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Title

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Permalink

<https://escholarship.org/uc/item/75m3g7z6>

Journal

Obesity, 16(2)

ISSN

1930-7381

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Publication Date

2008-02-01

DOI

10.1038/oby.2007.36

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Effect of Obesity on Short- and Long-term Mortality Postcoronary Revascularization: A Meta-analysis

Antigone Oreopoulos¹, Raj Padwal², Colleen M. Norris³, John C. Mullen¹, Victor Pretorius¹ and Kamyar Kalantar-Zadeh⁴

Objective: Overweight and obesity are often assumed to be risk factors for postprocedural mortality in patients with coronary artery disease (CAD). However, recent studies have described an “obesity paradox” – a neutral or beneficial association between obesity and mortality postcoronary revascularization. We reviewed the effect of overweight and obesity systematically on short- and long-term all-cause mortality post-coronary artery bypass grafting (CABG) and post-percutaneous coronary intervention (PCI).

Methods: We searched the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, Scopus, and Web of Science to identify cohort, case control, and randomized controlled studies evaluating the effect of obesity on in-hospital/short-term (within 30 days) and long-term (up to 5 years) mortality. Full-text, published articles reporting all-cause mortality between individuals with and without elevated BMI were included. Two reviewers independently assessed studies for inclusion and performed data extraction.

Results: Twenty-two cohort publications were identified, reporting results in ten post-PCI and twelve post-CABG populations. Compared to individuals with non-elevated BMI levels, obese patients undergoing PCI had lower short- (odds ratio (OR) 0.63; 95% confidence interval (CI) 0.54–0.73) and long-term mortality (OR 0.65; 95% CI 0.51–0.83). Post-CABG, obese patients had lower short-term (OR 0.63; 95% CI 0.56–0.71) and similar long-term (OR 0.88; 95% CI 0.60–1.29) mortality risk compared to normal weight individuals. Results were similar in overweight patients for both procedures.

Conclusions: Compared to non-obese individuals, overweight and obese patients have similar or lower short- and long-term mortality rates postcoronary revascularization. Further research is needed to confirm the validity of these findings and delineate potential underlying mechanisms.

Obesity (2008) **16**, 442–450. doi:10.1038/oby.2007.36

INTRODUCTION

Obesity is a highly and increasingly prevalent chronic condition associated with significant morbidity and mortality (1). Overweight and obese individuals are at greater risk for developing coronary artery disease (CAD), primarily as a consequence of obesity-related conditions such as diabetes, hypertension, and dyslipidemia (2). Accordingly, coronary revascularization is commonly performed in patients with increased BMI. Of the 197,105 isolated primary coronary artery bypass grafting (CABG) procedures performed nationally in the United States from 1997 to 2000, 31% were performed in moderately or severely obese individuals (BMI ≥ 35 kg/m²) (3). Furthermore, in a large, population-based registry >95,000 angioplasty

procedures in New York State, 43 and 24% of procedures were performed in overweight (BMI 25.0–29.9 kg/m²) and obese individuals (BMI ≥ 30 kg/m²), respectively (4). It is likely that the number of obese and overweight individuals undergoing such procedures will increase substantially in the future.

Although the association between excess adiposity and cardiovascular risk in the general population has been well established (1), the impact of overweight and obesity on mortality in patients with established CAD remains controversial and requires further investigation. Obesity is also often assumed to be a risk factor for postoperative morbidity/mortality following CABG and percutaneous coronary intervention (PCI) (5) because obesity predisposes toward chronic CAD, postprocedural wound

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Received 11 January 2007; accepted 7 June 2007. doi:10.1038/oby.2007.36

complications (6), 30-day readmission (7), and increased hospital length of stay (7). However, recent studies have described an “obesity paradox” in patients undergoing PCI or CABG, reporting similar or lower postoperative mortality rates in obese patients compared to patients of normal weight (8–11). If valid, these provocative findings may have important clinical implications, as it can be legitimately questioned whether or not overweight or obese patients should be counseled to lose weight before a revascularization intervention. This systematic review was conducted to further explore the association between increased adiposity and postoperative all-cause mortality.

METHODS

Search strategy

Detailed search strategies were designed with the help of a medical librarian to identify randomized controlled trials and observational studies evaluating the effect of overweight and obesity on postoperative mortality following PCI and CABG. A full search strategy is available upon request. The Cochrane Central Register of Controlled Trials (1900 to August 2006), MEDLINE (1966 to August 2006), EMBASE (1988 to August 2006), Scopus (1966 to August 2006), and Web of Science (1900 to August 2006) were searched, reference lists of primary studies and review articles were reviewed, and three experts in the field were contacted. No language or age restrictions were applied.

Inclusion and exclusion criteria

Studies were required to separately report mortality in obese and normal weight patients using BMI categories. *A priori*, we knew that not all studies would use the traditional World Health Organization BMI classification system of 18.5–24.9, 25.0–29.9, and ≥ 30.0 kg/m² for normal, overweight, and obesity, respectively. Therefore, to avoid eliminating studies with important information we considered BMI levels within 2 kg/m² of standard categories to be acceptable. However, studies comparing obese and non-obese (i.e., normal and overweight patients grouped together) were excluded unless outcomes in the normal weight population alone could be ascertained. Articles were also excluded if the total number of deaths was <5, the citation was a review or duplicate article, and if the study was published only in abstract form.

Outcomes

The primary outcome was all-cause mortality. As different factors may influence mortality in the immediate postoperative period vs. the long-term, we analyzed in-hospital/short-term (≤ 30 days) and longer term mortality separately. When studies reported mortality at two or more time intervals, the longest follow-up period was used for analysis. *A priori*, we planned a subgroup analysis examining the effect of moderate and/or severe obesity (BMI ≥ 35 kg/m²) on mortality.

Trial selection and data extraction

One author (A.O.) pre-screened the search results to remove citations that were clearly not relevant. Two reviewers (A.O. and R.P.) independently reviewed the remaining citations and performed data extraction. Cohen’s Kappa coefficients were calculated to assess inter-observer agreement for study inclusion and data extraction. Disagreements were resolved through consensus. Reviewers were not blinded to the authors’ names and institutions, journal of publication, or study results. When necessary, additional data were requested from the primary study authors. Study quality was assessed using the Ottawa–New Castle Assessment Scale for observational studies (12).

Data analysis

PCI and CABG procedures were analyzed separately. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using RevMan

(version 4.2.8) using a random effects model. If obesity was subclassified as “mild,” “moderate,” and “severe,” results were collapsed into a single “obese” category for the primary analysis. Heterogeneity was examined using the Higgins I^2 test (13). Roughly, Higgins I^2 values of 25, 50, and 75% can be interpreted as indicating low, moderate, and high heterogeneity.

RESULTS

Of the 3,477 initial citations, 262 were potentially relevant upon initial screening, 49 were potentially appropriate for inclusion, and 22 met final inclusion criteria (Figure 1). Inter-observer agreement was 0.9 for study inclusion and 0.82 for data extraction.

No randomized controlled trials (RCTs) evaluating the effects of pre-revascularization weight change on postprocedural mortality were found. Ten post-PCI (Table 1) and twelve post-CABG observational studies (Table 2) were identified. Two studies reported results for both PCI and CABG as separate analyses within the same publication (9,11). Four publications represented the posthoc analyses of RCTs (8,9,11,14) and the remainder were derived from primary cohorts.

Seventy percent of included studies were of high methodological quality (score 8–9/9) according to the Ottawa–New Castle criteria. Another 22% were of moderate methodological quality (score 6–7/9) and the remaining 8% were of low quality (score 4–5/9).

Main analysis

Post PCI. Five studies examined short-term/in-hospital mortality and eight studies reported long-term (1–5 year) mortality post-PCI (Figure 2). Compared to individuals without elevated BMI levels, both overweight (OR 0.71; 95% CI 0.62–0.81) and obese (OR 0.63; 95% CI 0.54–0.73) patients had lower short-term/in-hospital mortality. Similarly overweight

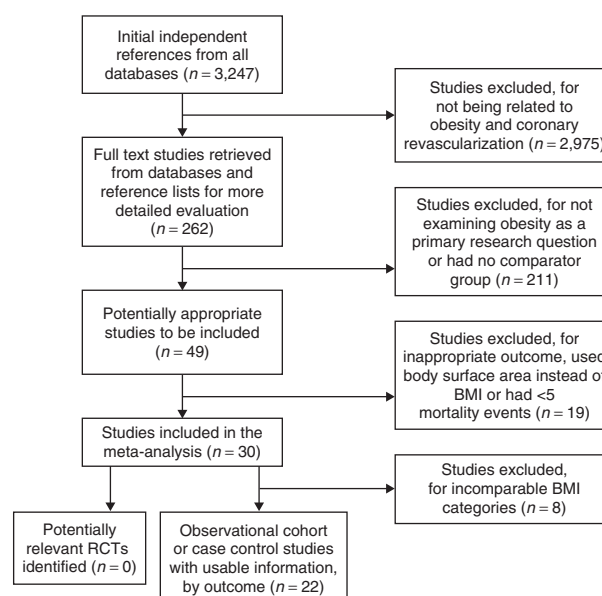


Figure 1 Quality of reporting of meta-analyses (QUOROM) statement flow diagram. RCTs, randomized controlled trials.

Table 1 Cohort studies evaluating the effect of obesity on mortality post-percutaneous coronary intervention (PCI)

Study	Population	Sample size ^a	Mean age (years), % female		BMI categories reported (kg/m ²)	Quality assessment score	Outcomes
Ellis <i>et al.</i> (US) (31)	Single surgical center	3,571	63, 28		Low-normal <25, moderate-severely obese ≥35	4	In-hospital
Gruberg <i>et al.</i> (US) (10)	Single surgical center	9,633	64, 31		Low-normal <25, overweight 25–29.9, obese ≥30	9	In-hospital, 1-year
Gruberg <i>et al.</i> (US) (11)	Posthoc analysis of the ARTS trial	599	61, 23		Low-normal <25, overweight 25–30, obese ≥30	8	3-year
Gurm <i>et al.</i> (US) (8)	Posthoc analysis of pooled data from 4 RCTs of glycoprotein IIb/IIIa inhibitors	11,071 for 30 day outcome (4 trials) and 7,131 for the 1 year outcome (3 trials)	61, 26		Underweight <18.5, normal 18.5–24.9, overweight 25–29.9, mild-moderately obese 30–39.9, severely obese ≥40	9	30-day, 1-year
Gurm <i>et al.</i> (US) (9)	Posthoc analysis of the BARI trial	2,072	Age ≥65 34%, 25% female		Underweight <20, normal 20–24.9, overweight 25–29.9, obese 30–35, severely obese ≥35	9	3-year, 5-year
Kelly <i>et al.</i> (US) (14)	Posthoc analysis of the CREDO trial	2,116	62, 29		Low-normal <25, overweight 25–29.9, mild-moderately obese 30.0–39.9 and severely obese ≥40	9	1-year
Minutello <i>et al.</i> (US) (4)	New York State Angioplasty Registry	94,511	63, 30		Underweight <18.5, normal 18.5–24.9, overweight 25–29.9, obese 30–34.9, moderate-severely obese ≥35	8	In-hospital
Nikolsky <i>et al.</i> (US) (35)	Posthoc analysis of the TAXUS-IV trial	1,307	63, 27		Low-normal <25, overweight 25–29.9, obese ≥30	8	1-year
Poston <i>et al.</i> (US) (36)	Single surgical center	1,569	65, 28		Underweight <20, normal 20–24.9, overweight 25–29.9, obese 30–34.9, moderate-severely obese ≥35	8	1-year
Powell <i>et al.</i> (US) (37)	Single surgical center	5,928	63, 29		Underweight <20, normal 20–25, overweight 25–29.9, obese 30–34.9, moderate-severely obese ≥35	7	In-hospital, 3-year

ARTS, arterial revascularization therapy study; BARI, bypass angioplasty revascularization investigation; CREDO, clopidogrel for the reduction of events during observation; RCTs, randomized controlled trials.

^aSample size excludes underweight patients (when reported).

(OR 0.66; 95% CI 0.55–0.79) and obesity (OR 0.65; 95% CI 0.51–0.83) were associated with lower long-term mortality post-PCI (Figure 3). In patients with moderate and/or severe obesity, both short-term/in-hospital (OR 0.76; 95% CI 0.61–0.95) and long-term (OR 0.62; 95% CI 0.41–0.96) mortality were reduced.

The short-term/in-hospital analyses demonstrated no heterogeneity. In the long-term analyses, heterogeneity was 39, 58, and 51% by Higgins *I*² for the overweight, obese, and moderate and/or severe obesity comparisons, respectively.

Post CABG. The effect of overweight and obesity on short-term/in-hospital and long-term mortality post-CABG was assessed in eight studies (Figure 4). Compared to individuals without elevated BMI levels, both overweight (OR 0.70; 95% CI 0.63–0.77) and obese (OR 0.63; 95% CI 0.56–0.71) patients had lower short-term/in-hospital mortality. In addition, moderately and/or severely obese patients were at lower risk of death (OR 0.66; 95% CI 0.51–0.86).

Five studies examined longer term outcomes, ranging from 1 to 5 years (Figure 5). Overweight (OR 0.78; 95% CI 0.60–1.00) and obesity (OR 0.88; 95% CI 0.60–1.29) were associated with lower long-term mortality post-PCI. Moderate and/or severe

obesity was associated with a neutral mortality risk (OR 1.42; 95% CI 0.76–2.65). There was no heterogeneity for the short-term/in-hospital mortality analyses, and heterogeneity was 47, 65, and 59% by Higgins *I*² for the overweight, obese, and moderate and/or severe comparisons for long-term mortality analyses, respectively.

Sensitivity analysis

Owing to the possible confounding effects of including underweight patients in the studies which classified normal BMI as <25 kg/m², a sensitivity analysis was conducted by excluding these studies (Table 3). The ORs and 95% CIs changed minimally in all analyses except the comparisons involving long-term mortality for moderately and/or severely obese individuals post-PCI and long-term mortality post-CABG. In the post-PCI sensitivity analysis, the CI for moderately and/or severely obese individuals changed to include one. In the post-CABG sensitivity analyses, obese patients were at significantly greater risk of death with long-term follow-up (Table 3). However, this result must be interpreted with caution, as four out of a possible five studies were excluded because they classified normal BMI as <25 kg/m².

Table 2 Cohort studies evaluating the effect of obesity on mortality post-coronary artery bypass grafting (CABG)

Study	Population	Sample size ^a	Age (years), % female	BMI categories reported (kg/m ²)	Quality assessment score	Mortality outcomes
Christakis <i>et al.</i> (Canada) (38)	Single surgical center	7,025	Mean age not provided, 19	Low-normal <24.9, overweight 25–30.4, obese >30.4	8	In-hospital
Enker <i>et al.</i> (Germany) (39)	Single surgical center	412	65, 32	Normal 20–25 and extreme obese ≥35	6	30-day
Gruberg <i>et al.</i> (US) (11)	Post-hoc analysis of the ARTS trial	604	61, 24	Low-normal <25, overweight 25–29.9, obese ≥30	8	3-year
Gurm <i>et al.</i> (US) (9)	Post-hoc analysis of the BARI trial	1,498	Age ≥65 34%, 25% female	Underweight <20, normal 20–24.9, overweight 25–29.9, obese 30–34.9, moderate–severely obese ≥35	9	3-year, 5-year
Kim <i>et al.</i> (Sweden) (40)	Single surgical center	6,728	61, gender not reported	Low-normal <25, overweight 25–29.9, obese ≥30	9	30-day, 1-year, 5-year
Orhan <i>et al.</i> (Turkey) (41)	Single surgical center	1,206	60, 18	Normal 18.5–24.9, overweight 25–29.9, obese ≥30	7	In-hospital
Pan <i>et al.</i> (US) (42)	Single surgical center	9,826	63, 25	Normal 20.0–24.9, overweight 25.0–29.9, mildly obese 30–34.9, moderately obese 35.0–39.9, severely obese ≥40	8	30-day
Potapov <i>et al.</i> (Germany) (43)	Single surgical center	22,666	63, 28	Low-normal <25.3 overweight 25.4–29.4, obese ≥29.5	6	30-day
Scwhann <i>et al.</i> (US) (44)	Single surgical center	3,560	63, 33	Low-normal <24, overweight 24–29.9, obese 30–34, ≥34 severely obese	7	5-year
Rapp-Kesek <i>et al.</i> (Sweden) (25)	Single surgical center	886	67, 26	Low-normal <24, overweight 24–29.9, obese 30–34, severely obese ≥34	9	2-year
Reeves <i>et al.</i> (UK) (45)	Prospective cohort of the National Cardiac Surgery Database	4,239	Mean not ascertainable, 18	Underweight <20, normal 20–24.9, overweight 25–29.9, obese 30–34.9, moderate–severely obese ≥35	9	In-hospital
Jin <i>et al.</i> (US) (46)	Nine surgical centers	16,128	66, 28	Underweight <18.5, normal 18.5–24.9, overweight 25–29.9, obese 30–34.9, moderate–severely obese ≥35	8	In-hospital

ARTS, arterial revascularization therapy study; BARI, bypass angioplasty revascularization investigation.

^aSample size excludes underweight patients (when reported).

DISCUSSION

We found no evidence of a detrimental association between overweight or obesity and short-term or long-term mortality post-PCI and post-CABG. In fact, quantitative meta-analyses of the available literature suggests a potentially beneficial effect of elevated BMI levels on mortality in these populations. This protective effect is inconsistently attenuated with longer term follow-up periods, when the level of obesity has progressed into the moderate or severe range and when studies involving underweight patients are excluded from the analysis.

Our results confirm the findings of a recently published meta-analysis examining the association between BMI and total mortality and cardiovascular events (15). This review, which quantitatively combined results from long-term studies (>6 months) involving post-PCI, CABG, and myocardial infarction (MI) patients, found the highest risk of mortality with BMI levels <20 kg/m² and the lowest risk of mortality in overweight patients. Our results are similar, although we also included short-term/in-hospital mortality as an endpoint, did not include studies published as abstracts only, and felt that

post-PCI and CABG populations were not similar enough to quantitatively combine into a single analysis. It is notable that combining these groups was associated with substantial statistical heterogeneity (15).

In contrast to our results, one might expect excess body weight to be associated with an increased risk of death in patients postcoronary revascularization because of previously documented associations between obesity and other cardiovascular risk factors, cardiovascular disease, prothrombosis, inflammation, sympathetic nervous system activation, and mortality in the general population (2,16,17). What, then, are the potential explanations for the “obesity paradox?” First, it is important to consider additional sources of bias. Obese patients consistently undergo revascularization procedures at a younger age than their non-obese counterparts and, consequently, may present with lower risk coronary anatomy (18). On the other hand, the paradox may be due to selection bias if only a subgroup of the “healthiest” obese patients are surviving to revascularization or being selected for revascularization (19,20). In addition, concern that obese patients may

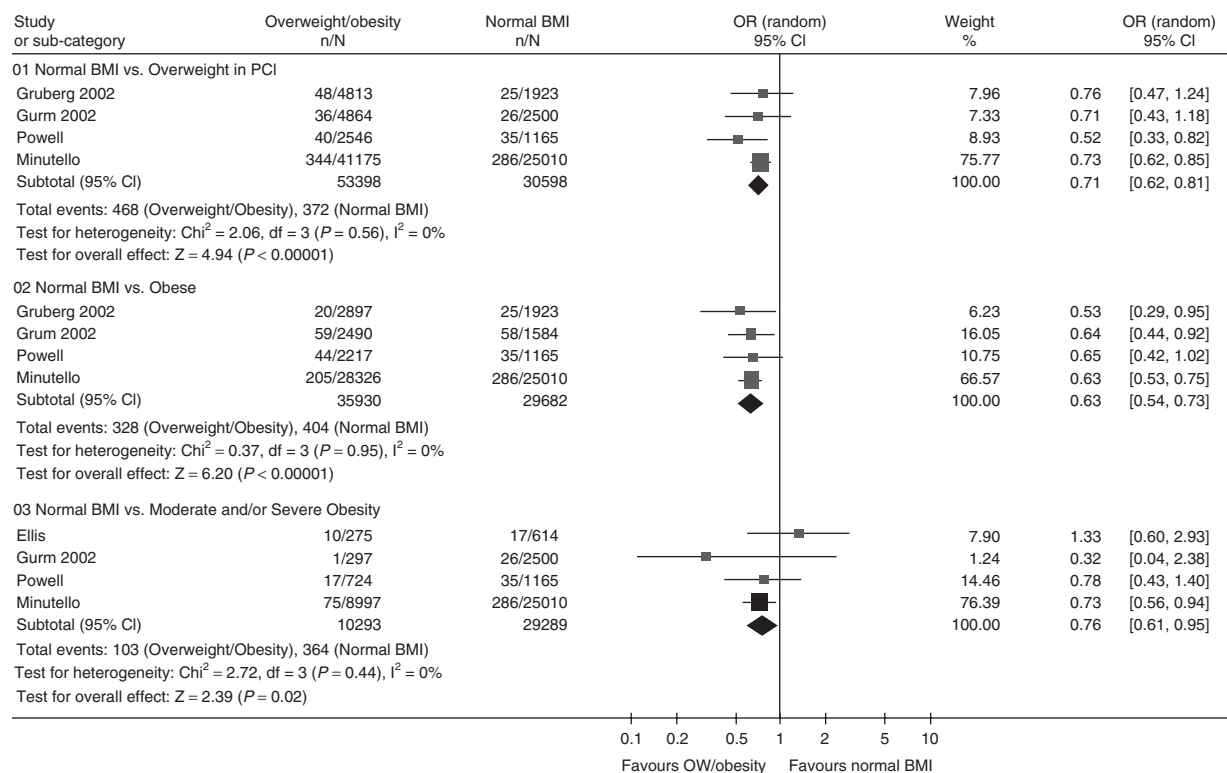


Figure 2 30-Day/in-hospital mortality post-percutaneous coronary intervention (PCI). OR, odds ratio; OW, overweight.

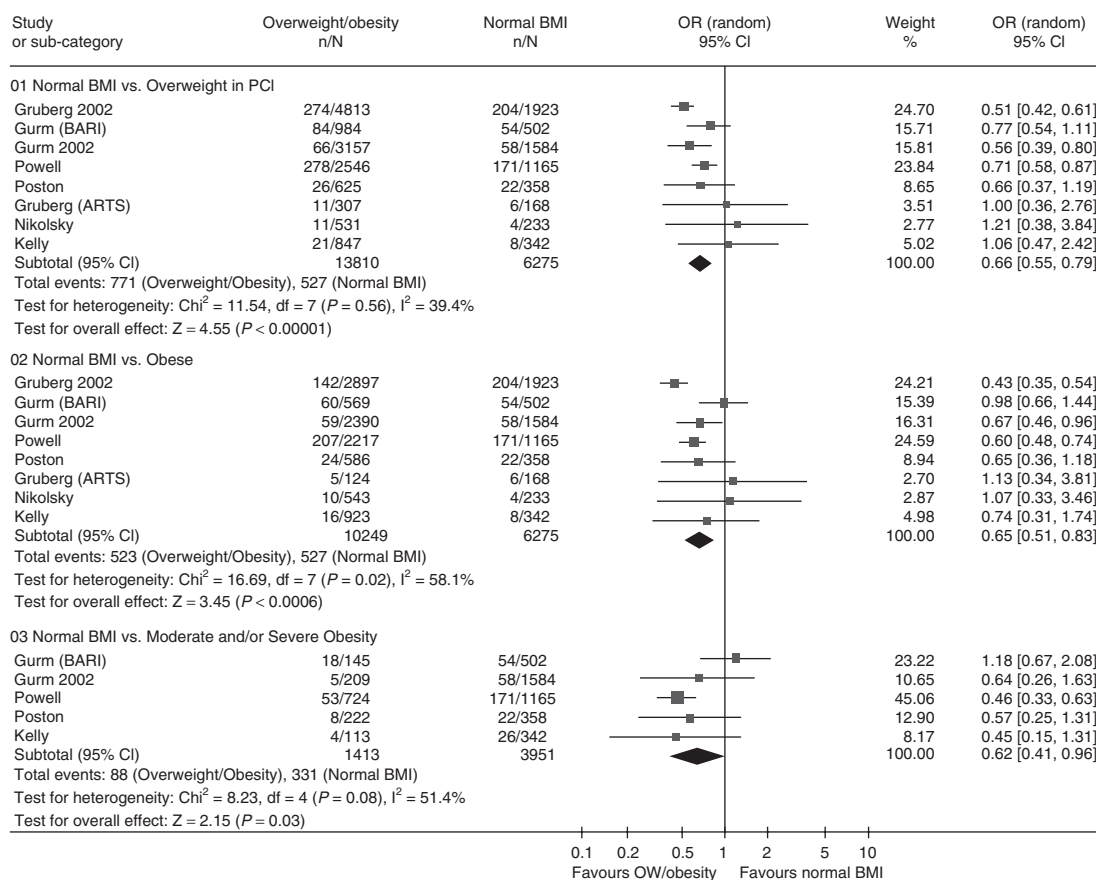


Figure 3 Long-term mortality (1–5 years) post-percutaneous coronary intervention (PCI). ARTS, arterial revascularization therapy study; BARI, bypass angioplasty revascularization investigation; OR, odds ratio; OW, overweight.

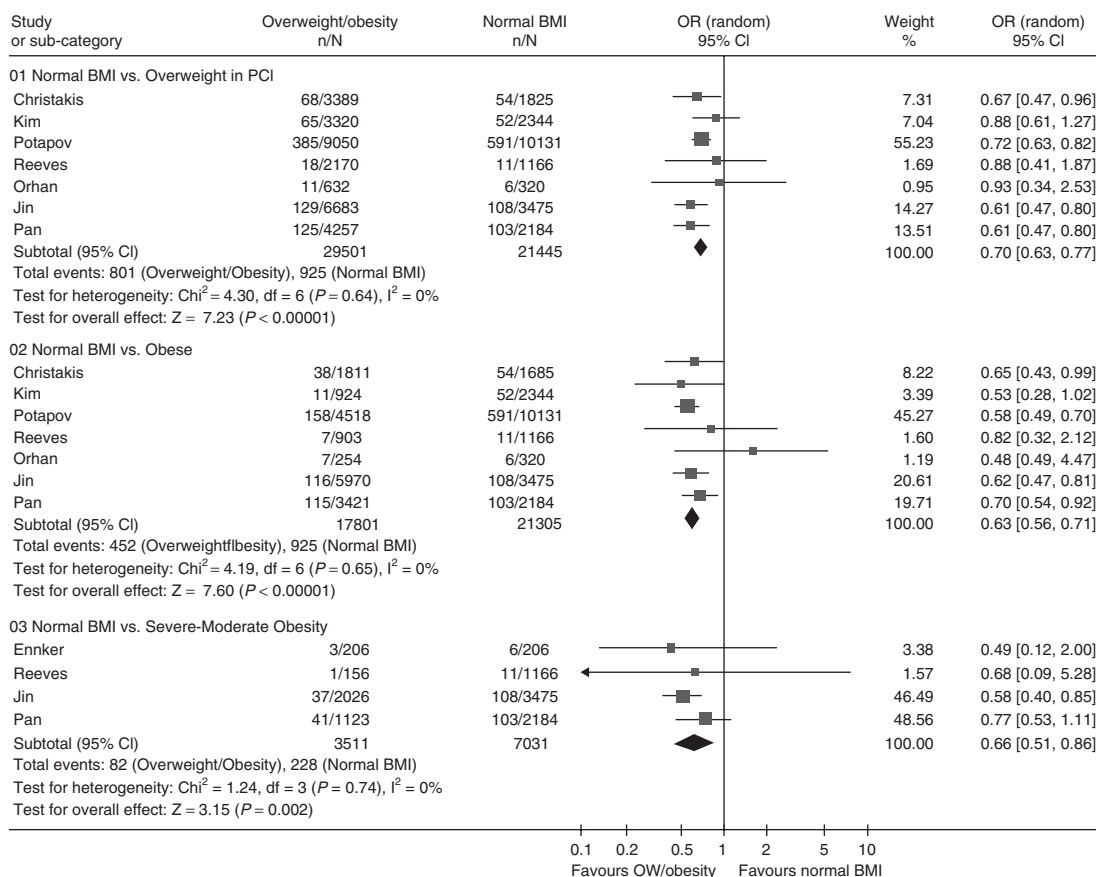


Figure 4 30-Day/in-hospital mortality post-coronary artery bypass graft (CABG). ARTS, arterial revascularization therapy study; BARI, bypass angioplasty revascularization investigation; OR, odds ratio; OW, overweight.

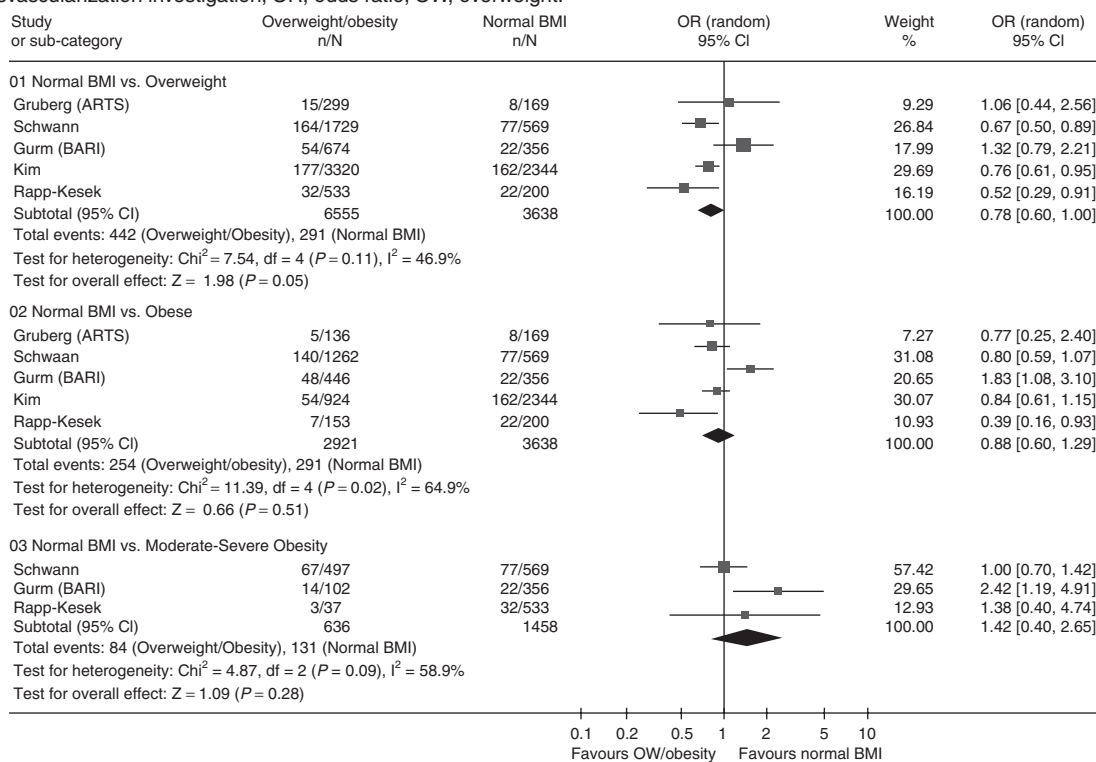


Figure 5 Long-term mortality (1–5 years) post-coronary artery bypass graft (CABG). ARTS, arterial revascularization therapy study; BARI, bypass angioplasty revascularization investigation; OR, odds ratio; OW, overweight.

Table 3 Sensitivity analysis

Mortality comparison	Analysis with or without studies classifying BMI as <25 kg/m ²	Number of studies in analysis	OR (95% CI) normal BMI vs. overweight	OR (95% CI) normal BMI vs. obese	OR (95% CI) normal BMI vs. moderate-severe obese
PCI short-term/ in-hospital	Studies included	5	0.71 (0.62–0.81)	0.63 (0.54–0.73)	0.76 (0.61–0.95)
	Studies excluded	3	0.70 (0.61–0.81)	0.63 (0.54–0.74)	0.73 (0.54–0.92)
PCI long-term	Studies included	8	0.66 (0.55–0.79)	0.65 (0.51–0.83)	0.62 (0.41–0.96)
	Studies excluded	4	0.69 (0.59–0.80)	0.69 (0.55–0.87)	0.66 (0.4–1.08)
CABG short-term/ in-hospital	Studies included	8	0.70 (0.63–0.77)	0.63 (0.56–0.71)	0.66 (0.51–0.86)
	Studies excluded	4	0.63 (0.53–0.76)	0.68 (0.56–0.82)	0.66 (0.51–0.86)
CABG long-term	Studies included	5	0.78 (0.60–1.0)	0.88 (0.60–1.29)	1.42 (0.76–2.65)
	Studies excluded	1	1.32 (0.79–2.21)	1.83 (1.08–3.10)	2.42 (1.19–4.91)

be at increased risk for vascular complications and cardiac events may result in increased diligence while obtaining vascular access, or provision of more aggressive treatment during hospitalization (21). Follow-up periods in studies to date may not be of sufficient length to demonstrate the expected negative impact of obesity on mortality. The confounding effects of smoking (which reduces body weight), the inclusion of underweight individuals, and unintentional weight loss due to (often unrecognized) chronic illness may increase mortality in patients with normal or underweight BMI categories (22).

To explore the possibility of selection bias, we determined the relative frequencies of selected baseline covariates known to affect survival in the post-PCI or post-CABG populations (Table 4). Obese patients were younger, but had a higher prevalence of comorbidities such as hypertension, hypercholesterolemia, and diabetes mellitus. Other comorbidities such as history of MI, chronic heart failure, smoking history, unstable angina, and left main disease were similar or slightly less frequent in obese patients compared to those of normal weight. Even social class (education level) was similar between groups. Although such an analysis cannot be regarded as definitive because other measured or unmeasured confounders may be affecting survival, these data provide evidence that there are both favorable (age) and unfavorable risk factors are present in obese patients with CAD. It is notable that even after adjustment for baseline covariates, overweight or obesity do not seem to increase mortality in this patient population (15).

Second, the possibility that the “obesity paradox” is a valid finding cannot be discounted. This paradox has been observed in a number of chronic disease states, including cancer, HIV infection, heart failure, rheumatic diseases, and end-stage renal failure (23). Furthermore, in patients undergoing myocardial perfusion imaging for suspected coronary disease, obesity, and overweight were associated with a neutral effect on cardiac mortality in patients with negative scans and *reduced* mortality in patients with positive scans and, therefore, proven CAD (24). Excess body weight may increase metabolic reserve and counteract the negative effects of chronic inflammation and cachexia (25,26). Specifically postrevascularization, obesity may improve outcomes because of larger vessel size and easier stent placement (27,28).

Table 4 Baseline patient characteristics

Clinical variable	Normal BMI	Overweight	Obese
Mean age <i>n</i> = 183,224 Studies = 15	66.1	62.9	60.4
Gender <i>n</i> = 187,339 Studies = 17	32.7% F	23.8% F	35.0% F
Education level (finished high school) <i>n</i> = 1,569 Studies = 1	84.4%	86.4%	81.3%
Diabetes <i>n</i> = 193,927 Studies = 18	17.0%	19.6%	33.2%
Hypertension <i>n</i> = 94,817 Studies = 16	50.8%	55.2%	67.0%
Hypercholesterolemia <i>n</i> = 33,709 Studies = 10	44.0%	52.8%	61.1%
Unstable angina <i>n</i> = 149,370 Studies = 13	48.8%	46.5%	49.2%
Chronic heart failure <i>n</i> = 143,182 Studies = 7	8.1%	7.1%	8.3%
History of myocardial infarction <i>n</i> = 85,821 Studies = 14	46.3%	45.6%	42.3%
Current smoker <i>n</i> = 124,287 Studies = 10	25.3%	24.3%	25.5%
Former smoker <i>n</i> = 5,928 Studies = 1	33.9%	46.3%	45.9%
Triple vessel disease <i>n</i> = 15,600 Studies = 5	58.2%	56.2%	52.0%
Left main disease <i>n</i> = 43,162 Studies = 6	25.6%	24.5%	22.5%
Peripheral vascular disease <i>n</i> = 122,071 Studies = 8	11.7%	9.4%	8.0%

Our results also suggest, albeit not definitively, that the potentially protective association between obesity and mortality is lost with longer follow-up periods and/or increasing severity of obesity. One may speculate that, with longer follow-up periods, the cumulatively detrimental effect of obesity on cardiovascular and metabolic (i.e., glycemic and lipid levels) function may manifest as increased mortality. In addition, severely obese individuals may have a higher risk of thrombosis (29), inflammation (17), endothelial dysfunction (30), under-dosing of anticoagulants (31), limited radiographic imaging of vessels, poor hemodynamic reserve (32), and failed resuscitation (33).

Several limitations of this meta-analysis should be noted. First, as with any systematic review, bias may occur due to selective study publication or if important studies were missed. We searched multiple databases and contacted content experts in an effort to minimize such bias. There were too few studies in each category to evaluate for potential publication bias using a funnel plot. However, publication bias tends to occur in the direction of non-neutral studies and, it is notable that no study found a positive association between obesity and mortality in overweight patients and only one study (9) found such an association in obese patients. Second, not all studies used the standard World Health Organization BMI classification system for body weight. In particular, several studies grouped normal and lower weight individuals together. As underweight (2), cachexia (34), and malnutrition (25,26) are associated with increased mortality, this may have resulted in an apparent relative benefit of overweight and obesity. However, our sensitivity analysis which excluded studies that classified $<25 \text{ kg/m}^2$ as normal BMI (and thus included underweight patients in this category), demonstrated that this did not have any major effect on the results. Third, although BMI is the most commonly used epidemiologic measure of obesity, it is imperfect and does not directly distinguish between adipose and lean tissue or central and peripheral adiposity. We were unable to determine if the apparent protective effects of obesity are due to increased fat or lean body mass. Misclassification of body composition using BMI would be expected to bias our ORs toward the null, thereby potentially masking a non-neutral association between BMI and mortality. Fourth, moderate statistical heterogeneity was found when quantitative pooling was performed for some of our outcomes. This is not surprising, because there are many potential clinical and methodological explanations for heterogeneity in postrevascularization studies. These may include differences in procedural techniques, operator and center experience, contemporary and local practice patterns, postoperative care, and patient selection. We used a random effects model in an effort to incorporate heterogeneity between trials in our analysis, but recognize that this does not eliminate the fact that heterogeneity was present. Again, it is notable that nearly all studies reported a neutral or beneficial effect of elevated BMI levels on mortality, providing supportive evidence that the summary effect sizes were the product of consistent results. Finally, the observational nature of the studies identified

provides associative, not causal, evidence, and mandates caution when interpreting the results.

CONCLUSIONS

In conclusion, observational studies suggest that obesity and overweight are associated with a neutral or beneficial effect on all-cause mortality postcoronary revascularization. This effect may be attenuated with longer follow-up periods and increasing severity of obesity. The underlying explanation for these results is unknown, although many potential explanations exist. Future prospective studies specifically designed to confirm or refute the “obesity paradox” and avoid potential bias inherent in previous research are required. Specifically, studies that more accurately quantify lean and fat tissue, central adiposity, temporal weight change, and intentionality of weight change should be performed. Until such data are available, the optimal weight-related treatment strategy for overweight and obese individuals postcoronary revascularization is unknown.

ACKNOWLEDGMENT

The lead author had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses.

DISCLOSURE

The authors declared no conflict of interest.

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REFERENCES

1. Haslam DW, James WP. Obesity. *Lancet* 2005;366:1197–1209.
2. Calle E, Thun MJ, Petrelli JM, Rodriguez C, Heath CW. Body mass index and mortality in a prospective cohort of U.S. adults. *N Eng J Med* 1999;341:1097–1105.
3. Prabhakar G, Haan CK, Peterson ED *et al*. The risks of moderate and extreme obesity for coronary artery bypass grafting outcomes. *Ann Thorac Surg* 2002;74:1125–1131.
4. Minutello RM, Chou ET, Hong MK *et al*. Impact of body mass index on in-hospital outcomes following percutaneous coronary intervention (report from the New York State Angioplasty Registry). *Am J Cardiol* 2004;93:1229–1232.
5. Parsonnet V, Dean D, Bernstein AD. A method of uniform stratification of risk for evaluation the results of surgery in acquired adult hear disease. *Circulation* 1989;79:13–112.
6. Cruse P, Foord R. A five-year prospective study of 23,649 surgical wounds. *Arch Surg* 1973;107:206–210.
7. Kuduvalli M, Grayson A, Oo A, Fabri B, Rashid A. Risk of morbidity and in-hospital mortality in obese patients undergoing coronary artery bypass surgery. *Euro J Cardiothorac Surg* 2002;22:787–793.
8. Gurm HS, Brennan DM, Booth J *et al*. Impact of body mass index on outcome after percutaneous coronary intervention. *Am J Cardiol* 2002;90:42–45.
9. Gurm HS, Whitlow PL, Kip KE, Investigators B. The impact of body mass index on short- and long-term outcomes inpatients undergoing coronary revascularization. *J Am Coll Cardiol* 2002;39:834–840.
10. Gruberg L, Weissman NJ, Waksman R *et al*. The impact of obesity on the short-term and long-term outcomes after percutaneous coronary intervention: the obesity paradox? *J Am Coll Cardiol* 2002;39:578–584.
11. Gruberg L, Mercado N, Milo S *et al*. Impact of body mass index on the outcome of patients with multivessel disease randomized to either coronary artery bypass grafting or stenting in the ARTS trial. *Am J Cardiol* 2005;95:439–444.
12. Wells G, Shea B, O’Connell D *et al*. The Newcastle-Ottawa Scale for Assessing the Quality of Nonrandomized Studies in Meta-Analysis. http://www.ohri.ca/programs/clinical_epidemiology/oxford_web.ppt (2006).

13. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–560.
14. Kelly RV, Hsu A, Topol E, Steinhilb S. The influence of body mass index on outcomes and the benefit of antiplatelet therapy following percutaneous coronary intervention. *J Invasive Cardiol* 2006;18:115–119.
15. Romero-Corral A, Montori VM, Somers VK *et al*. Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. *Lancet* 2006;368:666–677.
16. Misra A, Vikram NK. Clinical and pathophysiological consequences of abdominal adiposity and abdominal adipose tissue depots. *Nutrition* 2003;19:457–466.
17. Bray GA. Medical consequences of obesity. *J Clin Endocrinol Metab* 2004;89:2583–2589.
18. Rubishtein R, Halon DA, Jaffe R, Shahla J, Lewis BS. Relation between obesity and severity of coronary artery disease in patients undergoing coronary angiography. *Am J Cardiol* 2006;87:1277–1290.
19. Yancy WS Jr, Olsen MK, Curtis LH *et al*. Variations in coronary procedure utilization depending on body mass index. *Arch Int Med* 2005;165:1381–1387.
20. King KM, Southern DA, Cornuz J, Knudtson ML, Ghali WA. Elevated body mass index and access to coronary revascularization following cardiac catheterization. *Can J Cardiol* 2006;22(Suppl D):290.
21. Diercks DB, Roe MT, Mulgund J *et al*. The obesity paradox in non-ST-segment elevation acute coronary syndromes. *Am Heart J* 2006;152:140–148.
22. Yang D, Fontaine KR, Wang C, Allison DB. Weight loss causes increased mortality: cons. *Obes Rev* 2003;4:9–16.
23. Kalantar-Zadeh K, Block G, Horwich T, Fonarow GC. Reverse epidemiology of conventional cardiovascular risk factors in patients with chronic heart failure. *J Am Coll Cardiol* 2004;43:1439–1444.
24. Kang X, Shaw LJ, Hayes SW *et al*. Impact of body mass index on cardiac mortality in patients with known or suspected coronary artery disease undergoing myocardial perfusion single-photon emission computed tomography. *J Am Coll Cardiol* 2006;47:1418–1426.
25. Rapp-Kesek D, Stähle E, Karlsson TT. Body mass index and albumin in the preoperative evaluation of cardiac surgery patients. *Clin Nutr* 2004;23:1398–1404.
26. Engelman DT, Adams DH, Byrne JG *et al*. Impact of body mass index and albumin on morbidity and mortality after cardiac surgery. *J Thorac Cardiovasc Surg* 1999;118:866–873.
27. O'Connor NJ, Morton JR, Birkmeyer JD, Olmstead EM, O'Connor GT. Effects of coronary artery diameter in patients undergoing coronary bypass surgery. *Circulation* 1996;93:652–655.
28. Schunkert M, Harrell L, Palacios IF. Implications of small reference vessel diameter in patients undergoing percutaneous coronary revascularization. *J Am Coll Cardiol* 1999;93:40–48.
29. Juhan-Vague I, Alessi MC, Vague P. Increased plasma plasminogen activator inhibitor 1 levels: A possible link between insulin resistance and atherothrombosis. *Diabetologia* 1991;34:457–462.
30. Al Suwaidi J, Higano ST, Holmes DR Jr, Lennon R, Lerman A. Obesity is independently associated with coronary endothelial dysfunction in patients with normal or mildly diseased coronary arteries. *J Am Coll Cardiol* 2001;37:1523–1528.
31. Ellis SG, Elliott J, Horrigan M, Raymond RE, Howel G. Low-normal or excessive body mass index: Newly identified and powerful risk factors for death and other complications with percutaneous coronary intervention. *Am J Cardiol* 1996;78:642–646.
32. De Devitiis O, Fazio S, Pettito M *et al*. Obesity and cardiac function. *Circulation* 1981;64:477–482.
33. DeSilva R, Lown B. Energy requirements for defibrillation of a markedly overweight patient. *Circulation* 1978;57:827–830.
34. Anker SD, Negassa A, Coats AJ *et al*. Prognostic importance of weight loss in chronic heart failure and the effect of treatment with angiotensin-converting enzyme inhibitors: an observational study. *Lancet* 2003;361:1077–1083.
35. Nikolsky E, Kosinski E, Mishkel GJ *et al*. Impact of obesity on revascularization and restenosis rates after bare-metal and drug-eluting stent implantation. *Am J Cardiol* 2005;95:709–715.
36. Poston WS, Haddock CK, Conard M, Spertus JA. Impact of obesity on disease-specific health status after percutaneous coronary intervention in coronary disease patients. *Int J Obes* 2004;28:1011–1017.
37. Powell BD, Lennon RJ, Lerman A *et al*. Association of body mass index with outcome after percutaneous coronary intervention. *Am J Cardiol* 2003;91:472–476.
38. Christakis GT, Weisel RD, Buth KF *et al*. Is body size the cause for poor outcomes of coronary artery bypass operations in women? *J Thorac Cardiovasc Surg* 1995;110:1344–1358.
39. Ennker J, Schoeneich R, Schroder T, Schoeneich F, Ennker IC. The impact of morbidity obesity on the pre- and postoperative course after aortocoronary bypass surgery. *Deutsche Medizinische Wochenschrift* 2001;125:419–423.
40. Kim J, Hammar N, Jakobsson K *et al*. Obesity and the risk of early and late mortality after coronary artery bypass graft surgery. *Am Heart J* 2003;146:555–560.
41. Orhan G, Bicer Y, Aka SA *et al*. Coronary artery bypass graft operations can be performed safely in obese patients. *Euro J Cardiothorac Surg* 2004;25:212–217.
42. Pan W, Hinder K, Lee VV, Vaughn WK, Collard CD. Obesity in diabetic patients undergoing coronary artery bypass graft surgery is associated with increased postoperative morbidity. *Anesthesiology* 2006;104:441–447.
43. Potapov EV, Lowebe M, Anker S *et al*. Impact of body mass index on outcome in patients after coronary artery bypass grafting with and without valve surgery. *Euro Heart J* 2003;24:1933–1941.
44. Schwann TA, Habib RH, Zacharias A *et al*. Effects of body size on operative, intermediate, and long-term outcomes after coronary artery bypass operation. *Ann Thorac Surg* 2001;71:521–530.
45. Reeves BC, Ascione R, Chamberlain MH, Angelini GD. Effect of body mass index on early outcomes in patients undergoing coronary artery bypass surgery. *J Am Coll Cardiol* 2003;42(4):668–676.
46. Jin R, Grunkemeier GL, Furnary AP, Handy JR Jr. Is obesity a risk factor for mortality in coronary artery bypass surgery? *Circulation* 2005;111:3359–3365.