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Title: Impact of initial hospital diagnosis on mortality for acute myocardial infarction: a national cohort study.

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Abstract

Aims: Early and accurate diagnosis of acute myocardial infarction is central to successful treatment and improved outcomes. We aimed to investigate the impact of the initial hospital diagnosis on mortality for patients with acute myocardial infarction.

Methods and results: Cohort study using data from the Myocardial Ischaemia National Audit Project of patients discharged with a final diagnosis of ST-elevation myocardial infarction (STEMI, n=221,635) and non-STEMI (NSTEMI, n=342,777) between 1st April 2004 and 31st March 2013 in all acute hospitals (n = 243) in England and Wales. Overall, 168,534 (29.9%) patients had an initial diagnosis which was not the same as their final diagnosis. After multivariable adjustment, for STEMI a change from an initial diagnosis of NSTEMI (time ratio (TR) 0.97, 95% CI 0.92–1.01) and chest pain of uncertain cause (0.98, 0.89–1.07) was not associated with a significant reduction in time to death, whereas for other initial diagnoses the time to death was significantly reduced by 21% (0.78, 0.74–0.83). For NSTEMI, after multivariable adjustment, a change from an initial diagnosis of STEMI was associated with a reduction in time to death of 10% (TR 0.90, 95% CI 0.83–0.97), but not for chest pain of uncertain cause (0.99, 0.96–1.02). Patients with NSTEMI who had other initial diagnoses had a significant 14% reduction in their time to death (TR 0.86, 95% CI 0.84–0.88). STEMI and NSTEMI with other initial diagnoses had low rates of pre-hospital ECG (24.3% and 21.5%), aspirin on hospitalisation (61.6% and 48.5%), care by a Cardiologist (60.0% and 51.5%), invasive coronary procedures (38.8 % and 29.2%), cardiac rehabilitation (68.9% and 62.6%) and guideline indicated medications at time of discharge from hospital. Had the 3.3% of patients with STEMI and 17.9% of NSTEMI who were admitted with other initial diagnoses received an initial diagnosis of STEMI and NSTEMI, then 33 and 218 deaths per year might have been prevented, respectively.

CONCLUSION: Nearly one in three patients with acute myocardial infarction had other diagnoses at first medical contact, who less frequently received guideline indicated care and had significantly higher mortality rates. There is substantial potential, greater for NSTEMI than STEMI, to improve outcomes through earlier and more accurate diagnosis of acute myocardial infarction.

Registration: ClinicalTrials.gov NCT02600962.

Introduction

Acute myocardial infarction is a common cause of hospital admission and a major burden on healthcare resources.[1,2] Its early and accurate diagnosis is central to successful treatment and improved outcomes.[3,4] Typically, on admission to hospital an initial diagnosis is made for each patient which determines their treatment. In addition to pharmacological therapies, this includes primary percutaneous coronary intervention or fibrinolysis for ST-elevation myocardial infarction (STEMI) and invasive coronary imaging and revascularisation for non-STEMI (NSTEMI). Even though a prerequisite for the diagnosis of acute myocardial infarction is the detection of a rise and fall in troponin,[5] the preliminary hospital diagnosis is usually made in the absence of this information – being derived from pre-hospital data and that obtained from the history, clinical examination and 12-lead electrocardiograph (ECG) in an emergency environment.

Our previous work found that patients with acute myocardial infarction who failed to receive evidence-based care at the pre-hospital phase were less likely to receive hospital treatments, and that this was associated with premature death.[6,7] Yet, we are not aware of any studies which have quantified the impact of an initial hospital diagnosis which is not acute myocardial infarction on clinical outcomes among patients who have had an acute myocardial infarction. Clarifying the extent to which patients with acute myocardial infarction received different initial diagnoses is important given data suggesting that high sensitivity troponins may increase the diagnosis of acute myocardial infarction and reduce rates of death.[8,9] In this study, we sought to determine the degree to which an initial non-specific / non-cardiac diagnosis impacted on mortality for patients hospitalised with acute myocardial infarction. Specifically, we aimed to describe the baseline characteristics, investigations performed, cardiovascular treatments received and mortality at 1 year for

patients hospitalised with STEMI or NSTEMI who also had an initial diagnosis of 'chest pain of unknown cause' or 'other initial diagnosis'.

Methods

Setting and design

We included all NHS hospitals (n=243) in England and Wales which provided care for patients (n=564,412) aged between 18 and 100 years at time of hospitalisation and discharged from hospital alive with acute myocardial infarction between 1st April 2004 and 31st March 2013. Patient-level data were extracted from the Myocardial Ischaemia National Audit Project (MINAP), a comprehensive registry of hospitalisations for acute coronary syndrome in England and Wales, which was started in 2000 and is now mandated by the Department of Health.[10] For multiple admissions, we used the earliest record to reduce potential bias form pre-existing treatments. Details of MINAP have been described previously.[6,10] The data flow for the derivation of the analytical cohort can be seen in Supplement Figure 1.

Study variables

We included demographic factors (age, sex, year of hospital admission), past medical history (coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), heart failure, diabetes mellitus, hypertension, hyperlipidaemia, previous acute myocardial infarction and smoking status), markers of acute myocardial infarction severity at time of hospitalisation (heart rate, systolic blood pressure, serum creatinine, cardiac arrest, elevated cardiac biomarkers and ST segment depression on the ECG), investigations (pre-hospital ECG, any ECG, coronary angiography), acute treatments (aspirin, fibrinolysis, primary PCI), medications prescribed at hospital discharge (aspirin, $P2Y_{12}$ inhibitors, angiotensin

converting enzyme inhibitors (ACEi)/angiotensin-receptor blockers (ARB), β blockers, HMG Co-A reductase inhibitors (statins) and care (cardiac rehabilitation, care by a Cardiologist). For each patient, we extracted information about their initial diagnosis (STEMI, NSTEMI, chest pain of unknown cause, other initial diagnoses). For each hospital we calculated its average annual volume and deprivation level (mean Townsend score) across all patients recorded in MINAP as attending that hospital during 2004-2013.

Initial and final diagnoses

The final diagnosis of STEMI and NSTEMI was based on guidelines from the European Society of Cardiology (ESC), American College of Cardiology (ACC) and American Heart Association (AHA) and determined at local level by the attending Consultant.[5] The initial diagnosis was made by the emergency medical services or other clinicians in a position to provide definitive treatment. It was based on information (such as the history of the presenting complaint, physical examination and initial ECG) gathered in the acute setting and was not modified on the basis of further ECGs or cardiac biomarkers. The initial diagnoses included STEMI, NSTEMI, chest pain of uncertain origin and other initial diagnoses. Chest pain of unknown origin was defined as a single episode of chest pain thought to be cardiac in nature where hospital admission was felt appropriate to exclude an ischaemic event. It covered admissions where no clear initial diagnosis was made, but where there was suspicion that a patient's symptoms were ischaemic in nature. Other initial diagnoses included non-cardiac diagnoses (such as pancreatitis) as well as non-acute myocardial infarction diagnoses (such as acute aortic dissection).

We created a variable called 'change in diagnosis' to represent combinations of initial to final diagnoses, made at hospital admission and discharge, respectively. The change in diagnosis categories included; STEMI→STEMI, NSTEMI→STEMI, chest pain of unknown cause→STEMI,

other initial diagnoses→STEMI, STEMI→NSTEMI, NSTEMI→NSTEMI, chest pain with unknown cause→NSTEMI, other initial diagnoses→NSTEMI.

Mortality

The primary clinical outcome was mortality from all causes at 1 year after discharge from hospital. National unique identifiers were used to link patients with the Office for National Statistics, and we accessed the registry to ascertain vital status or date of death at 1-year. The survival duration was derived from the date of death or censorship and date of discharge from hospital.

Statistical analysis

Baseline characteristics, investigations and treatments were stratified by initial and final diagnosis and described using median (interquartile range, IQR) for numerical variables and count (%) for categorical variables. Odds ratios (OR) or median difference (MD) were calculated for patient variables between stratified groups and the Chi-squared test or Wilcoxon rank-sum tests used to test the significance of the differences between strata. We categorised all numerical variables. We used a survival tree model to determine age cut-offs (≤61, 62-73, 74-82, and ≥83 years) to maximise mortality differences between age groups and to mitigate non-linear effects; whereas serum creatinine, heart rate, systolic blood pressure and length of hospital stay were split by tertiles.

We compared mortality rates at 1 year by age and sex, stratified by the change in diagnosis categories. We used Kaplan–Meier survival curves to depict unadjusted survival estimates to 1 year by change in diagnosis category. We investigated the association between the change in diagnosis and time to death at 1 year using accelerated failure time models (Cox models violated the proportional hazards assumption). Separate models for final diagnosis STEMI and NSTEMI included change in diagnosis as the explanatory variable adjusted for patient

baseline clinical and treatment characteristics; including age, sex, CABG, heart failure, diabetes, hypertension, hyperlipidaemia, previous myocardial infarction, percutaneous coronary intervention, prior or current smoking, creatinine, heart rate and systolic blood pressure on admission, cardiac arrest, elevation of cardiac enzymes, ST segment depression on the ECG, emergency reperfusion therapy (fibrinolysis or primary percutaneous coronary intervention), acute or chronic aspirin, pre-hospital or any ECG, care by a cardiologist, coronary angiography, cardiac rehabilitation and at discharge from hospital the prescription of aspirin, $P2Y_{12}$ inhibitors, β blocker, statin and ACEi/ARB. We also adjusted for length of hospital stay, hospital volume, Townsend score per hospital and year of hospital admission. A random intercept representing each hospital was added to the model to account for the clustering of patients within hospitals.

We used linear mixed effects logistic regression models, separately for patients with a final diagnosis of STEMI and NSTEMI, to investigate which factors were associated with a change in diagnosis. Therefore, to predict a change from STEMI→STEMI (no change) compared with other initial diagnoses→STEMI (change), we built models that included the same patient clinical variables as we had used for the survival models but excluded treatment variables. We included a random intercept representing the participating hospitals. Model selection was performed to eliminate the covariates that were not significant. We applied the same model to predict changes for the NSTEMI combinations of diagnoses.

We estimated the total number of deaths that might have been prevented if the initial diagnosis was correct by multiplying the adjusted time ratio of a change in diagnosis by the 1 year mortality rate for STEMI and NSTEMI respectively. This was then multiplied by the proportion of patients who received an incorrect diagnosis out of the total number of cases between 2004 and 2013.

The accelerated time failure and logistic regression models were applied to complete cases and estimates presented with 95% confidence intervals (CI). Where not specified, a *P*-value <0.05 was considered to indicate statistical significance. Statistical analyses were performed with R (version 3.2.2).

Sensitivity analysis

To assess the impact of incomplete data on the results of the modelling (under the assumption that data were not missing at random), for each variable we created an extra level called "missing" to represent missing or unknown values. We applied each model to the new data containing the "missing" category. To investigate the influence of the "missing" category, we combined the "missing" group either to the reference group or to the highest level group for each variable, and repeated our main analysis to the newly formed variables. This gave us the possible range of coefficients (eTable 5-6).

Results

Of 564,412 patients with acute myocardial infarction (mean age 68.4 (SD 13.7) years, 66.8% male), the majority (86.4%) were white, one fifth (19.1%) had diabetes and one fifth (21.5%) previous myocardial infarction (Table 1). Nearly two thirds (64.1%) were prior or current smokers, 48.8% had hypertension, 33.3% hyperlipidaemia. For the cohort, 3.8% had a cardiac arrest, and 16.3% had ST depression on their ECG. The median (IQR) hospital stay was 5 (3-9) days. Table 1 shows that patients with a final diagnosis of NSTEMI were more frequently co-morbid, and had longer hospital stays. In total, 168,534 (29.9%) patients had an initial diagnosis which was not the same as their final diagnosis. For final diagnosis STEMI and NSTEMI, the proportions with other initial diagnoses (3.3% and 17.9%) was higher than

the proportions with chest pain of uncertain cause (2.9% and 16.1%), but lower than the proportion with initial diagnosis NSTEMI (14.2%) and STEMI (19.7%).

Baseline characteristics

eTables 1 and 2 show the baseline characteristics of patients with STEMI and NSTEMI according to their initial diagnoses. For STEMI, patients who had an initial diagnosis of NSTEMI, chest pain of uncertain cause or another initial diagnosis were older, more frequently female with heart failure, diabetes, previous myocardial infarction, higher creatinine and heart rates, cardiac arrest, ST depression on their ECG and longer lengths of hospital stay. These findings were more pronounced among patients with other initial diagnoses whose length of hospital stays was more than twice that of patients who had an initial diagnosis of STEMI (9 vs. 4 days). For NSTEMI, the findings were very similar; those who did not have an initial diagnosis of NSTEMI were more frequently older, female and co-morbid. Lengths of hospital stays for those with other initial diagnoses were nearly double that of NSTEMI (11 vs. 6 days).

For patients with other initial diagnoses, the strongest predictors for change to a final diagnosis of STEMI were, ST segment depression (OR 2.97, 95% CI 2.26-3.89), age ≥83 years (2.81, 2.42-3.25), heart rate >86 bpm (2.12, 1.90-2.37) and heart failure (1.96, 1.58-2.44) (Figure 1). The use of a pre-hospital ECG was associated with an 85% chance of not changing diagnosis to STEMI (OR 0.15, 95% CI 0.14-0.17). Having a length of hospital stay over 7 days increased the likelihood of being diagnosed with STEMI by 4-fold (4.34, 3.83-4.91). For NSTEMI who presented with other initial diagnoses, the strongest predictors for change of their diagnosis were, age ≥83 years (OR 3.16, 95% CI 2.98-3.35), cardiac arrest (2.77, 2.48-3.09), heart rate >86 bpm (2.38, 2.28-2.48) and heart failure (1.55, 1.47-1.64). The use of a

pre-hospital ECG was the strongest predictor for not changing to a diagnosis of NSTEMI (OR 0.36, 95% CI 0.35-0.37) and having a length of hospital stay over 7 days increased the likelihood of being diagnosed with NSTEMI by 4-fold (4.05, CI 3.84-4.27). The adjusted risk of a change in diagnosis from other initial diagnoses to that of final STEMI or NSTEMI diagnosis varied significantly by hospital (eFigure 2).

Treatments

eTables 3 and 4 show the treatments for STEMI and NSTEMI according to their initial diagnoses. For STEMI, patients who had an initial diagnosis of NSTEMI, chest pain of uncertain cause or other initial diagnoses less frequently received reperfusion therapy, aspirin on hospital admission or a pre-hospital ECG. They less frequently were under the care of a Cardiologist, received coronary angiography, cardiac rehabilitation and any guideline indicated medication at the time of discharge from hospital. For NSTEMI, a similar pattern of care was evident, with particularly low rates of coronary angiography among those with other initial diagnoses.

Mortality

At 1 year following hospital discharge, the mortality rate among STEMI who had an initial diagnosis of STEMI was 5.6% compared with a higher rate for those with an initial diagnosis of NSTEMI (8.4%), chest pain of uncertain cause (8.3%) and other initial diagnoses (21.3%) (Figure 2). For NSTEMI, the contrast in mortality at 1 year between patients with an initial diagnosis of NSTEMI (10.7%) and those with STEMI (11.4%) and chest pain of uncertain cause (11.5%) was less evident. Patients with NSTEMI who had other initial diagnoses, however, had mortality rates at 1 year more than double (25.5%) that of patients with an initial diagnosis of NSTEMI. With increasing age, but not by sex, these differences were accentuated (Figure 3).

After adjustment for case mix, investigations and treatments (Table 2), for STEMI a change from an initial diagnosis of NSTEMI (time ratio (TR) 0.97, 95% CI 0.92–1.01) and chest pain of uncertain cause (0.98, 0.89–1.07) was not associated with a significant reduction in time to death, whereas for other initial diagnoses the time to death was significantly reduced by 21% (0.78, 0.74–0.83). For NSTEMI, after multivariable adjustment (Table 3), a change from an initial diagnosis of STEMI was associated with a reduction in time to death of 10% (TR 0.90, 95% CI 0.83–0.97), but not for chest pain of uncertain cause (0.99, 0.96–1.02). Patients with NSTEMI who had other initial diagnoses had a significant 14% reduction in their time to death (TR 0.86, 95% CI 0.84–0.88).

Further, if the 7,411 patients with STEMI who were admitted with other initial diagnoses had received an initial diagnosis of STEMI then 332 deaths (33 deaths per year) at 1 year might have been prevented. Equally, if the 61,204 patients with NSTEMI who were admitted with other initial diagnoses had received an initial diagnosis of NSTEMI then 2,185 deaths (218 deaths per year) at 1 year might have been prevented.

Sensitivity analysis

Sensitivity analysis was performed for each model using all available cases as described in methods section. The results are presented in eTable 5-6 for logistic regression models for predicting the change of diagnosis, and Table 2-3 for accelerated time failure models for predicting the 1-year survival. The results show a narrow range of the coefficients containing the coefficient values from the corresponding models using complete cases.

Discussion

Acute myocardial infarction is a common reason for hospitalisation and a medical emergency that requires early access to specialist treatment.[11,12] Evidence from clinical and

basic science studies reveals that delays to guideline-indicated care (such as timely reperfusion for STEMI and risk-stratified revascularisation for NSTEMI) are associated with increased mortality.[3,4,13] The diagnosis of acute myocardial infarction, however, is not always apparent at first medical contact. Our study of over 500,000 patients with a diagnosis of STEMI or NSTEMI shows that a preliminary diagnosis made at initial medical contact which was not of acute myocardial infarction was not infrequent. Among the one in three cases where there was inconsistency between the initial and final diagnosis, the chance of receiving guideline indicated treatments for the management of acute myocardial infarction was significantly reduced and associated high rates of premature death. We estimated that, over the decade of study, had patients with acute myocardial infarction who were admitted with other initial diagnoses received an initial diagnosis of acute myocardial infarction, then over 250 deaths per year might have been prevented, respectively.

Whilst a preliminary diagnosis of STEMI is readily made among patients with chest pain who have ST-segment elevation or new left bundle branch block on their presenting ECG, its timely diagnosis relies on the early use of the ECG. In the UK, as with other modern healthcare systems, the emergency management of STEMI has become institutionally operationalised – patients bypass local hospital to receive primary PCI at Heart Attack Centres – and this has been associated with the decline in the rates of death following STEMI.[14-16] Even so, our study shows that a proportion of patients (who, typically, were more co-morbid) did not receive an early diagnosis of STEMI. In turn, this was associated with premature death because they were much less likely to receive evidence-based care. Our earlier work revealed sub-optimal use of the pre-hospital ECG, which is a critical step in the 'perfect patient pathway' for the management of STEMI.[7] Moreover, early missed care opportunities such as the provision of a pre-hospital ECG are associated with the failure to provide guideline-indicated care later on, which in turn is associated with significantly higher

rates of death compared with patients who receive interventions early in the STEMI pathway.[6]

Survival was reduced by up to a fifth among patients with acute myocardial infarction who had other initial diagnoses at first medical contact. These findings were upheld after adjusting for case mix, cardiovascular risk and treatments received, suggesting that either other factors are responsible for the reduced survival or our adjustment was not comprehensive. Other factors may include delays to rather than the receipt of treatments or the availability of specialist hospital facilities and staffing[16]. By comparison we found, after adjustment, no survival disadvantage for NSTEMI who initially were diagnosed as STEMI, and STEMI who were initially diagnosed with NSTEMI. This may have been because, although the risk of receiving guideline-indicated care was lower for patients who changed between STEMI and NSTEMI diagnoses, treatment use among these groups was comparably high and our models captured the multimorbidity of patients with NSTEMI. Similarly, we did not find a survival disadvantage following adjustment for case mix, risk and treatments received for patients who had an initial diagnosis of chest pain of uncertain cause. Again, whilst these patients were less likely to receive care interventions, overall they had high rates of use of guideline-indicated treatments for acute myocardial infarction. Moreover, it was among patients who had initial other diagnoses that treatments were less frequent compared with patients with chest pain of uncertain cause and those who did not have a change of diagnosis.

We found that the proportion of patients with NSTEMI who did not have an initial diagnosis of NSTEMI was at least five-fold higher than for patients with STEMI. Such patients, whilst being more co-morbid, were less likely to receive guideline-indicated care and more likely to die sooner than patients who had an initial diagnosis of NSTEMI. Even though it is not unusual for patients with NSTEMI to have a normal ECG, we found that a quarter of those

with other initial diagnoses had electrocardiographic ST-segment depression, which was of similar frequency to that for patients who had an initial diagnosis of NSTEMI. In contrast to STEMI, the diagnosis of NSTEMI is more dependent upon the results of the troponin assay, which is rarely available at first medical contact. Therefore, approaches to reduce potential harm through omission of care would include the early use of high-sensitivity troponin which is associated with higher and earlier rates of diagnosis of NSTEMI, more frequent use of guideline-indicated care and better clinical outcomes.[9] By increasing diagnostic certainty, emergency department congestion would be reduced and there would be fewer unnecessary non-cardiac hospitalisations.[17,18]

Our investigation has a number of other important clinical implications. In the absence of early troponin results, physicians are reliant on the clinical history and results of the ECG. Yet, over half of patients will have a non-diagnostic ECG and atypical symptoms of acute myocardial infarction are not uncommon in the elderly, women and in patients with diabetes, chronic renal failure or dementia.[19-21] Furthermore, the history of chest pain has been shown to be of limited value in cases of suspected acute coronary syndrome.[22,23] For NSTEMI, where the diagnostic yield from the ECG is, by definition, lower than for STEMI, physicians are even more reliant on the typicality of the history of chest pain. Our observational evidence of potentially avoidable deaths associated with delayed STEMI and NSTEMI diagnoses serves to remind clinicians of the importance of being aware of the range of characteristics with which patients with acute myocardial infarction present to hospital. Specifically for NSTEMI, our results in light of other recent cohort data call for the earlier use and wider adoption of high sensitivity troponins as well as a focus on the systematic application of accelerated diagnostic protocols using risk scores rather than subjective clinical assessment.[9,24-26]

There are some limitations to this study. We did not have data regarding the type and timing of the troponin assay and therefore, we could not determine their effect on the change in diagnosis. Nonetheless, there is good evidence for the impact of troponins on diagnostic yield.[8,9,24] We were reliant on the accurate recording of the diagnoses and we did not have data for the specific clinical diagnosis under the category other initial diagnoses. Even though MINAP performs annual data validation,[10] this could have led to misclassification bias and precluded higher resolution interrogation of specific preliminary diagnoses (such as the frequency of pancreatitis as an initial diagnosis). Nonetheless, we were careful in our selection of patients with a final diagnosis of acute myocardial infarction (eFigure 1), and one of the strengths of the cohort was the ability to determine STEMI and NSTEMI among a very large cohort of patients. Also, we excluded patients who died in hospital because we were unsure as to what treatments they had received. In doing so, we may have underestimated the effects of a change in diagnosis because the risk of dying from acute myocardial infarction is higher early after the event[27]. Finally, MINAP does not record data for all patients with acute myocardial infarction.[1] Given this, our calculation of the numbers of preventable deaths is underestimated and the potential for improvement is likely to be much greater.

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Figure 1. Odds ratios for predicting change in diagnosis for patients with an initial diagnosis of 'other initial diagnosis' and final diagnosis STEMI (a) or NSTEMI (b).

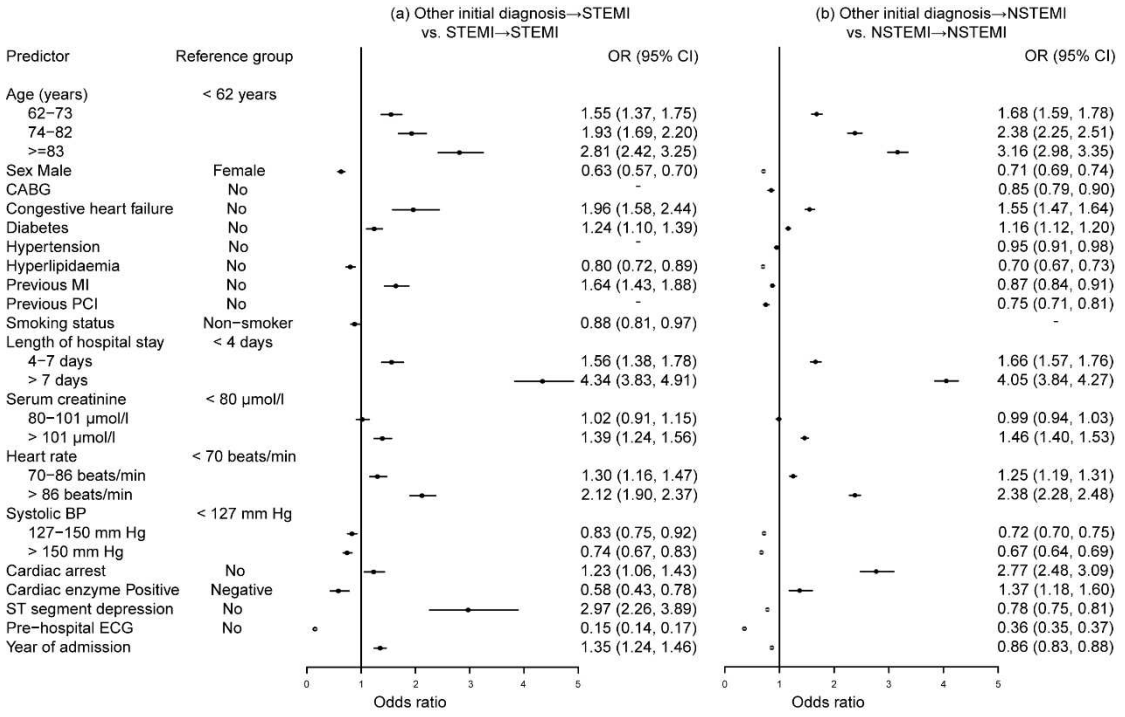


Figure1 footnote: A random intercept representing participating hospitals was included in each model to adjust for clustering effect; the hospital level variables including hospital volume and Townsend score/hospital were not statistically significant in both models.

Figure 2. Unadjusted survival rates for patients with STEMI and NSTEMI, stratified by initial diagnosis

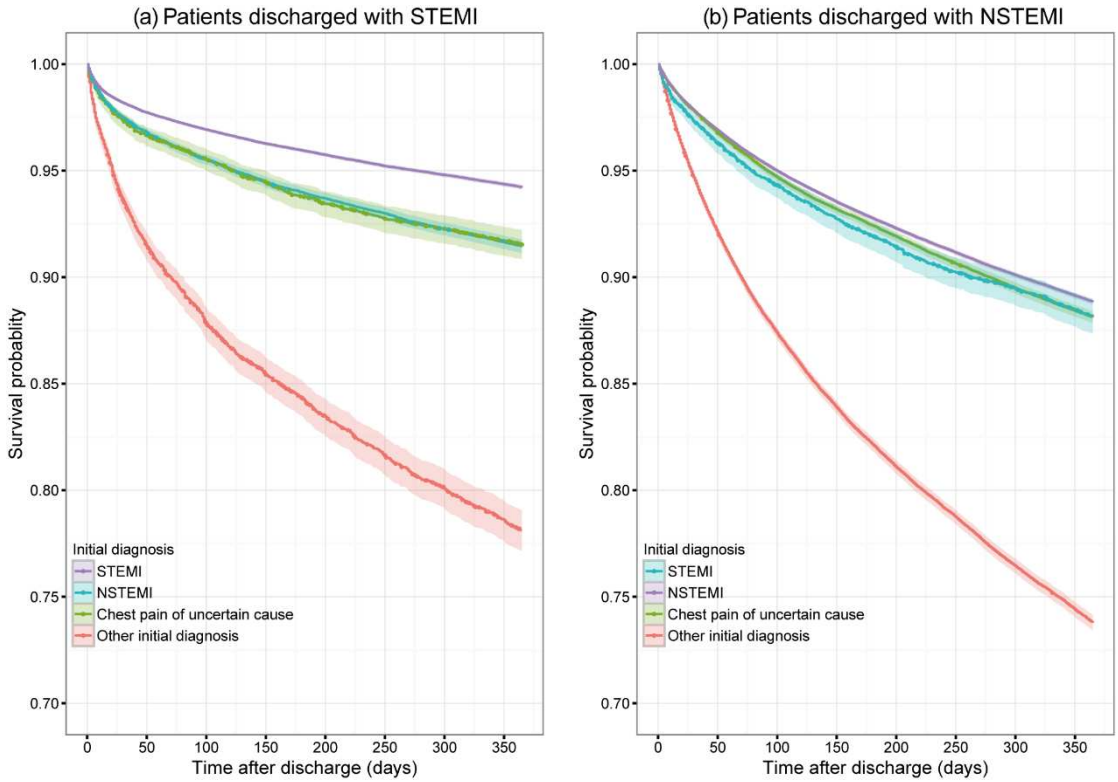
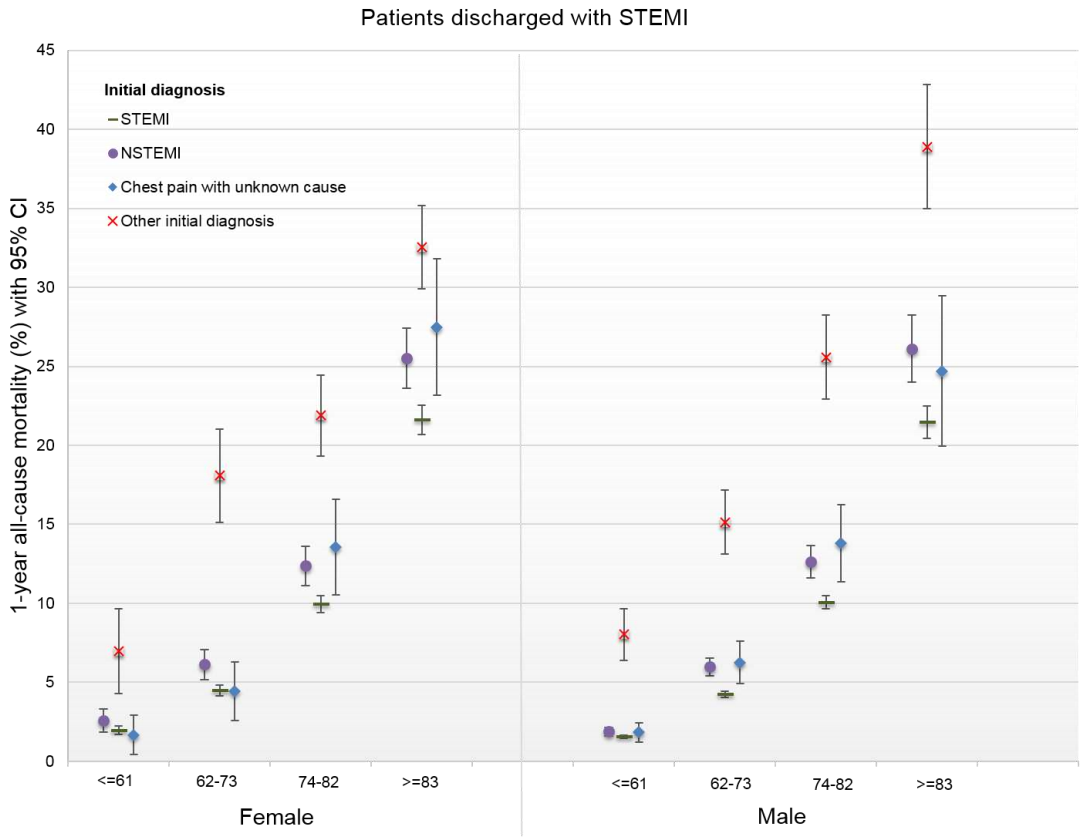


Figure 3. All-cause mortality at 1 year for patients with STEMI and NSTEMI, stratified by age, sex and initial diagnosis



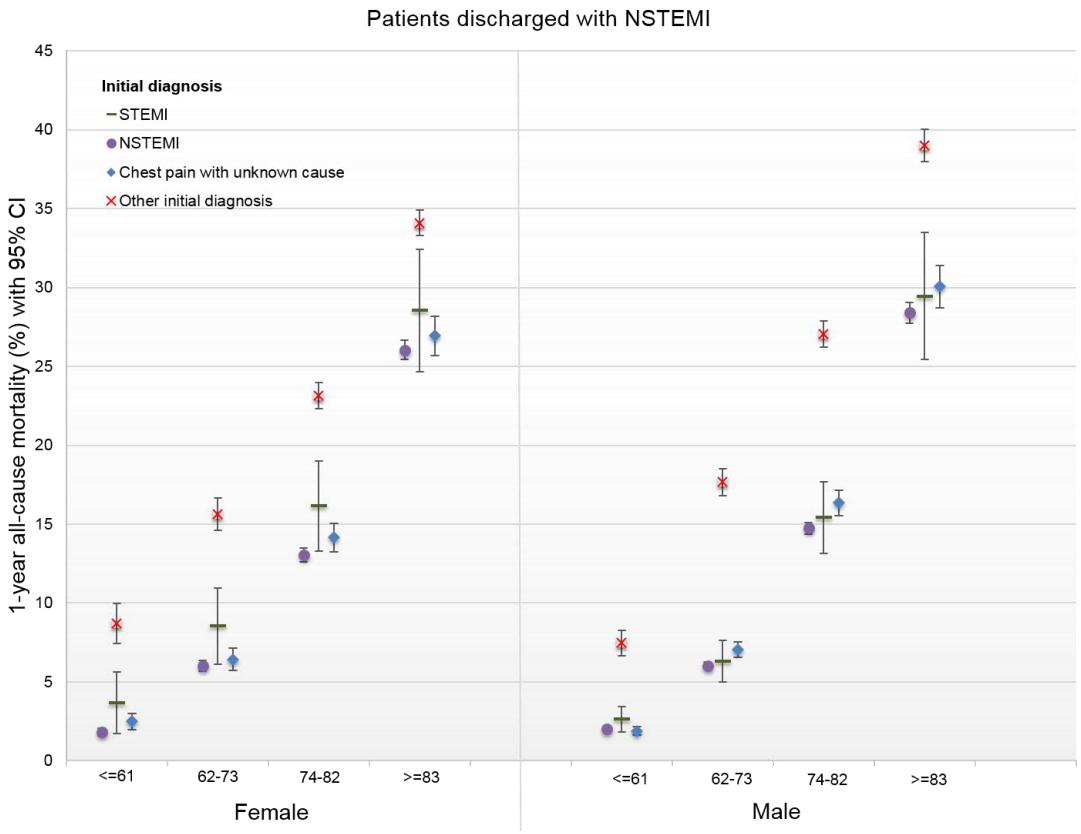

Patients discharged with NSTEMI
Initial diagnosis
STEMI
NSTEMI
Chest pain with unknown cause
Other initial diagnosis
1-year all-cause mortality (%) with 95% CI
0
5
10
15
20
25
30
35
40
45
<=61
62-73
74-82
>=83
Female
Male

Table 1. Baseline characteristics, by final diagnosis

Baseline characteristic	Final diagnosis	
	STEMI N = 221635	NSTEMI N = 342777
Age in years, median (IQR)	64.5 (55.0, 74.8)	72.5 (61.5, 81.1)
Men (%)	159923 (72.2)	216937 (63.3)
Medical history		
CABG (%)	5022 (2.5)	25714 (8.0)
Congestive heart failure (%)	3407 (1.7)	22019 (6.9)
Diabetes (%)	27703 (13.4)	75244 (22.6)
Hypertension (%)	84252 (41.8)	173629 (53.1)
Hyperlipidaemia (%)	58512 (30.1)	112416 (35.3)
Previous MI (%)	25703 (12.7)	88156 (26.9)
PCI (%)	11599 (5.9)	30607 (9.5)
Prior or current smoking (%)	137983 (68.2)	196493 (61.5)
AMI severity variables		
Serum creatinine (µmol/l)*	87.0 (74.0, 103.0)	92.0 (76.0, 114.0)
Heart rate (beats/min)	75.0 (64.0, 89.0)	80.0 (67.0, 94.0)
Systolic BP (mm Hg)	135.0 (118.0, 154.0)	141.0 (123.0, 160.0)
Cardiac arrest (%)	15000 (7.2)	5351 (1.6)
Cardiac enzyme positive (%)	190013 (96.0)	314310 (95.3)
ST segment depression (%)	4058 (1.9)	82478 (26.0)
Length of hospital stay in days^	4 (2, 7)	6 (4, 11)
Initial diagnosis		
STEMI (%)	176269 (79.5)	6764 (2.0)
NSTEMI (%)	31436 (14.2)	219568 (64.1)
Chest pain of uncertain cause (%)	6519 (2.9)	55241 (16.1)
Other initial diagnosis (%)	7411 (3.3)	61204 (17.9)

Continuous variables are presented with median (IQR);

Categorical variables are presented with count (%);
* µmol/l can be converted into mg/dl by dividing 88.4
^ Length of hospital stay rounded to nearest single day

Table 2.1-year survival according to change in diagnosis for patients discharged with STEMI. Model 1 includes 'Missing' category representing unknown or missing values for each variable; model 2 combines the 'Missing' category with reference group; model 3 combines the 'Missing' category with the highest level category of that variable.

		Adjusted survival time ratio with 95% CI		
Variable	**Reference group**	**Model 1**	**Model 2**	**Model 3**
Change in diagnosis	STEMI->STEMI	1	1	1
NSTEMI->STEMI		0.97(0.92,1.01)	0.99(0.94,1.03)	0.94(0.90,0.98)**
Chest pain of uncertain cause->STEMI		0.98(0.89,1.07)	0.98(0.90,1.07)	0.95(0.86,1.03)
Other initial diagnosis->STEMI		0.78(0.74,0.83)**	0.76(0.72,0.81)**	0.75(0.71,0.80)**

Note: Each model was further adjusted for patients' casemix, investigations and treatments and hospital level covariates; a random intercept representing participating hospitals was included in each model to adjust for clustering effect; ** p < 0.01

Table 3. 1-year survival according to change in diagnosis for patients discharged with NSTEMI. Model 1 includes 'Missing' category representing unknown or missing values for each variable; model 2 combines the 'Missing' category with reference group; model 3 combines the 'Missing' category with the highest level category of that variable.

		Adjusted survival time ratio with 95% CI		
Variable	**Reference group**	**Model 1**	**Model 2**	**Model 3**
Change in diagnosis	NSTEMI->NSTEMI	1	1	1
STEMI->NSTEMI		0.90(0.83,0.97)**	0.90(0.83,0.97)**	0.83(0.71,0.96)**
Chest pain of uncertain cause->NSTEMI		0.99(0.96,1.02)	0.99(0.96,1.02)	1.06(0.99,1.13)
Other initial diagnosis->NSTEMI		0.86(0.84,0.88)**	0.85(0.83,0.87)**	0.85(0.80,0.89)**

Note: Each model was further adjusted for patients' casemix, investigations and treatments and hospital level covariates; a random intercept representing participating hospitals was included in each model to adjust for clustering effect; ** p < 0.01