The impact of obesity on mortality in UA/non-ST-segment elevation myocardial infarction

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Aims Obesity is associated with diabetes mellitus and advanced coronary artery disease (CAD). Once a non-ST-elevation acute coronary syndrome has occurred, the association between obesity and prognosis is poorly defined. This study was designed to assess the impact of obesity on outcome after unstable angina/non-ST-segment elevation myocardial infarction (UA/NSTEMI) treated with early revascularization.

Methods and results In a prospective cohort study in 1676 consecutive patients with UA/NSTEMI we examined the association between presence of obesity and all-cause mortality. All patients underwent coronary angiography and, if appropriate, early catheter-based revascularization. Patients were divided into four groups according to body mass index (BMI): normal, 18.5–24.9 (n = 551); overweight, 25–29.9 (n = 824); obese, 30–34.9 (n = 244); and very obese, above 35 (n = 48). Obese and very obese patients were younger and had a higher incidence of hypertension, diabetes mellitus, elevated cardiac troponin T, and C-reactive protein levels. The angiographic extent of CAD was similar among the BMI groups. Median follow-up was 17 (interquartile range 6–31) months. Cumulative 3-year mortality rates were 9.9% for normal BMI, 7.7% for overweight, 3.6% for obese, and 0 (no death) for very obese (log-rank P = 0.043). Obese and very obese patients had less than half the long-term mortality when compared with normal BMI patients [hazard ratio (HR) 0.38, 95% confidence interval (CI) 0.18–0.81, P = 0.012]. This result remained significant after adjustment for confounding prognostic factors including coronary status and left ventricular function (adjusted HR 0.27, 95% CI 0.08–0.92, P = 0.036).

Conclusion Obesity is associated with improved outcome after UA/NSTEMI treated with early revascularization.

KEYWORDS Unstable angina; Myocardial infarction; Obesity; Revascularization

Introduction

The epidemic of obesity has attained increasing recognition. One in five Europeans and more than half of US adults are overweight or obese.1 Annual health-care costs attributable to obesity have been estimated to be approximately $68 billion, with an additional $30 billion being spent on weight-reduction programmes and special diets.1 Obesity is associated with higher levels of insulin resistance, as well as hyperinsulinaemia, increases in triglyceride and cholesterol levels, and increases in sympathetic nervous system activity. Moreover, obesity is an important risk factor for the development of diabetes mellitus, hypertension, coronary artery disease, ventricular dysfunction, congestive heart failure, stroke, and cardiac arrhythmias.2–5

In patients with established coronary atherosclerosis, the body mass index (BMI) was associated with unstable angina and myocardial infarction (MI).6 In addition, long-term studies had shown that obesity is associated with excess mortality in the general population.7–10

Approximately 2–2.5 million patients Worldwide are hospitalized for unstable angina/non-ST-segment elevation myocardial infarction (UA/NSTEMI) each year.11–13 Within the last 3 years, early coronary angiography and revascularization has been established as the most appropriate management strategy in these patients.11–13 The impact of obesity on outcomes in UA/NSTEMI receiving contemporary treatment with an early invasive strategy remains unknown.

The purpose of this study was to evaluate the impact of obesity on long-term outcomes following UA/NSTEMI in a large cohort of consecutive unselected patients treated with an early invasive strategy.

Methods

Study population

Consecutive patients admitted to our centre with UA/NSTEMI from January 1996 to December 1999 were included in this analysis. The study protocol required typical chest pain at rest and early...
coronary intervention or coronary artery bypass grafting and on least three times the upper limit of normal. All patients underwent over the previous trough level in at least two samples reaching at the upper limit of normal after coronary artery bypass grafting) or CK-MB beyond two times the upper limit of normal and five times death and non-fatal MI. MI was defined as typical chest pain at secondary endpoints, we assessed non-fatal MI and the composite of The primary endpoint was defined as death from all causes. As secondary endpoints, we assessed non-fatal MI and the composite of death and non-fatal MI. MI was defined as typical chest pain after angiography. We excluded patients with de novo angina pectoris on exertion or worsening angina during exertion only, patients with persistent ST-elevation, patients in whom angiography was not performed due to patient refusal (n = 6) or extremely severe concomitant disease (n = 9) with severe dementia or advanced malignancy, and patients with no information regarding body weight or height (n = 24). The study was carried out according to the principles of the Declaration of Helsinki and approved by the Institutional Review Board. Informed consent was obtained from all participating patients. Arterial hypertension was defined as a known history of hypertension or treatment with blood pressure lowering drugs. Hypercholesterolaemia was defined as a known history of hypercholesterolaemia, admission LDL cholesterol levels above 130 mg/dL, or treatment with cholesterol-lowering drugs. Diabetes was defined as a known history of diabetes mellitus treated currently with either diet, oral glucose-lowering agents, or insulin. At hospital discharge, all patients were counselled to use a low-cholesterol diet and statins if necessary to achieve an LDL cholesterol below 100 mg/dL during follow-up.

Body mass index
BMI was calculated as weight in kilograms divided by the square of height in metres. Of the commonly used measures of obesity, BMI is the body size measurement that correlates best with body fat content. As recommended by the World Health Organization, a BMI below 18.5 was classified as underweight, between 18.5 and 24.9 as normal, between 25 and 29.9 as overweight, between 30 and 34.9 as obese, and ≥ 35 as very obese.

Patient management
Patients with persistent chest pain underwent immediate coronary angiography. In patients asymptomatic while on medical therapy, coronary angiography was performed within 24 h of admission. Whenever possible, coronary stenting of the culprit lesion was performed immediately after angiography. Stenting was not restricted to patients with one- and two-vessel disease, but also favoured in patients with three-vessel disease with suitable lesions. If revascularization was indicated, but percutaneous coronary intervention was not considered the optimal treatment option (unprotected left main disease, diffuse three-vessel disease), patients were scheduled for early coronary artery bypass grafting.

Follow-up
All patients were scheduled for outpatient visits at 6 months. In addition, patients were contacted by questionnaire on a regular basis. For patients reporting cardiac symptoms, at least one clinical and electrocardiographic examination was performed at the outpatient clinic or by the referring physician. All information derived from contingent hospital re-admission records or provided by the referring physician or by the outpatient clinic was reviewed and entered into the computer database.

Endpoints and statistical analysis
The primary endpoint was defined as death from all causes. As secondary endpoints, we assessed non-fatal MI and the composite of death and non-fatal MI. MI was defined as typical chest pain at rest followed by an increase in creatine phosphokinase (CK and CK-MB beyond two times the upper limit of normal and five times the upper limit of normal after coronary artery bypass grafting) or new Q-waves in the electrocardiogram. To meet this endpoint criterion, patients who had initially presented with MI had to have new ST-segment changes and an increase in CK of at least 50% over the previous trough level in at least two samples reaching at least three times the upper limit of normal. All patients underwent electrocardiographic recordings immediately after percutaneous coronary intervention or coronary artery bypass grafting and on the following morning. In addition, cardiac markers (CK and CK-MB) were determined at 8-24 h after the intervention, and additionally whenever ischaemic symptoms developed. The statistical analyses were performed using the SPSS/PC (version 12.0, SPSS Inc., Chicago, IL, USA) software package. A statistical significance level of 0.05 was used. Comparisons were made using analysis of variance for independent samples and χ² tests as appropriate. All hypothesis testing was two-tailed. Cox proportional-hazards regression analysis was used as the appropriate method throughout. Multivariable Cox regression analysis was performed to identify independent predictors of death. Together with BMI, all baseline, demographic, clinical, laboratory, and angiographic variables were entered in a univariable Cox regression analysis. All variables associated with long-term mortality in univariable analysis (P < 0.05) were entered into the multivariable model. The linearity assumption was assessed by additionally including the square of the respective covariate in the regression model. For each of the predictor variables, we tested the proportional hazard assumption by including its interaction with time of follow-up into the regression model. As measure of overall kidney function, the glomerular filtration rate was entered. We calculated the glomerular filtration rate with the use of the abbreviated Modification of Diet in Renal Disease study equation: Glomerular filtration rate (in mL/min/1.73 m² of body surface area) = 186 × (serum creatinine in mg/dL)⁻¹.⁵⁵ × (age in years)⁻².⁰³ × 0.₇₄₂ in female subjects × 1.₂₁₀ in black subjects. Additionally, the range of hazard ratios obtained for obesity from all possible models with two predictors, including those that were not significant in a univariable setting, was calculated. The cumulative survival curves were constructed with the use of the Kaplan–Meier method.

Results
Baseline characteristics
A total of 1676 unselected consecutive patients with symptoms of myocardial ischaemia at rest without persistent ST-segment elevation were enrolled in the study. The median BMI was 26.4 (inter-quartile range 24.3–28.8). Table 1 describes the baseline, demographic, clinical, angiographic, and procedural characteristics of the cohort divided into groups according to their BMI. One-third of the patients had a normal BMI (n = 551), half of the patients were overweight (n = 824), and 18% were obese or very obese (n = 292). Obese and very obese patients were younger, had less often a prior MI, had a higher incidence of hypertension and diabetes mellitus, and more often elevated levels of troponin T and C-reactive protein. The angiographic extent of coronary artery disease and left ventricular function was similar among the groups. Discharge medication was different among BMI groups with a higher use of statins, ACE-inhibitors, and beta-blockers in obese and very obese patients.

Only nine patients (0.5% of the study cohort) were underweight with a BMI below 18.5. Because of the small number of patients and limited statistical power in this group, all analyses were restricted to normal, overweight, obese, and very obese patients.

Revascularization
About 70% of patients underwent revascularization. Percutaneous coronary intervention was the predominant revascularization strategy and was performed very early at a median of 5.3 h from admission. Percutaneous coronary intervention was not restricted to patients with one- or
Table 1  Baseline patient, angiographic, and procedural characteristics according to body mass index on admission

|                          | Underweight (BMI < 18.5) | Normal (BMI 18.5–24.9) | Overweight (BMI 25–29.9) | Obese (BMI 30–34.9) | Very obese (BMI ≥ 35) | All obese (BMI ≥ 30) | P-value*
|--------------------------|--------------------------|------------------------|--------------------------|----------------------|-----------------------|----------------------|----------------------
| Age (years)              | 66.1 ± 12                | 65.9 ± 11              | 64.7 ± 10                | 63.6 ± 10            | 58.4 ± 11             | 62.7 ± 11            | <0.001               |
| Female sex (%)           | 5 (56)                   | 182 (33)               | 203 (25)                 | 73 (30)              | 17 (35)               | 90 (31)              | 0.002                |
| Body mass index          | 17.7 ± 0.6               | 23.1 ± 1.4             | 27.2 ± 1.4               | 31.8 ± 1.3           | 37.0 ± 2.0            | 32.7 ± 2.4           | <0.001               |
| Prior myocardial infarction (%) | 0                      | 203 (37)               | 315 (38)                 | 76 (31)              | 6 (13)                | 82 (28)              | 0.007                |
| Prior coronary bypass grafting (%) | 0                      | 72 (13)                | 107 (13)                 | 27 (11)              | 2 (4)                 | 29 (10)              | 0.349                |
| Prior coronary angioplasty (%) | 0                      | 104 (19)               | 179 (22)                 | 42 (17)              | 7 (15)                | 49 (17)              | 0.145                |
| T-wave inversion (%)     | 4 (44)                   | 171 (31)               | 235 (29)                 | 65 (27)              | 15 (31)               | 80 (27)              | 0.463                |
| Cardiogenic shock (%)    | 0                        | 4 (0.7)                | 109 (13)                 | 41 (17)              | 13 (27)               | 54 (19)              | 0.187                |
| Female sex (%)           | 5 (56)                   | 309 (56)               | 475 (58)                 | 145 (58)             | 19 (40)               | 160 (55)             | 0.007                |
| Current cardiac disease (%) | 0                      | 75 (14)                | 109 (13)                 | 41 (17)              | 13 (27)               | 54 (19)              | 0.187                |
| Angina at rest >48 h     | 8 (89)                   | 317 (58)               | 487 (59)                 | 141 (58)             | 19 (40)               | 160 (55)             | 0.007                |
| Non-Q myocardial infarction (%) | 0                      | 62 (11)                | 99 (12)                  | 33 (14)              | 8 (17)                | 41 (14)              | 0.155                |
| Angina at rest >48 h to 8 weeks post-myocardial infarction (%) | 11 (11)          | 97 (18)                | 126 (19)                 | 29 (12)              | 8 (17)                | 37 (13)              | 0.007                |
| Angina at rest >48 h     | 0                        | 4 (0.7)                | 9 (1.1)                  | 0                    | 0                    | 0                    | 0.187                |
| ST-depression >0.1 mV (%) | 0                        | 57 (10)                | 81 (10)                  | 22 (9)               | 2 (4)                 | 24 (8)               | 0.605                |
| Aspirin (%)              | 8 (89)                   | 463 (87)               | 702 (88)                 | 207 (88)             | 39 (83)               | 246 (87)             | 0.024                |
| Oral anticoagulation (%) | 0                        | 23 (4)                 | 38 (5)                   | 16 (7)               | 3 (6)                 | 19 (7)               | 0.001                |
| Oral hypoglycaemic agents (%) | 0                      | 39 (7)                 | 64 (8)                   | 21 (9)               | 3 (6)                 | 24 (9)               | 0.820                |
| Insulin (%)              | 0                        | 23 (4)                 | 41 (5)                   | 19 (8)               | 0                    | 19 (7)               | 0.349                |

*Comparison between BMI groups normal, overweight, and all obese.

BMI, body mass index; ACE, angiotensin-converting enzyme.
two-vessel disease but was also performed in patients with three-vessel disease and suitable lesions. Coronary stents were implanted in about 80% of the PCI patients. Percuta-
neous coronary intervention was performed almost four
times more often than coronary artery bypass grafting.
Patients received 3.2 ± 0.9 distal bypass graft anastomoses
including left internal mammary artery grafts in 89%
Pro-
portions of invasive treatment with percutaneous coronary
intervention or coronary artery bypass grafting were
similar among the BMI groups (Table 1).

Outcome
Ninety-one deaths and 74 non-fatal MI occurred during a
median follow-up of 17 (inter-quartile range 6–31) months.
Ninety-two per cent of deaths were from cardiovascular
causes. In-hospital rates for mortality and non-fatal MI
were low and similar in all groups (Table 2). In-hospital
stroke occurred in one (0.1%) patient with overweight BMI
and in two (0.7%) patients with obese BMI.

During total follow-up, all-cause and cardiovascular mor-
tality was significantly lower among obese and very obese patients. Obese and very obese patients had less than half the
long-term mortality when compared with normal BMI
patients (for all-cause mortality HR 0.38, 95% CI
0.18–0.81, P = 0.012; for cardiovascular mortality HR
0.37, 95% CI 0.16–0.82, P = 0.014). There was also a signif-
cicant reduction in the combined endpoint of all-cause death
or non-fatal MI during total follow-up for obese and very
obese compared with normal BMI patients (HR 0.51, 95% CI
0.29–0.89, P = 0.017). The number of events per person-
year of follow-up was 0.046 in normal, 0.030 in overweight,
and 0.018 in obese or very obese patients for all-cause mor-
tality, and 0.067, 0.061, and 0.035 for the combined end-
point of death or MI, respectively.

The Kaplan–Meier survival analysis showed cumulative all-
cause mortality rates at 3 years of 9.9% for patients with
normal BMI, 7.7% for overweight, 3.6% for obese, and
0 (no death) for very obese patients (log-rank P = 0.043)
(Figure 1). The corresponding mortality rates at 1 year were
6.5, 4.1, 2.5 and 0%, and the mortality rates at 2
years were 8.7, 5.5, 3.6, and 0%. When examined as a con-
tinuous variable, BMI was significantly associated with
mortality (hazard ratio 0.91, 95% CI 0.85–0.97, P = 0.003
for each unit increase in BMI).

Subgroup analysis
Figure 2 shows the reductions in all-cause mortality for
obese patients during total follow-up among subgroups. Sur-

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Survival benefit for obese patients compared with normal BMI
patients was realized for all subgroups irrespective of
gender, age, prior MI, diabetes mellitus, hypertension, the
extent of coronary artery disease, the elevation of
markers of myocardial necrosis or inflammation, or treat-
ment modalities.

Multivariable analysis
Baseline variables associated with mortality in univariable
analysis were: age, ST-segment depression, previous MI,
elevated cardiac troponin T, elevated white blood count,
platelet count, kidney function, left ventricular function,
angiographic extent of coronary artery disease, C-reactive
protein, and obesity. In a multivariable Cox regression analy-
sis that adjusted for all these variables, obesity (BMI ≥ 30)
remained a significant independent predictor of all-cause
mortality during long-term follow-up (adjusted HR 0.27,
95% CI 0.08–0.92, P = 0.036) (Table 3). For none of the
predictor variables in question, there was evidence for a viola-
tion of the proportional hazard assumption. All interaction
terms between the predictor variables and time of follow-up
had P-values above 0.1. The range of hazard ratios obtained
for obesity from all possible models with two predictors,
including those that were not significant in a univariable
setting, was 0.166–0.512.

Discussion
This large prospective study in consecutive unselected
patients with UA/NSTEMI receiving contemporary treatment
with early revascularization evaluated the impact of obesity
on long-term mortality. Our major finding was that obese
and very obese patients had less than half the mortality
when compared with normal BMI patients. The reduction
in mortality rates was consistent among all subgroups and
persisted after multivariable adjustment. This contrasts
with primary prevention studies that implicate BMI as a
strong risk factor for mortality.

The findings of this study complement and extend our
knowledge regarding the impact of obesity on cardiovascular
disease by suggesting that the prognostic impact of obesity
is confounded by a cardiovascular event.1–10 Obesity is a
risk factor for the development of diabetes mellitus and cor-

With coronary artery disease is present, obesity is associated with unstable angina and cor-

However, once unstable angina/non-ST-segment
elevation MI develops and is treated with an early revascu-
larization strategy as in our study, obesity is associated
with a significant reduction in long-term mortality. The
hypothosis that the history of a coronary event may
change the association between obesity and mortality is sup-
ported by several recent studies.17–21 In the GUSTO IV-ACS
trial examining the glycoprotein IIb/IIIa inhibitor abciximab
in patients with UA/NSTEMI not scheduled for coronary
intervention, higher body weight was even associated with
reduced 1-year mortality.20 Patients with body weight
<75 kg had a 1-year mortality of 9.6% compared with 7.4%
in patients with body weight 75–90 kg and 6.6% in patients
with body weight >90 kg (P < 0.001).20 Moreover, similar
results were reported in a combined analysis of the
SYMPHONY and 2nd SYMPHONY trials.21 These trials eval-
uated the oral platelet glycoprotein IIb/IIIa inhibitor sibrafi-
ban, which was never approved for clinical use. Eisenstein
et al. found that overweight and obese BMI classifications
were associated with better intermediate-term survival. Our
findings extend this observation to patients treated with
the most contemporary management strategy and
importantly documents that the association between
obesity and mortality persists after multivariable adjust-
ment including left ventricular function, angiographic
extent of coronary artery disease, and C-reactive protein
levels.

This finding of a better prognosis of obese patients with
UA/NSTEMI receiving contemporary treatment is supported
by predominately favourable short-term data from large
angioplasty registries and the BARI trial.22–25 Moreover, a

Impact of obesity on mortality in UA/NSTEMI

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recent study including 9633 patients with predominately stable coronary artery disease undergoing percutaneous coronary intervention showed that obese patients had a lower risk of in-hospital and 1-year mortality when compared with patients with a normal BMI. However, in-hospital mortality seemed to be increased in patients with severe obesity. Although only a moderate number of patients with severe obesity were included in this study, our data do not support this finding of a worse outcome in very obese patients. In contrast, the very obese patients showed the lowest mortality of all BMI groups examined, suggesting a linear association between BMI and mortality in patients with UA/NSTEMI receiving contemporary treatment.

It is important to note that mortality in our study was lower than reported for a comparable cohort of patients with UA/NSTEMI treated with medical therapy and similar to studies applying contemporary early revascularization strategy.

The improved long-term outcome of obese patients observed in our study cannot be explained by an excess mortality in underweight patients, as they were excluded from our analysis. Underweight patients have consistently been shown to have increased in-hospital mortality, both after percutaneous coronary intervention and coronary artery bypass grafting.

Given the observational nature of our cohort, we were limited to describe the association between obesity and improved outcome in UA/NSTEMI. Thus, further research is necessary to elucidate the underlying pathophysiological mechanisms responsible for the more favourable outcome in obese patients. Possible mechanisms may include the following.

Because obese patients have more detectable and potentially modifiable risk factors for cardiovascular disease, medical treatment of the underlying clinical conditions including hypercholesterolaemia, diabetes, and hypertension, eventually combined with increased exercise, change in diet, and intentional weight loss, might have a stronger impact on prognosis in obese when compared with non-obese patients. Corresponding to their higher incidence of arterial hypertension and hypercholesterolaemia, obese patients in our study were treated more often with statins, ACE-inhibitors, and beta-blockers when compared with normal weight patients. As these agents have been shown to reduce mortality in patients with CAD, medical treatment differences might account for some of the difference in long-term prognosis. In addition, even a modest intentional weight loss can improve or prevent obesity-related cardiovascular risk factors like diabetes mellitus and arterial hypertension. Exercise, even in the absence of weight loss, decreases insulin resistance in obese individuals.

Other potential mediators of the improved outcome of obese patients with UA/NSTEMI include the endogenous cannabinoids, lower platelet count, excess triglyceride content in heart tissue including areas of healed MI, and lower age.
Endogenous cannabinoids, which are upregulated in obese patients, might have important protective cardiovascular effects.\textsuperscript{30–34} Besides their central nervous effects, endogenous cannabinoids are also present in other cell types like endothelial cells, activated macrophages, and platelets.\textsuperscript{30,31} They are potent vasodilators in the coronary and cerebrovascular beds.\textsuperscript{32} Endocannabinoid receptor agonists exert a cardioprotective effect in ischaemia–reperfusion models with a delay in the formation of necrotic zones and an improved cardiac resistance to arrhythmias that is mediated mainly through CB\textsubscript{(2)} cannabinoid receptors.\textsuperscript{33} In addition, low-dose oral cannabinoid therapy reduced the progression of atherosclerosis in an animal model.\textsuperscript{34}

Platelets seem to play a major role in the pathophysiology of acute coronary syndromes, as well as the outcome after percutaneous coronary intervention with stent implantation.\textsuperscript{11–13,35} Interestingly, our data indicate that obese patients with UA/NSTEMI have a significantly lower platelet count when compared with normal weight patients. In addition to the lower platelet count, platelet magnesium depletion\textsuperscript{36} may contribute to reduced platelet function in obese patients with UA/NSTEMI. Obesity alters the levels of procoagulant and anticoagulant plasma proteins. The net effect of obesity on haemostasis in UA/NSTEMI remains unknown.\textsuperscript{37,38}

Sudden cardiac death due to malignant ventricular arrhythmias is responsible for the majority of deaths in patients with UA/NSTEMI.\textsuperscript{13} Excess triglyceride content in heart tissue including areas of healed MI might influence the vulnerability to ventricular arrhythmias in obese compared with normal weight patients.\textsuperscript{39}

As possible indicators for an earlier stage of coronary artery disease, obese patients were younger compared with normal and overweight patients and less often had

### Table 3

**Independent predictors of long-term mortality in multivariable analysis**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Hazard ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count (continuous)</td>
<td>1.006 (1.002–1.009)</td>
<td>0.001</td>
</tr>
<tr>
<td>White blood count (&gt;10^3) µL(^{-1})</td>
<td>3.17 (1.36–7.39)</td>
<td>0.008</td>
</tr>
<tr>
<td>Age (continuous)</td>
<td>1.05 (1.00–1.10)</td>
<td>0.033</td>
</tr>
<tr>
<td>Obesity (body mass index (&gt;30))(^a)</td>
<td>0.27 (0.08–0.92)</td>
<td>0.036</td>
</tr>
</tbody>
</table>

Baseline variables associated with mortality in univariable analysis and entered into the multivariable model were: age, ST-segment depression, previous MI, elevated cardiac troponin T, elevated white blood count, platelet count, kidney function, left ventricular function, angiographic extent of coronary artery disease, C-reactive protein, and obesity. CI, confidence interval.

\(^a\)All obese vs. normal body mass index.
prior MI. On the other hand, the angiographic extent of coronary artery disease was similar among the groups. Furthermore, the association between obesity and lower long-term mortality persisted in multivariable analysis after adjustment for age, left ventricular function, and angiographic extent of coronary artery disease.

Limitations
Several limitations apply to this study. First, the present study does not take into account the recent weight loss and shifts in body weight, which may be associated with risk. Unfortunately, this information is not available in our data set. However, even without this additional information, our findings have considerable clinical impact as risk is typically assessed according to actual BMI rather than BMI changes. In addition, cumulative mortality rates seem to separate early after the index event. Changes in body weight seem less likely to account for a difference in early when compared with late mortality. Secondly, the percentage of patients with a BMI of 40 or greater in this study was similar to other European studies and lower than in some previous US studies resulting in a low absolute number of patients in this extreme group. Therefore, the finding of an improved outcome after UA/NSTEMI should not be extrapolated to patients with very severe obesity. Thirdly, BMI may reflect also muscle mass. Other measures of obesity such as waist-to-hip ratio might better reflect body fat content and distribution when compared with BMI. Fourthly, the presented results based on the categorization of BMI rely on a simplification of the relation between BMI and mortality.

Our analysis has five particular strengths. First, it is derived from a prospective study of consecutive unselected patients rather than a randomized trial. This eliminates selection bias and eases the extrapolation of findings into clinical practice. Secondly, it includes long-term follow-up. Thirdly, coronary angiography was performed in all patients. The incidence of significant CAD was 87% in obese patients when compared with 84% in normal weight patients. Moreover, 62% had coronary multivessel disease and 66% had an elevated cardiac troponin following their chest pain episode. Therefore, we can reliably exclude that obese patients had a higher incidence of non-coronary causes of chest pain that might have resulted in the favourable prognosis observed. Fourthly, a uniform revascularization strategy was applied in all patients. Fifthly, the extent of coronary artery disease and left ventricular function was quantified in all patients and included in the multivariable analysis as potential cofounder.

Conclusions
This large prospective study in consecutive unselected patients with UA/NSTEMI receiving contemporary treatment with early revascularization showed that obese and very obese patients had less than half the mortality when compared with normal BMI patients. This observation was consistent among all subgroups and persisted after multivariable adjustment.

Conflict of interest: none declared.

References
22. Minutello RM, Chou ET, Hong MK, Bergman G, Parikh M, Iacovone F, Wong SC. Impact of body mass index on in-hospital outcomes following
Impact of obesity on mortality in UA/NSTEMI