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Prognostic value of admission blood glucose concentration and diabetes diagnosis on survival after acute myocardial infarction
Results from 4702 index cases in routine practice

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Short title : Glucose, diabetes and prognosis after myocardial infarction

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ABSTRACT

The diagnosis of diabetes and admission blood glucose concentration are associated with adverse outcome after acute coronary syndromes. We compared the relative association with survival after ST-elevation acute myocardial infarction of admission blood glucose concentration and of diabetes diagnosis.

We carried out a retrospective cohort study in 4702 consecutive patients with ST elevation AMI (STEMI) occurring April 1st 1993 - December 31st 2005, assessed for mortality at 30 days and 1 year. Patients were classified according to antecedent diabetes, and by blood glucose concentration at admission (quartile 1, <7mmol/L; quartile 2, 7 - 8.2 mmol/L; quartile 3, 8.3 - 10.9 mmol/L; quartile 4, ≥11 mmol/L). Multivariable models were constructed for determinants of mortality, including year of STEMI and demographic variables, entering blood glucose concentration and antecedent diabetes individually, and together.

All-cause 30-day and 1-year mortality were 22.8% and 31.3% for patients with antecedent diabetes, compared to 16.3% and 23.0% respectively for those without. For glucose quartiles 1, 2, 3, and 4, crude 30-day mortality was 9.0%, 10.6%, 17.9% and 31.0%. Adjusted 30-day mortality risk was similar in quartile 2, higher by >80% in quartile 3 and by >150% in quartile 4, compared to glucose quartile 1. Antecedent diabetes was associated with an increase in mortality (unadjusted odds ratio (OR) 1.52 (95% CI 1.24 , 1.86)). On multivariable analysis (excluding glucose quartile), this reduced to 1.24 (0.98 , 1.58) and changed to a small, statistically non-significant reduction in risk when glucose quartile was added to the analysis (adjusted OR 0.87 (0.67 , 1.13)). Inclusion of antecedent diabetes in multivariable models did not add to the predictive value for mortality of glucose quartile (p=0.368). Similar relationships were observed for 1 year mortality.

In patients with STEMI, blood glucose concentration shows graded association with risk of 30-day and 1-year mortality and is of greater prognostic relevance than antecedent diabetes diagnosis. Moderate elevation of blood glucose, below levels previously considered to be clinically relevant, is associated with adverse impact on survival.

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Introduction

Abnormalities of glucose metabolism have powerful association with adverse prognosis for patients with coronary heart disease. In the setting of acute myocardial infarction (AMI), the diagnosis of diabetes is associated with adverse outcome [1, 2]. In addition, elevated blood glucose ('stress hyperglycaemia') is common among patients hospitalised with AMI, irrespective of diabetes status, and is also associated with adverse outcome [2, 3, 4, 5, 6, 7]. In most studies considering the influence of diabetes on prognosis after AMI, patients have been categorised based upon a history of the condition prior to the index event, an approach likely to underestimate prevalence. Similarly, studies assessing the association with prognosis of hyperglycaemia have for the most part considered blood glucose concentration as a dichotomised variable, using varying cut-off values [5, 8, 9]. Those studies considering blood glucose as a graded variable have been in selected cohorts, considering only patients with prior diabetes diagnosis [3, 7, 18] or aged > 65 years [6], or used fasting glucose[(9, 10] or glycated haemoglobin [11].
It remains unclear whether it is diabetes per se, or the severity of the acute glycaemic response at the time of the event, which impacts on prognosis [4]. Indeed the relative influence upon outcome after AMI of these factors has not been assessed in routine practice. The aim of the current study was to assess the relative association with survival after ST segment elevation AMI (STEMI) of antecedent diabetes diagnosis and of admission blood glucose concentration.

Methods

Data are from consecutive admissions (January 1st 1993 – December 31st 2005) to the coronary care unit (CCU) of a large teaching hospital (Leicester Royal Infirmary), one of two serving the population of Leicestershire, UK (approximately 946,000 residents in 2004). For all patients we record routine clinical and demographic data including information on diagnosis (STEMI/NSTEMI), electrocardiographic (ECG) site of infarct and details of medical history, coronary heart disease risk-factors, and medication prescribed prior to and during admission. Mortality is recorded prospectively, as described previously [12]. For patients with multiple admissions, we considered data pertaining only to the first. Pre-defined outcome measures were the individual and relative strength of association with 30-day and 1-year, all-cause mortality of antecedent diabetes and admission blood glucose concentration.

Patient identification
On a background of changes during the study period in the definition of AMI, we maintained consistent inclusion criteria by restricting the analysis to patients with STEMI. The diagnosis required (i) ECG evidence of dynamic ST segment elevation together with (ii) appropriate symptoms and (iii) increase in serum levels of CK to greater than twice the upper limit of the laboratory reference range (ie >400 IU/L). Troponin concentrations were not available for the full study period . Patients were categorised according to (i) a pre-existing diagnosis of diabetes (reported by the patient, or on the basis of prescribed medication) and (ii) by blood glucose concentration at the time of index admission.
The data used in this analysis were gathered during routine care of the patients. Although predating the Myocardial Ischaemia National Audit Project (MINAP), our database is that used by our hospital for this purpose. In this context, data collection does not require individual patient consent. The project was approved by the local research ethics committee.

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Statistical analysis

Baseline differences between groups were examined using independent two-sample t-tests for continuous variables and chi-squared tests for categorical variables. Data are presented as differences in means and proportions, with 95% confidence intervals (CI). We calculated 30-day mortality proportions for the complete population with follow-up censored at January 30th 2006. One-year mortality proportions were calculated for patients admitted (n=4876) up to December 31st 2004, the most recent date at which complete 1-year follow-up data were available.

The association between year of index AMI and all-cause mortality was assessed using unconditional logistic regression analysis with covariate effects reported as odds ratios (OR) with 95% CI. An interaction term representing year of admission was included to explore the impact of temporal trends in the management of ACS [13, 14], As indications for, and proportions of patients receiving (70% - 77% annually) thrombolysis, were consistent throughout the study period, this variable was included in the model. In all cases a linear effect for year of admission (log odds scale) provided the best fitting model. Other continuous variables (age, glucose, creatinine and peak creatine kinase) showed non-linear relationships with outcome and for initial univariate analyses were categorised to ease interpretation. Glucose, creatinine and peak creatine kinase were grouped by quartile, and age was divided into <65, 65-74, and ≥75 years.

The blood glucose concentration used was that first recorded for the index admission, assayed as part of routine investigations. Glucose was divided by quartiles of the range observed over the study period: Quartile 1, <7mmol/L; Quartile 2, 7 - 8.2 mmol/L; Quartile 3, 8.3 - 10.9 mmol/L; Quartile 4, ≥11 mmol/L. We initially assessed the unadjusted, univariate association with mortality of antecedent diabetes and of glucose quartile. Differential effects over time were assessed by fitting interactions between these covariates and year of diagnosis. We then fitted models adjusted for age, sex, peak CK, creatinine, previous AMI, smoking status, year of index AMI and administration of thrombolysis. Fractional polynomials were used to model continuous variables to allow for potential non-linearity. To quantify the effects of antecedent diabetes and of glucose quartile, separate models were fitted including these individually, and in combination. Demographic features and outcomes were assessed for the subcohort of patients for whom admission glucose was not recorded. Analyses were performed using Stata 9 (StataCorp. 2005. Stata Statistical Software: Release 9, College Station, TX).

RESULTS

From January 1st 1993 – December 31st 2004, we recorded 4876 consecutive, index admissions with STEMI. Excluding from analysis 174 (3.6%) individuals not normally resident locally, the study population consisted of 4702 patients (3198, 68.0% male; mean age 66.7, SD 12.7, range 21-107 years). Female (72.2 ± 11.4 years) were older than male patients (64.1 ± 12.4, $p<0.001$). For 683 (14.0%) and 2 patients respectively, details of admission blood glucose concentration and antecedent diabetes status were not available.

Antecedent Diabetes

Antecedent diabetes was recorded for 749 (15.9%) patients, increasing from 13.9% in 1993 to 20.3% in 2005. Patients with antecedent diabetes were older by an average of 1.4 years and more often female (Table 1). Mean admission glucose and creatinine concentrations were higher, but peak CK lower, in these patients, who were less likely to receive thrombolysis or to be prescribed aspirin or beta-blocker during the index admission, but more likely to receive diuretic therapy, inhibitors of the renin-angiotensin system and insulin.

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Admission blood glucose

Table 2 shows characteristics of patients according to glucose quartile, and for the subcohort in whom admission blood glucose was not recorded. Even in quartiles 3 (10.3%) and 4 (42.7%) of blood glucose, a minority of patients had antecedent diabetes.

Patients with glucose in quartile 4 were on average 5.6 years older than those in quartile 1. Higher glucose quartile was associated with higher serum creatinine and lower admission systolic blood pressure. Thrombolysis was administered in fewer patients in quartile 4 compared to quartiles 1-3. In-hospital diuretic prescription increased, and beta-blocker prescription fell, as glucose quartile increased. There was little variation among quartiles in the use of inhibitors of the renin-angiotensin system.

In patients for whom admission blood glucose was not recorded, demographic and treatment features were broadly similar to those seen in the population as a whole. In terms of proportions with antecedent diabetes, treatment with insulin, and case-fatality, these patients most closely resembled those in quartile 3 (Table 2).

Survival

During follow up, case fatality was 42.2% (1992/4702). By 30 days 841 (17.9% of the population, 42.2% of all events), and by 1 year 1136 (24.2% of the population, 57.0% of events) deaths had occurred. The univariate strengths of association with mortality for important clinical and demographic variables are shown in Table 3.

Antecedent Diabetes and Survival

Overall 30-day mortality was 22.8% and 1-year mortality was 31.3% for patients with antecedent diabetes, compared to 16.3% and 23.0% respectively for those without. Antecedent diabetes was associated with a univariate, unadjusted increase in the odds of death of approximately 50%, at both 30-days (OR 1.52, 95% CI 1.24 , 1.86) and 1-year (OR 1.52, 95% CI 1.24 , 1.84)(Table 3).

Blood glucose and Survival

Figure 1 shows the fully adjusted odds of mortality by 30 days and admission blood glucose considered as a continuous variable.

Blood glucose above the median (8.3mmol/L) was associated with increased mortality (Table 3). For patients with glucose in quartile 4 (≥11 mmol/L), 30-day mortality (31%) was over 3-fold higher than in quartile 1 (9.0%). For 30-day mortality, compared to quartile 1, the OR for quartile 2 was 1.20 (95% CI 0.89 , 1.61), for quartile 3 was 2.20 (95% CI 1.67 , 2.91) and quartile 4 was 4.54 (95% CI 3.50 , 5.88).

Similar associations were evident for 1-year mortality. Compared to quartile 1, the OR for quartile 2 was 1.29 (95% CI 1.00 , 1.66), for quartile 3 was 2.05 (95% CI 1.61 , 2.62) and quartile 4 was 4.04 (95% CI 3.21 , 5.07).

Glucose concentration and antecedent diabetes – relative impact on prognosis

Using multivariable, unconditional logistic regression models, we assessed the association with prognosis of antecedent diabetes, glucose quartile, and year of index AMI (Table 4). Unadjusted analyses for diabetes and glucose quartile were followed by analysis adjusted for age, sex, previous MI, peak CK, creatinine, thrombolysis, smoking status and year of index AMI, considering diabetes or glucose separately in individual analyses. Finally, modelling was carried out adjusting for these covariables and including both diabetes and glucose.

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As noted above, unadjusted odds of mortality by 30 days and 1year was approximately 50% higher for patients with antecedent diabetes compared to patients without this diagnosis. Adjustment for covariates abolished the estimated early and late mortality risk associated with an antecedent diagnosis of diabetes and the addition of blood glucose concentration did not contribute further to the model build (Table 4).

Although attenuated by covariables adjustment, higher blood glucose concentrations retained association with mortality. Compared to quartile 1, adjusted risk was similar in quartile 2, and approximately 75% and 150% higher in quartile 3 and 4 respectively. The addition of antecedent diabetes did not materially alter the odds ratio associated with the degree of glycaemia (p=0.368), or the overall model fit (Table 4).

Discussion

Key findings

This is the first study to assess, in a large, unselected cohort of patients with ACS, the relative impact upon prognosis of pre-existing diabetes diagnosis and of admission glucose level. Our study presents two novel, clinically important findings. First, blood glucose concentration at admission to hospital with STEMI had more powerful association with prognosis than did antecedent diabetes. Even minor elevation of blood glucose concentration above the normal range was associated with adverse impact on outcome. Second, the adverse impact upon mortality of antecedent diabetes was markedly attenuated when adjusted for covariables, and was completely absent when correction included admission blood glucose. In contrast, the prior diagnosis of diabetes had no meaningful impact upon the risk associated with glucose concentration at the time of index admission.

Our data lend indirect support to the recent statement from the American Heart Association that optimum blood glucose levels after AMI have yet to be established and should be the focus of future clinical trials [15]. While we observed little variation in outcome for blood glucose below 8.2mmol/L, mortality risk was increased above this level. This may be considered in the context of the target, and achieved, concentrations in trials of intensive glycaemic control after AMI. These studies recruited patients with admission glucose >11mmol/L [16, 17], had target levels of 7-10.9 mmol/L [16] or 7-10 mmol/L [17], and achieved mean glucose levels of 9-10mmol/L [16, 17]. In a previous study, mortality was lowest in patients for whom blood glucose at 24 hours after AMI was below 7mmol/L [18]. Taken together, these observations suggest that in patients with STEMI both the threshold at which active intervention is applied and target blood glucose levels may be lower than previously considered.

The benefit of active lowering of blood glucose after AMI has been demonstrated in a number of studies [8, 9, 10, 19], and greater falls in blood glucose in the period following admission with AMI is associated with better survival [16, 18, 19]. In both DIGAMI studies, effective glucose lowering soon after AMI was associated with improved survival [16, 17], and recently, prescription of insulin in patients with AMI, not previously known to have diabetes, is associated with improved outcome [20]. It is noteworthy that the only controlled study of glucose lowering after AMI which achieved lower blood glucose compared to standard management was the first DIGAMI study [16]; this was also the only such study in which active intervention was associated with improved outcome.

It may be argued that some of our cohort, patients in quartile 4 for example, should be considered as having diabetes. However in many patients with hyperglycaemia at admission with AMI, the diagnosis of diabetes is not confirmed on formal testing at a later time [21]. Our study was designed as a pragmatic assessment of the impact on prognosis of admission

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blood glucose values. Moreover, if the degree of dysglycaemia impacts directly on prognosis, it is this, rather than later diagnosis of diabetes, to which the clinician should respond.
Our observation of associations between higher blood glucose and a number of markers of adverse prognosis, eg lower blood pressure, higher creatinine and greater age, may support the contention that hyperglycaemia is only a marker of adverse prognosis. However hyperglycaemia may be directly detrimental to the ischaemic myocardium through a variety of mechanisms, including free radical release and endothelial dysfunction [22], exaggerated reperfusion injury [23], the abolition of ischaemic preconditioning [24] and increased oxygen demand due to reliance on free fatty acid metabolism [25]. Further evidence for direct myocardial toxicity of hyperglycaemia during ischaemia comes from a recent report in a large cohort of patients undergoing CABG, in which suboptimal perioperative blood glucose control (≥ 11.1 mmol/L) showed graded association with increased risk of adverse outcome, irrespective of diabetes status [26]. Overall, these data are strongly suggestive of at least some direct toxic influence of elevated blood glucose in ischaemic myocardium.

Study limitations

Our database lacks information on some important variables, including objective assessment of left ventricular function and regarding clinical evidence of heart failure. Although information on blood glucose was missing in a proportion of patients, the distribution of demographics and outcomes were similar between those with and without a glucose measure, making it unlikely that the missing information would bias our results. In a proportion of our population, elevated blood glucose undoubtedly represents hitherto unrecognised diabetes, a limitation applying to the vast majority of studies classifying patients based upon antecedent diagnosis. The blood glucose concentrations considered were measured on admission and thus represent non-fasting measurements made at varying times of the day and from the onset of the index event. However, this measurement is the one available to physicians soon after admission and is the only measurement upon which early therapeutic decisions may be based. We did not adjust for prescription of individual secondary prevention therapies, the impact of which was not the focus of this analysis. Consideration of individual treatment effects may introduce bias for a number of reasons. In the most severely ill patients, early mortality and adverse clinical features in survivors will limit treatment prescription. Our study is limited by assessment of survival up to 1-year, and consideration of the influence of dysglycaemia and diabetes on longer term prognosis would be appropriate. We have no information on therapy or interventions after discharge. However, as the risk of death was greatest in the first 30 days, it is unlikely that changes after discharge impacted on overall outcome in a major way. Finally, our findings are based upon a historical cohort, admitted over a prolonged period during which the management of ACS evolved considerably. While we have corrected for such changes by inclusion of year of AMI in multivariable analysis, this may not have adjusted fully for such changes.

In summary, admission blood glucose concentration is a powerful, readily available marker of adverse outcome after ST elevation AMI, and is prognostically more informative than consideration of antecedent diabetes status. Minor elevation of blood glucose outwith the normal range is associated with adverse impact upon survival. Admission blood glucose concentration should be considered in the early assessment of prognosis after AMI. Further studies of intensive blood glucose management after AMI are merited.

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Conflicts of Interest: None

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	Antecedent Diabetes		
	Yes N=749 (15.9%)	**No N=3951 (84.1%)**	**Difference** (Diabetes – No Diabetes)
Male (%)	460 (61.4)	2737 (69.3)	-7.9 (-11.6 , -4.1)*
Age (years)	67.9 ± 0.4	66.5 ± 0.2	1.4 (0.5 , 2.3)†
Plasma glucose (mmol/L)[1]	14.7 ± 0.3	8.9 ± 0.1	5.7 (5.2 , 6.3)†
Creatinine (µmol/L)[2]	120.7 ±2.3	109.2 ±0.7	11.5 (6.8 , 16.3)†
Peak CK (IU/L)[3] ; Normal range < 200	1818 ± 62	2115 ± 31	-296 (-433 , -159)†
History of			
Smoking			
Current (%)	156 (20.8)	1312 (33.2)	-12.4 (-15.7 , -9.1)*
Former (%)	183 (24.4)	992 (25.1)	-0.7 (-4.0 , 2.7)*
Never (%)	410 (54.7)	1645 (41.6)	13.1 (9.2 , 17.0)*
Not known (%)	0	2	
Previous AMI (%)	175 (23.4)	571 (14.5)	8.9 (5.7 , 12.1)*
Angina (%)	230 (30.7)	862 (21.8)	8.9 (5.3 , 12.4)*
Hypertension (%)	368 (49.1)	1296 (32.8)	16.3 (12.5 , 20.2)*
Hyperlipidaemia (%)	151 (20.2)	451 (11.4)	8.7 (5.7 , 11.8)*
Cerebrovascular disease (%)	83 (11.1)	191 (4.8)	6.2 (3.9 , 8.6)*
Treatment			
Thrombolysis (%)	468 (62.5)	2883 (73.0)	-10.5 (-14.2 , -6.8)*
Diuretic (%)	457 (61.0)	1743 (44.1)	16.9 (13.1 , 20.7)*
Aspirin (%)	528 (70.5)	3099 (78.4)	-7.9 (-11.5 , -4.4)*
Beta Blocker (%)	282 (37.7)	1798 (45.5)	-7.9 (-11.7 , -4.1)*
Insulin (%)	510 (68.1)	280 (7.1)	61.0 (57.6 , 64.4)*
ACE Inhibitor / ARB (%)	385 (51.4)	1580 (40.0)	11.4 (7.5 , 15.3)*
Statin (%)	196 (26.2)	1054 (26.7)	-0.5 (-3.9 , 2.9)*

Table 1: Demographic and in-hospital treatment characteristics of patients with and without antecedent diagnosis of diabetes. Table shows mean ± standard error or number (%). CK = Creatine Kinase; ACE = Angiotensin converting Enzyme; ARB = Angiotensin Receptor Blocker.

[1] 101 missing values for diabetes and 581 missing values for no diabetes;

[2] 9 missing values for diabetes and 39 missing values for no diabetes;

[3] 9 missing values for diabetes and 39 missing values for no diabetes

* Calculated difference in proportions (with 95% confidence intervals)

† Calculated difference in means (with 95% confidence intervals)

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		GQ1 <7		GQ2 7-8.3		GQ3 8.3-11		GQ4 ≥11		Missing Glucose		Overall	
		n	%	n	%	n	%	n	%	n	%	n	%
Sex	Male	713	76.7	776	72.1	609	63.9	643	60.7	457	66.9	3,198	68.0
	Female	217	23.3	300	27.9	344	36.1	417	39.3	226	33.1	1,504	32.0
Diabetes	No	882	94.8	1,027	95.4	855	89.7	606	57.2	581	85.1	3,951	84.0
	Yes	48	5.2	49	4.6	98	10.3	453	42.7	101	14.8	749	15.9
	Missing	0	0	0	0	0	0	1	0.1	1	0.1	2	0.04
Statin	No	567	61.0	803	74.6	714	74.9	859	81.0	508	74.4	3,451	73.4
	Yes	363	39.0	273	25.4	239	25.1	201	19.0	175	25.6	1,251	26.6
ACE or ARB	No	499	53.7	655	60.9	547	57.4	608	57.4	427	62.5	2,736	58.2
	Yes	431	46.3	421	39.1	406	42.6	452	42.6	256	37.5	1,966	41.8
Diuretic	No	596	64.1	645	59.9	483	50.7	418	39.4	360	52.7	2,502	53.2
	Yes	334	35.9	431	40.1	470	49.3	642	60.6	323	47.3	2,200	46.8
Beta Blocker	No	373	40.1	578	53.7	534	56.0	733	69.2	403	59.0	2,621	55.7
	Yes	557	59.9	498	46.3	419	44.0	327	30.8	280	41.0	2,081	44.3
Thrombolysis	No	272	29.2	248	23.0	193	20.2	408	38.5	229	33.5	1,350	28.7
	Yes	658	70.8	828	77.0	760	79.8	652	61.5	454	66.5	3,352	71.3
Insulin	No	895	96.2	1046	97.2	877	92.0	493	46.5	600	87.9	3911	83.2
	Yes	35	3.8	30	2.8	76	8.0	567	53.5	83	12.2	791	16.8
	n	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Overall Mean(SD)**	
Age	4,702	63.8	13.27	65.3	12.88	67.6	12.10	69.4	11.54	67.4	13.06	66.7(12.69)	
SBP	4,627	141.8	28.06	139.8	28.49	137.6	31.71	135.4	36.48	137.2	31.02	138.4(31.44)	
Creatinine (µmol/L)	4,654	103.3	47.33	102.6	35.78	109.1	38.73	126.3	56.83	113.8	5.64	111.0(48.19)	

Table 2: Demographic and in-hospital treatment characteristics of patients according to glucose quartile. ACE = Angiotensin converting Enzyme; ARB = Angiotensin Receptor Blocker; SBP = Systolic Blood Pressure. † 1-year survival was assessed on patients admitted up to 31st December 2004, being the last date for which 1-year follow-up was available. Therefore the total number of patients included in the one-year analysis (n=4474) is fewer than in the 30-day analysis (n=4702).

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Variable		30 Day Mortality		1 Year Mortality	
		No. Deaths/ No. at risk (%)	Odds Ratio (95% CI)	No. Deaths/ No. at risk (%)	Odds Ratio (95% CI)
Antecedent Diabetes	No	550/3370 (16.3)	1	743/3225 (23.0)	1
	Yes	148/648 (22.8)	1.52(1.24 , 1.86)	192/614 (31.3)	1.52 (1.24 , 1.84)
Sex	Female	316/1278 (24.7)	1	403/1224 (32.9)	1
	Male	382/2740 (13.9)	0.49 (0.42 , 0.58)	532/2615 (20.3)	0.52 (0.45 , 0.61)
Thrombolysis	No	307/1120 (27.4)	1	405/1065 (38.0)	1
	Yes	391/2898 (13.5)	0.41 (0.35 , 0.49)	530/2774 (19.1)	0.38 (0.33 , 0.45)
Previous MI	No	541/3388 (16.0)	1	704/3231 (21.7)	1
	Yes	157/630 (24.9)	1.75 (1.43 , 2.14)	231/608 (38.0)	2.20 (1.83 , 2.64)
Age (years)					
	<65	117/1669 (7.0)	1	150/1574 (9.5)	1
	65-74	187/1153 (16.2)	2.57 (2.01 , 3.02)	256/1111 (23.0)	2.84 (2.28 , 3.54)
	≥75	394/1196 (32.9)	6.52 (5.21 , 8.15)	529/1154 (45.8)	8.04 (6.55 , 9.86)
Glucose (mmol/L, quartile)					
	<7.3	84/930 (9.0)	1	122/871 (14.0)	1
	7.3-8.2	114/1076 (10.6)	1.20 (0.89 , 1.61)	180/1037 (17.4)	1.29 (1.00 , 1.66)
	8.3-10.9	171/953 (17.9)	2.20 (1.67 , 2.91)	228/910 (25.1)	2.05 (1.61 , 2.62)
	≥11	329/1059 (31.1)	4.54 (3.50 , 5.88)	405/1021 (39.7)	4.04 (3.21 , 5.07)
Creatinine (μmol/L, quartile)					
	<87	80/972 (8.2)	1	114/927 (12.3)	1
	87-100.9	97/1032 (9.4)	1.16 (0.85 , 1.58)	135/971 (13.9)	1.15 (0.88 , 1.50)
	101-120.9	139/1000 (13.9)	1.80 (1.35 , 2.41)	203/961 (21.1)	1.91 (1.49 , 2.45)
	≥121	381/1009 (37.8)	6.76 (5.21 , 8.79)	483/976 (49.5)	6.99 (5.54 , 8.82)
Peak CK (IU/L, quartile)					
	<752	253/997 (25.4)	1	299/927 (32.3)	1
	752-1567	131/989 (13.3)	0.45 (0.36 , 0.57)	196/940 (20.9)	0.55 (0.45 , 0.68)
	1568-2808	140/1000 (14.0)	0.48 (0.38 , 0.60)	202/971 (20.8)	0.55 (0.45 , 0.68)
	≥2809	168/1019 (16.5)	0.58 (0.47 , 0.72)	232/990 (23.4)	0.64 (0.53 , 0.79)
Year	Annual		0.94 (0.92 , 0.96)		0.95 (0.93 , 0.97)

Table 3. Univariate association with 30-day and all-cause mortality

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Parameter		Unadjusted (n=4018)	Adjusted[1] (Excluding Diabetes) (n=4001)	Adjusted[2] (Excluding Glucose) (n=4001)	Adjusted[3] (n=4001)
30 DAY					
Glucose	Q1	1	1	-	1
	Q2	1.19 (0.89 , 1.61)	1.07 (0.77 , 1.49)	-	1.07 (0.77, 1.49)
	Q3	2.20 (1.67 , 2.91)	1.70 (1.20 , 2.37)	-	1.73 (1.27 , 2.36)
	Q4	4.54 (3.50 , 5.88)	2.458 (1.80 , 3.32)	-	2.58 (1.90 , 3.52)
Diabetes	No	1	-	1	1
	Yes	1.52 (1.24 , 1.87)	-	1.24 (0.98 , 1.58)	0.87 (0.67 , 1.13)
Year		0.937 (0.92 , 0.96)	0.936 (0.90 , 0.92)	0.93 (0.90 , 0.95)	0.94 (0.91 , 0.96)
AIC			0. 716135	0.7286741	0.7163706
Parameter		Unadjusted (n=3839)	Adjusted (n=3825)	Adjusted (n=3825)	Adjusted[1] (n=3825)
ONE YEAR					
Glucose	Q1	1	1	-	1
	Q2	1.29 (1.00 , 1.66)	1.24 (0.93 , 1.65)	-	1.24 (0.93 , 1.65)
	Q3	2.05 (1.61 , 2.62)	1.64 (1.24 , 2.17)	-	1.64 (1.24 , 2.17)
	Q4	4.04 (3.21 , 5.07)	2.28 (1.74 , 2.99)	-	2.34 (1.76 , 3.11)
Diabetes	No	1	-	1	1
	Yes	1.52 (1.26 , 1.84)	-	1.24 (0.99 , 1.57)	0.93 (0.73 , 1.20)
Year		0.93 (0.93 , 0.97)	0.95 (0.93 , 0.98)	0.94 (0.92 , 0.97)	0.95 (0.93 , 0.98)
AIC			0.841869	0.8519422	0.8423143

Table 4:
Results of modelling proportions surviving to 30 days and one year.
Adjusted models are adjusted for age at MI, sex, previous AMI, CK, creatinine, thrombolysis, smoking status and year of hospitalisation : [1] for blood glucose concentration (quartile); [2] antecedent diabetes and [3] for both blood glucose concentration (quartile) and antecedent diabetes.
Year = Odds ratio per year 1993-2005 (30-day) or 1993-2004 (1-year)
AIC = Akaike's information criterion (lower values indicate a better fitting model).

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Legend Figure 1

Adjusted odds of 30-day mortality according to admission blood glucose concentration

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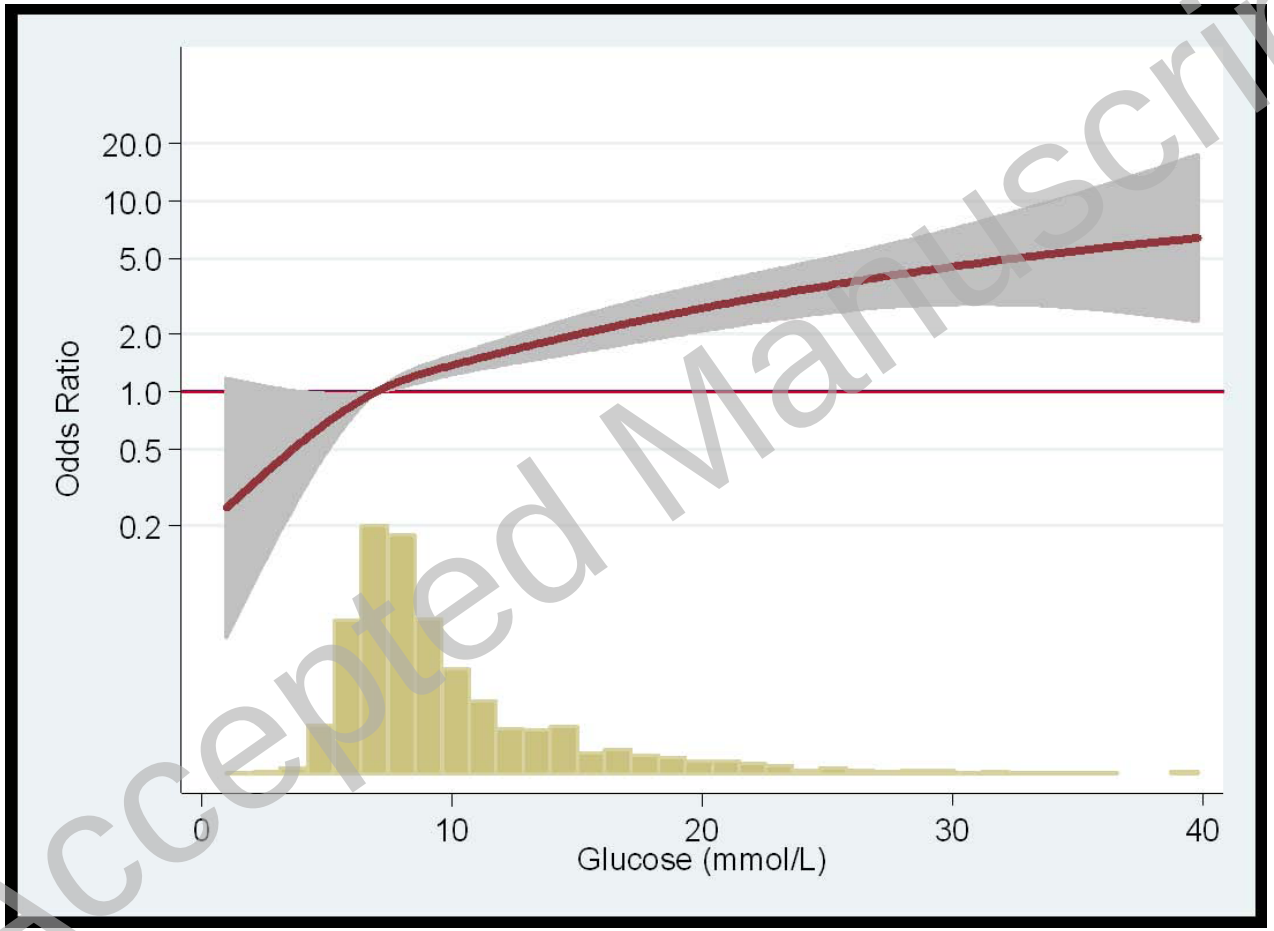

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