SUPPLEMENTAL MATERIAL

Data S1. Supplemental Methods

MACE and mortality definitions

Non-fatal AMI

Any patient who was found to have a subsequent troponin elevation or coronary revascularisation was considered to have potential for achieving the end point myocardial infarction. An adjudication pack was produced for all patients who had a troponin elevation providing details of the admission (age, gender, admission observations, blood results, ECGs, relevant excerpts of clinical history and past medical history, relevant imaging up to 6 weeks following admission, and discharge details). Adjudication was then performed by an independent cardiologist (AK/RD/TH) who were blinded to the novel biomarker results. Details of the universal definition were provided in the pack and they were asked if they felt this presentation was due to a Type 1 Myocardial Infarction, Type 2 Myocardial Infarction, acute myocardial injury, chronic myocardial injury or other. An option for requiring more information was given. Patients who presented as part of the PPCI pathway activation who went onto have emergency coronary angiography and revascularisation were considered as having an AMI. The admission details for any patient who had undergone revascularisation, or any patients transferred for revascularisation were reviewed to look for the potential of MACE.

Unstable angina and revascularization

The end point unstable angina and revascularization was defined as any patient, with myocardial infarction excluded or normal troponin levels, who required inpatient coronary revascularization, by means of percutaneous intervention or coronary artery bypass grafting, after presenting with symptoms felt to be cardiac in nature by the treating physicians. Patients who had 'early' or expedited outpatient revascularization after presenting were recorded, but not considered a primary outcome event; as this was felt a softer endpoint.

Mortality

The cause of death was determined in one of two methods, review of hospital records and official death certification. Hospital records of all patients who had died were reviewed. For patients who were in hospital at the time of death and the cause of death was clear from diagnostic information and had been documented in the notes, this cause was used. If a patient was under the care of a palliative care team with a clear terminal condition (such as metastatic malignancy) in the 6 weeks prior to death, the cause of death was attributed to that condition. If no information was available from hospital notes, copies of the official death certificates were retrieved from the General Register Office. All-cause mortality was defined as any patient who had died within the follow up period of any cause. Cardiovascular mortality was defined as having a cause of death in section I(a) on the official death certificate due to coronary artery disease, myocardial infarction, and heart failure due to coronary heart disease.

Risk score calculations

HEART SCORE

The HEART Score was determined by using the online HEART Score calculator found at the URL: https://www.mdcalc.com/heart-score-major-cardiac-events
The history graded as ‘Highly suspicious’ if all features of pain were in the high-risk features, 'slightly suspicious' if no high-risk features were present and 'moderately suspicious' if features from both groups were present. If a patient only had 1 feature from the high-risk category and no features from the low-risk features of chest pain then the pain was graded as ‘moderately suspicious’. ECG changes were counted, repolarization abnormalities if they had T wave inversion.

TIMI score

TIMI Score for Unstable Angina / NSTEMI was calculated using the online software found at the URL: https://www.mdcalc.com/timi-risk-score-ua-nstemi

Table S1. Outcome at varying time points

	Inpt	30-day	8-week	6-mo	12-mo	24-mo	36-mo	48-mo	Long-term
UA/ revasc	7 (1.44)	9 (1.85)	9 (1.85)	11 (2.26)	11 (2.26)	14 (2.87)	14 (2.87)	14 (2.87)	16 (3.29)
MI	6 (1.23)	7 (1.44)	7 (1.44)	9 (1.85)	12 (2.46)	15 (3.08)	23 (4.72)	29 (5.95)	29 (5.95)
CV death	0	0	0	0	0	0	0	0	4 (0.82)
MACE	13 (2.67)	16 (3.29)	16 (3.29)	19 (3.90)	22 (4.52)	28 (5.75)	36 (7.39)	41 (8.42)	48 (9.86)
Mortality	0	0	2 (0.41)	5 (1.03)	11 (2.26)	14 (2.87)	18 (3.70)	26 (5.34)	42 (8.62)

Table showing outcome at different time points according to type of adverse outcome. Data is expressed in total number experiencing the outcome with percentage of total cohort in parentheses.

Table S2. Biomarker median value and range

Biomarker	Median	IQ range
HFABP (ng/ml)	4.25	3.12-7.04
GDF-15 (pg/ml)	281.82	184.52-494.54
NTproBNP (mg/dl)	110.7	50.50-252.45
hs-CRP (ng/ml)	0.23	0.10-0.66
Galectin-3 (pg/ml)	14	11.5-17.18
hs-cTnT (ng/l)	4	3-8
hs-cTnI (ng/l)	3.2	2.2-5.5

Median values and interquartile range of each biomarker.

Table S3. Relative risk of biomarker for MACE

Biomarker	Cut off	RR for given biomarker
HFABP	6.4ng/ml	1.130 (0.677-1.886) 0.760
NTproBNP	Age/gender adjusted[10]	1.39 (0.959-2.034) 0.071
Galectin-3	25.2ng/ml[12]	NA
hs-CRP	3mg/l[11]	1.294 (0.325-5.308) 0.985
hs-cTnI	♀17ng/l[13] ♂35ng/l	1.012 (0.970-1.056)

RR for each biomarker according to established cut offs or 99th percentile values. The RR associated with a biomarker above this cut off is displayed with 95% CI for RR and where possible following this p value. NTproBNP was calculated using published age/gender associated cut-offs. There were no events in patients with Galectin-3 above this threshold therefore this was not calculable.

Table S4. Univariable Cox Regression analysis for MACE

Variable	HR	95% CI	Significance
ln(HFABP)	1.048	0.632-1.735	0.857
ln(GDF-15)	**1.851**	**1.319-2.598**	**<0.001**
ln(NTproBNP)	**1.407**	**1.116-1.773**	**0.004**
ln(hs-CRP)	0.963	0.784-1.183	0.720
ln(Galectin-3)	1.362	0.659-2.813	0.394
ln(hs-cTnT)	**3.650**	**2.153-6.190**	**<0.001**
ln(hs-cTnI)	**1.814**	**1.275-2.580**	**<0.001**
TIMI	**1.908**	**1.562-2.329**	**<0.001**
HEART	**1.774**	**1.439-2.188**	**<0.001**

Univariable analysis of variables showing hazard ratios, 95% confidence intervals and significance.

Table S5. Univariable Cox Regression analysis for all-cause mortality

Variable	HR	95% CI	Significance
ln(HFABP)	1.049	0.633 – 1.738	0.852
ln(hs_cTnT)	**3.669**	**2.164 – 6.221**	**<0.001**
ln(GDF15)	**1.851**	**1.319 – 2.597**	**<0.001**
ln(NTproBNP)	**1.408**	**1.117 – 1.775**	**0.004**
ln(hs_cTnI)	**1.821**	**1.281 – 2.588**	**<0.001**
ln(HSCRP)	0.964	0.785 – 1.183	0.725
ln(Galectin_3)	1.566	0.538 – 4.560	0.411
TIMI	**1.928**	**1.576 – 2.360**	**<0.001**
GRACE	**1.016**	**1.004 – 1.028**	**0.007**
HEART	**1.777**	**1.441 – 2.192**	**<0.001**
Charlson Comorbidity Index	**1.364**	**1.207 – 1.542**	**<0.001**