlusion >3 months
Smoothness of contour	Irregularity of contour	Inability to protect major side branches
Little or no calcification	Moderate/severe calcification	Degeneration of older vein grafts with friable lesions
Absence of total occlusion	Presence of thrombus	
Non ostial location	Ostial location	
Absence of major branch involvement	Bifurcation lesions requiring double guide wires	
Absence of thrombus	Total occlusions <3 months	

Table E: American College of Cardiology/American Heart Association Lesion Classification.

[5,6]

Grade	Definition
0	None
1	Filling of side branches of the artery to be dilated via collateral channels without visualization of the epicardial segment
2	Partial filling of the epicardial segment via collateral channels
3	Complete filling of the epicardial segment of the artery being dilated via collateral channels

Table F: Rentrop classification of collateral circulation [7]

REPORTING GUIDELINES

Title and abstract		
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) <i>Cohort study</i> - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross sectional study</i> - Give the eligibility criteria, and the sources and methods of selection of participants
		(b) <i>Cohort study</i> - For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> - For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group

Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding
		(b) Describe any methods used to examine subgroups and interactions
		(c) Explain how missing data were addressed
		(d) <i>Cohort study</i> - If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> - If applicable, explain how matching of cases and controls was addressed <i>Cross sectional study</i> - If applicable, describe analytical methods taking account of sampling strategy
		(e) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study - eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) <i>Cohort study</i> - Summarise follow-up time (eg average and total amount)
Outcome data	15*	<i>Cohort study</i> - Report numbers of outcome events or summary measures over time
		<i>Case-control study</i> - Report numbers in each exposure category, or summary measures of exposure
		<i>Cross sectional study</i> - Report numbers of outcome events or summary measures

Main results	16	(a) Report the numbers of individuals at each stage of the study - eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Other analyses	17	Report other analyses done - eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

TABLE G STROBE statement: checklist of items that should be included in reports of observational studies [8]

References

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- 3 Henriques JPS, Zijlstra F, Van 't Hof AWJ, *et al.* Angiographic assessment of reperfusion in acute myocardial infarction by myocardial blush grade. *Circulation* 2003;**107**:2115–9. doi:10.1161/01.CIR.0000065221.06430.ED
- 4 Sianos G, Papafaklis MI, Serruys PW. Angiographic thrombus burden classification in patients with ST-segment elevation myocardial infarction treated with percutaneous coronary intervention. *J Invasive Cardiol* 2010;**22**:6B–14B.
- 5 Ryan T, Faxon D, Gunnar R, *et al.* Guidelines for percutaneous transluminal coronary angioplasty. A report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Percutaneous Translu. *Circulation* 1988;**78**:486–502.
- 6 Ellis S, Vandormael M, Cowley M, *et al.* Coronary morphologic and clinical determinates of procedural outcome with angioplasty for multivessel coronary disease: implications for patient selection. *Circulation* 1990;**82**:1193–202.
- 7 Rentrop K, Cohen H, Blanke R, *et al.* Changes in collateral channel filling immediately after controlled coronary artery occlusion but an angioplasty balloon in human subjects. *J Am Coll Cardiol* 1985;**5**:587–92.
- 8 Elm E Von, Altman DG, Egger M, *et al.* Strengthening the reporting of observational studies in epidemiology (STROBE) statement : guidelines for reporting observational studies. *Br Med J* 2007;**335**:806–8. doi:10.1136/bmj.39335.541782.AD