ORIGINAL RESEARCH

Body Mass Index, Outcomes, and Mortality Following Cardiac Surgery in Ontario, Canada

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***Background*—**The "obesity paradox" reflects an observed relationship between obesity and decreased morbidity and mortality, suggesting improved health outcomes for obese individuals. Studies examining the relationship between high body mass index (BMI) and adverse outcomes after cardiac surgery have reported conflicting results.

***Methods and Results*—**The study population (N=78 762) was comprised of adult patients who had undergone first-time coronary artery bypass (CABG) or combined CABG/aortic valve replacement (AVR) surgery from April 1, 1998 to October 31, 2011 in Ontario (data from the Institute for Clinical Evaluative Sciences). Perioperative outcomes and 5-year mortality among pre-defined BMI (kg/m^2) categories (underweight <20, normal weight 20 to 24.9, overweight 25 to 29.9, obese 30 to 34.9, morbidly obese >34.9) were compared using Bivariate analyses and Cox multivariate regression analysis to investigate multiple confounders on the relationship between BMI and adverse outcomes. A reverse J-shaped curve was found between BMI and mortality with their respective hazard ratios. Independent of confounding variables, 30-day, 1-year, and 5-year survival rates were highest for the obese group of patients (99.1% [95% Confidence Interval {CI}, 98.9 to 99.2], 97.6% [95% CI, 97.3 to 97.8], and 90.0% [95% CI, 89.5 to 90.5], respectively), and perioperative complications lowest. Underweight and morbidly obese patients had higher mortality and incidence of adverse outcomes.

***Conclusions*—**Overweight and obese patients had lower mortality and adverse perioperative outcomes after cardiac surgery compared with normal weight, underweight, and morbidly obese patients. The "obesity paradox" was confirmed for overweight and moderately obese patients. This may impact health resource planning, shifting the focus to morbidly obese and underweight patients prior to, during, and after cardiac surgery. **(*J Am Heart Assoc*. 2015;4:e002140 doi: 10.1161/JAHA.115.002140)**

Key Words: body mass index • bypass graft • coronary artery bypass graft • mortality • obesity

Obesity is a risk factor for premature death due to cardiovascular disease and cancer.[1–4] An "obesity paradox" has been described,[5] which reflects a relationship between obesity, compared with normal weight, and decreased mortality. It refers to counter-intuitive epidemiological evidence suggesting improved health outcomes for obese individuals in a variety of clinical situations.[1] This paradoxical association has been demonstrated in diabetes, end-stage renal disease, hypertension, heart failure, established coronary artery disease (CAD) and peripheral arterial disease.[2,6,7]

Studies examining the relationship between obesity and adverse outcomes following cardiac surgery have reported conflicting results. For example, underweight and morbidly obese patients were shown to require longer postoperative ventilation than moderately obese patients.[8–10] Recent studies demonstrate that obesity affects coronary artery bypass graft surgery (CABG) patients in an advantageous or neutral manner,[7,11] but are at odds with prior studies which suggest a higher mortality and morbidity in obese patients compared with normal weight patients following CABG.[3] Our group previously demonstrated that obesity is a risk factor for failure of "fast track" extubation following CABG.[8] However, most of these studies have small samples and short-term follow-up. Given these limitations, we designed the current study to investigate the relationship between body mass index (BMI) and mortality and other outcomes following cardiac surgery, in a large sample with long-term follow-up, using administrative datasets housed at the Institute for Clinical Evaluative Sciences (ICES) in Ontario, Canada. We sought to determine if BMI is a predictor in determining outcomes following cardiac surgery.

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Methods

Study Population

The study population included patients over 18 years old who had an initial CABG or combined CABG and open chest aortic valve replacement (AVR), from April 1, 1998 to October 31, 2011 in Ontario. The date of first cardiac surgery was the index date, and eligible patients were followed for 1 year with respect to major outcomes, and 5 years for mortality. Preoperative data were included for 1 year prior to surgery, and outcomes for 1 year postoperatively. Patients for whom sex, age, height, weight were missing, and patients living outside of Ontario or of unknown residence were excluded. Cardiac Care Network of Ontario (CCN) data were used to identify baseline characteristics such as cardiac ejection fraction, number of grafts bypassed, prior myocardial infarction (MI), emergency or elective surgery, and other comorbidities. CCN data and the following datasets were combined from ICES using deterministic linkage by unique ICES key number identifiers: Ontario Health Insurance Plan, Canadian Institute of Health Information (CIHI) Discharge Abstract Database, National Ambulatory Care Reporting System, Same Day Surgery, and the Registered Persons Database. This study received ethics approval from the Queen's University Research Ethics Board.

Patients who had undergone either isolated CABG or combined CABG/AVR were selected from the CIHI Discharge Abstract Database. Data for which other cardiac procedures had been performed during the same admission were excluded (eg, percutaneous coronary intervention or other valve procedures).

Baseline Characteristics and Comorbidities

Baseline characteristics on index date included age, sex, and BMI. BMI was calculated as weight (kg)/height (m^2), and patients were divided into groups: underweight (BMI <20 kg/m^2), normal weight (BMI 20.0 to 24.9 kg/m^2), overweight (BMI 25.0 to 29.9 kg/m^2), obese (BMI 30.0 to 34.9 kg/m^2), and morbidly obese (BMI >34.9 kg/m^2), closely based on World Health Organization (WHO) and Health Canada guidelines.[12–14] The following comorbidities were assessed for presence within 1 year prior to index date: diabetes, smoking history (current or ever smoked), peripheral vascular disease (PVD), chronic obstructive pulmonary disease (COPD), dialysis within 1 year prior to surgery, cerebrovascular disease (CVD), congestive heart failure (CHF, from CIHI), hypertension, elective or emergent surgery, creatinine. Within 30 days prior to surgery, the following cardiac characteristics were captured: ejection fraction, prior MI, left main coronary disease, and previous CABG at date of surgery. At index date, the cardiac characteristics were number of grafts, off-pump surgery, and type of operation. The Elixhauser index, a measurement score that includes 30 co-existing conditions, was used to account for baseline comorbidities that are predictive of long-term mortality.[15,16]

Outcome Definition

From index date to date of discharge, outcomes of interest were surgery type, total length of stay (LOS) in hospital, LOS excluding Alternative Level of Care-LOS, surgery duration, reoperation, time in intensive care unit (ICU), postoperative creatinine, blood transfusion, dialysis, stroke, MI, and death at discharge during hospital admission, and transfusion of blood products. Post-discharge outcomes collected included readmission rates within 60 days of discharge, dialysis, stroke, and MI within 60 days and 1 year of discharge, and mortality at 30 days, 1 and 5 years.

Statistical Analysis

Mean and standard deviation (SD) were used for continuous variables, and categorical variables were expressed as percentages. To detect differences between the BMI groups, ANOVA was used, and Mann-Kendall trend test was used to test significant differences in BMI over time. Five-year mortality was compared using bivariate analyses, and Cox multivariate regression analysis to investigate multiple confounders on the relationship between BMI and patient mortality, providing hazard ratios and 95% confidence intervals (CI). Age, gender, diabetes, smoking history, PVD, COPD, dialysis, hypertension, serum creatinine, CVD, CHF, Elixhauser index, surgery type, LOS, reoperation, blood transfusion, stroke in hospital, MI in hospital, dialysis within 1 year, stroke within 1 year, MI within 1 year, ejection fraction, prior MI, elective or emergent surgery, left main coronary disease, previous CABG, and BMI were included in the model. For missing values, analyses were conducted adjusting the denominator. SAS software (version 9.3, Statistical Analysis System Institute) was used for statistical analyses, with $P<0.05$ considered significant.

Results

The study population consisted of 78 762 patients. Tables 1 through 3 show preoperative characteristics and postoperative outcomes. Where specific values were not available for all study years, total sample size analyzed is indicated.

Baseline Characteristics

Table 1 lists baseline characteristics of the BMI groups. Twenty-two percent of the patients were classified as normal

Table 1. Baseline Characteristics

Variable	Under Weight (n=1228)	Normal Weight (n=17 162)	Over Weight (n=34 597)	Obese (n=18 147)	Morbidly Obese (n=7628)	Total (n=78 762)	*P* Value*
Age at admission							
Mean±SD	67.81±10.95	66.86±10.23	65.37±9.90	63.67±9.73	61.78±9.61	64.99±10.04	<0.001
Sex							
Female, n (%)	501 (40.8)	3985 (23.2)	6156 (17.8)	3790 (20.9)	2261 (29.6)	16 693 (21.2)	<0.001
Weight, kg							
Mean±SD	53.17±7.50	66.87±8.15	79.71±9.27	92.28±10.86	109.32±18.08	82.26±16.54	<0.001
Body mass index							
Mean±SD	18.72±1.34	23.29±1.26	27.45±1.39	32.03±1.38	39.69±9.67	28.65±5.80	<0.001
Diabetes							
n (%)	410 (33.4)	5990 (34.9)	12 560 (36.3)	8253 (45.5)	4409 (57.8)	31 622 (40.1)	<0.001
Smoke history							
n (%)	696 (56.7)	9341 (54.4)	20 705 (59.8)	11 531 (63.5)	4934 (64.7)	47 207 (59.9)	<0.001
Peripheral vascular disease							
n (%)	213 (17.3)	2249 (13.1)	3993 (11.5)	2099 (11.6)	814 (10.7)	9368 (11.9)	<0.001
Chronic obstructive pulmonary disease							
n (%)	174 (14.2)	1262 (7.4)	2219 (6.4)	1380 (7.6)	792 (10.4)	5827 (7.4)	<0.001
Dialysis within 1 year prior to surgery							
n (%)	17 (1.4)	130 (0.8)	127 (0.4)	62 (0.3)	38 (0.5)	374 (0.5)	<0.001
Cerebrovascular disease							
n (%)	143 (11.6)	1817 (10.6)	3269 (9.4)	1557 (8.6)	654 (8.6)	7440 (9.4)	<0.001
CHF status							
n (%)	43 (3.5)	344 (2.0)	506 (1.5)	239 (1.3)	129 (1.7)	1261 (1.6)	<0.001
Number of grafts							
Mean±SD	2.55±0.78	2.61±0.76	2.63±0.74	2.61±0.75	2.57±0.77	2.61±0.75	<0.001
Median (IQR)	3 (2 to 3)	3 (2 to 3)	3 (2 to 3)	3 (2 to 3)	3 (2 to 3)	3 (2 to 3)	<0.001
Off pump							
n (%)	69 (5.6)	657 (3.8)	1196 (3.5)	612 (3.4)	256 (3.4)	2790 (3.5)	<0.001
Elixhauser index							
Mean±SD	2.88±2.04	2.35±1.84	2.22±1.75	2.45±1.83	3.02±1.96	2.39±1.83	<0.001
Median (IQR)	3 (1 to 4)	2 (1 to 3)	2 (1 to 3)	2 (1 to 3)	3 (2 to 4)	2 (1 to 3)	<0.001
Hypertension (n=30 931)†							
n (%)	342 (63.3)	4619 (66.3)	8952 (69.1)	5304 (74.2)	2646 (79.7)	21 863 (70.7)	<0.001
Ejection fraction (n=40 349)†							
1, n (%)	253 (43.5)	3985 (47.2)	8767 (48.4)	4444 (47.0)	1752 (46.6)	19 201 (47.6)	0.007
2, n (%)	168 (28.9)	2445 (28.9)	5285 (29.2)	2883 (30.5)	1125 (30.0)	11 906 (29.5)	
3 or 4, n (%)	118 (20.3)	1433 (17.0)	2891 (16.0)	1481 (15.7)	603 (16.1)	6526 (16.2)	
Prior myocardial infarction							
n (%)	68 (26.4)	886 (25.1)	1360 (23.2)	793 (24.5)	385 (24.7)	3492 (24.2)	0.214
Left main disease (n=34 994)†							
n (%)	141 (28.0)	1878 (26.6)	3771 (24.2)	1809 (21.9)	747 (21.0)	8346 (23.8)	<0.001

Continued

Table 1. Continued

Variable	Under Weight (n=1228)	Normal Weight (n=17 162)	Over Weight (n=34 597)	Obese (n=18 147)	Morbidly Obese (n=7628)	Total (n=78 762)	*P* Value*
Emergent or non-emergent (n=53 230)†							
Emergent, n (%)	7 (0.9)	126 (1.1)	202 (0.8)	87 (0.7)	25 (0.5)	447 (0.8)	0.004
Non-emergent, n (%)	767 (98.5)	11 103 (98.4)	23 687 (98.7)	12 123 (98.9)	4864 (99.2)	52 544 (98.7)	
Creatinine, μmol/L (n=30 886)†							
Mean±SD	99.59±82.00	98.15±61.29	96.44±55.26	96.35±55.08	95.07±48.60	96.76±56.71	0.102
>180, n (%)	27 (5.1)	164 (2.3)	236 (1.8)	115 (1.6)	59 (2.0)	601 (1.9)	<0.001

ANOVA indicates analysis of variance; CHF, congestive heart failure; SD, standard deviation.
*Overall, by ANOVA.
†Where data are missing, total n is indicated in the variable cell.

Table 2. Perioperative Characteristics Occurring Between Surgery and Discharge, Unless Otherwise Indicated

Variable	Under Weight (n=1228)	Normal Weight (n=17 162)	Over Weight (n=34 597)	Obese (n=18 147)	Morbidly Obese (n=7628)	Total (n=78 762)	*P* Value*
Surgery type							
CABG only, n (%)	1074 (87.5)	15 611 (91.0)	31 809 (91.9)	16 587 (91.4)	6911 (90.6)	71 992 (91.4)	<0.001
CABG+aortic, n (%)	154 (12.5)	1551 (9.0)	2788 (8.1)	1560 (8.6)	717 (9.4)	6770 (8.6)	
Length of hospital stay, days							
Mean±SD	8.6±8.5	7.6±7.7	7.2±7.0	7.4±7.5	8.1±8.6	7.4±7.5	<0.001
Length of hospital stay excluding alternative level of care, days							
Mean±SD	8.3±8.0	7.4±7.0	7.1±6.1	7.3±7.0	7.9±8.3	7.3±6.8	<0.001
Surgery duration, hours							
Mean±SD	4.4±1.3	4.3±1.3	4.4±1.5	4.5±1.4	4.7±1.3	4.5±1.4	<0.001
Reoperation							
n (%)	26 (2.1)	204 (1.2)	304 (0.9)	126 (0.7)	46 (0.6)	706 (0.9)	<0.001
Intensive care unit time, hours (n=52 715)†							
Mean±SD	95.4±156.2	77.3±124.5	70.0±124.8	75.8±159.6	84.1±157.0	74.8±137.7	<0.001
Postoperative creatinine, μmol/L (n=30 887)†							
Mean±SD	99.6±82.0	98.2±61.3	96.4±55.3	96.4±55.1	95.1±48.6	96.8±56.7	0.101
Blood transfusion (red blood cells) (n=72 631)†							
n (%)	810 (71.1)	8582 (54.4)	13 095 (41.2)	5743 (34.3)	2360 (32.8)	30 590 (42.1)	<0.001
Blood transfusion (platelets or plasma) (n=72631)†							
n (%)	453 (39.8)	5277 (33.4)	8845 (27.8)	4045 (24.2)	1639 (22.8)	20 259 (27.9)	<0.001
Dialysis							
n (%)	28 (2.3)	204 (1.2)	339 (1.0)	196 (1.1)	105 (1.4)	872 (1.1)	<0.001
Stroke							
n (%)	≤5 (0.3)	54 (0.3)	101 (0.3)	41 (0.2)	18 (0.2)	218 (0.3)	0.486
Myocardial infarction							
n (%)	245 (20.0)	2944 (17.2)	4828 (14.0)	2234 (12.3)	933 (12.2)	11 184 (14.2)	<0.001
Death							
n (%)	42 (3.4)	256 (1.5)	356 (1.0)	168 (0.9)	88 (1.2)	910 (1.2)	<0.001

ANOVA indicates analysis of variance; CABG, coronary artery bypass graft, SD, standard deviation.
*Overall, by ANOVA.
†Where data are missing, total n is indicated in the variable cell.

Table 3. Patient Outcomes After Discharge

Variable	Under Weight (n=1228)	Normal Weight (n=17 162)	Over Weight (n=34 597)	Obese (n=18 147)	Morbidly Obese (n=7628)	Total (n=78 762)	*P* Value*
1-year mortality	107 (8.7)	663 (3.9)	906 (2.6)	447 (2.5)	235 (3.1)	2358 (3.0)	<0.001
5-year mortality	275 (22.4)	2053 (12.0)	3263 (9.4)	1697 (9.4)	826 (10.8)	8114 (10.3)	<0.001
Readmission within 60 days	244 (19.9)	2600 (15.1)	4754 (13.7)	2649 (14.6)	1412 (18.5)	11 659 (14.8)	<0.001
Dialysis within 1 year	19 (1.5)	161 (0.9)	237 (0.7)	122 (0.7)	83 (1.1)	622 (0.8)	<0.001
Stroke within 1 year	≤5 (0.4)	82 (0.5)	148 (0.4)	72 (0.4)	38 (0.5)	345 (0.4)	0.722
MI within 60 days	18 (1.5)	242 (1.4)	363 (1.0)	166 (0.9)	87 (1.1)	876 (1.1)	<0.001
MI within 1 year	42 (3.4)	434 (2.5)	708 (2.0)	333 (1.8)	166 (2.2)	1683 (2.1)	<0.001

Variables are reported as n (%). ANOVA indicates analysis of variance; MI, myocardial infarction.
*Overall difference, by ANOVA.

weight (N=17 162), with 44% overweight (N=34 597), 23% obese (N=18 147), 10% morbidly obese (N=7628), and 2% underweight (N=1228). Underweight patients were the oldest (mean±SD: 68±11), constituted the largest number of females (41%), had the highest rates of PVD, COPD, dialysis, CVD, CHF, left ventricular grades 3 or 4, and left main coronary disease, creatinine. The morbidly obese group was the youngest, and experienced the highest rates of diabetes and hypertension. Although more obese/morbidly obese patients had any smoking history, more underweight patients were current smokers at the time of surgery, compared with normal weight patients. There was no difference in mean serum creatinine, but a significant difference in creatinine concentration >180 μmol/L. The median number of bypass grafts for all BMI groups was 3; and 3.5% of patients had off-pump surgery, with the underweight group having the most at

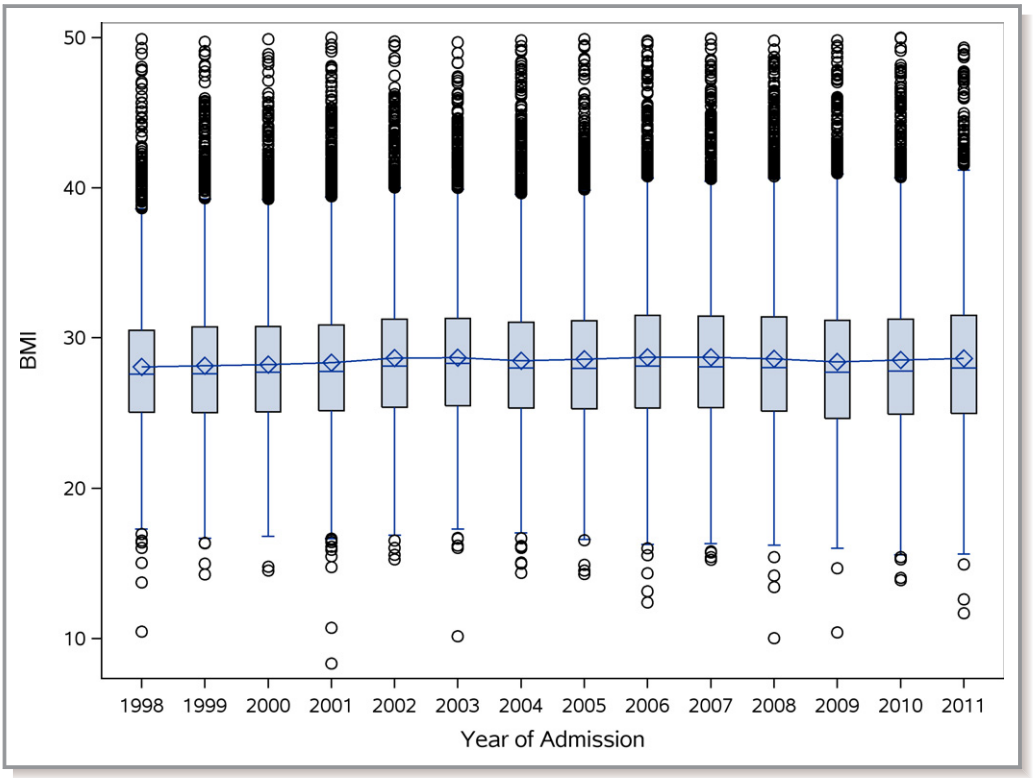

Figure 1. The box in the boxplot displays the median (diamonds), mean (dashes), and encompasses the 25th and the 75th percentiles; lines include × 1.5 interquartile range beyond the 25th and 75th percentiles; the outer circles represent outliers. There was no significant trend found over the years of the study (*P*=0.1005) using the Mann-Kendall trend test. BMI indicates body mass index.

Table 4. Proportion of Patients Alive at 3 Time Intervals Following Date of Surgery (95% Confidence Intervals)

BMI Category	30 Days	1 Year	5 Years
Under weight (n=1228)	0.965 (0.954, 0.977)	0.914 (0.896, 0.932)	0.759 (0.730, 0.787)
Normal weight (n=17 162)	0.985 (0.983, 0.987)	0.962 (0.959, 0.965)	0.872 (0.866, 0.878)
Over weight (n=34 597)	0.990 (0.988, 0.991)	0.974 (0.972, 0.976)	0.900 (0.896, 0.903)
Obese (n=18 147)	0.991 (0.989, 0.992)	0.976 (0.973, 0.978)	0.900 (0.895, 0.905)
Morbidly obese (n=7628)	0.988 (0.985, 0.990)	0.970 (0.965, 0.974)	0.883 (0.874, 0.892)

BMI indicates body mass index.
N=78 762.

5.6%. There was an overall statistical difference between BMI groups in all baseline characteristics, except for mean serum creatinine and prior MI.

In-Hospital Clinical Outcomes

Table 2 presents outcomes from index (surgery) date to date of discharge. Ninety-one percent of patients had CABG only and 9% combined surgery. The underweight group had the greatest hospital LOS, reoperation rates, ICU hours, dialysis, MI, and blood (red cell, platelet) transfusion, and number of deaths. The morbidly obese group experienced the longest surgery duration. The difference between BMI groups in postoperative serum creatinine and stroke was non-significant.

Table 3 shows post-discharge outcomes with an overall statistical difference between BMI groups for all events, except stroke within 1 year of discharge. The underweight group experienced the highest rates of surgery readmission, MI, and mortality.

BMI Trend by Year and Mortality

Figure 1 shows a trend analysis for BMI from 1998 to 2011. The mean period of follow-up was 7.8±4 years, with 12 392 deaths. Overall, 30-day, 1- and 5-year survival rates were highest for the obese group (99.1% [95% CI, 98.9 to 99.2], 97.6% [95% CI, 97.3 to 97.8], and 90.0% [95% CI, 89.5 to 90.5]), respectively, and lowest for the underweight group

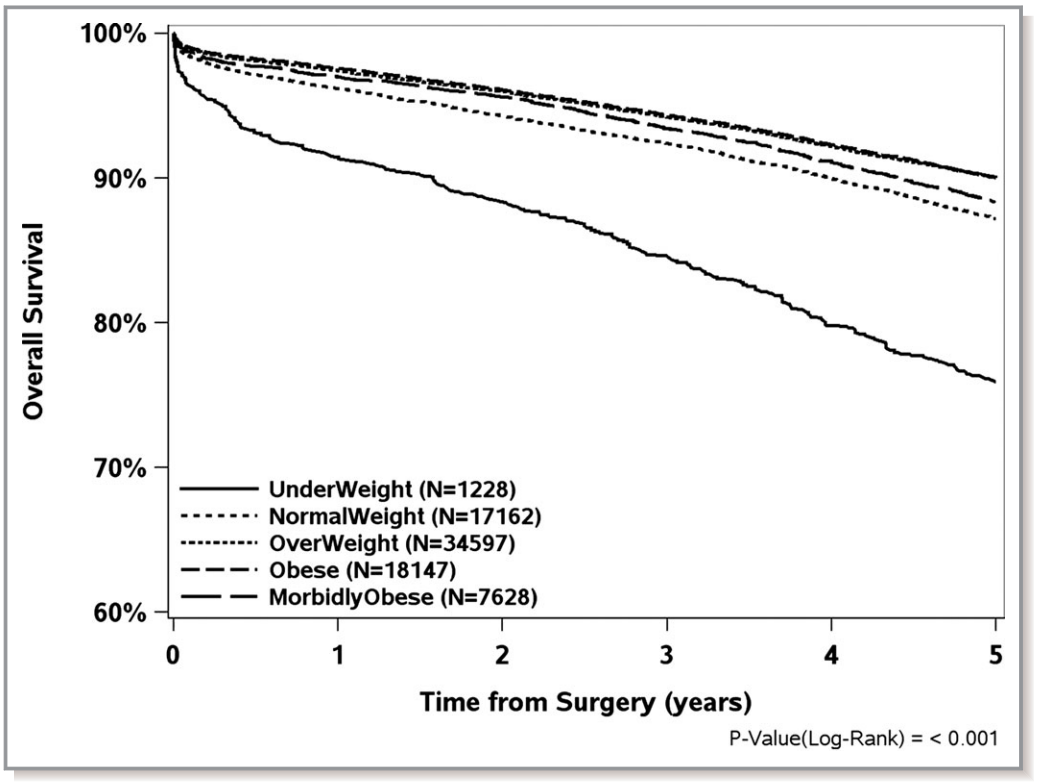

Figure 2. Kaplan-Meier Curves indicating overall 5-year survival from date of surgery, by body mass index category.

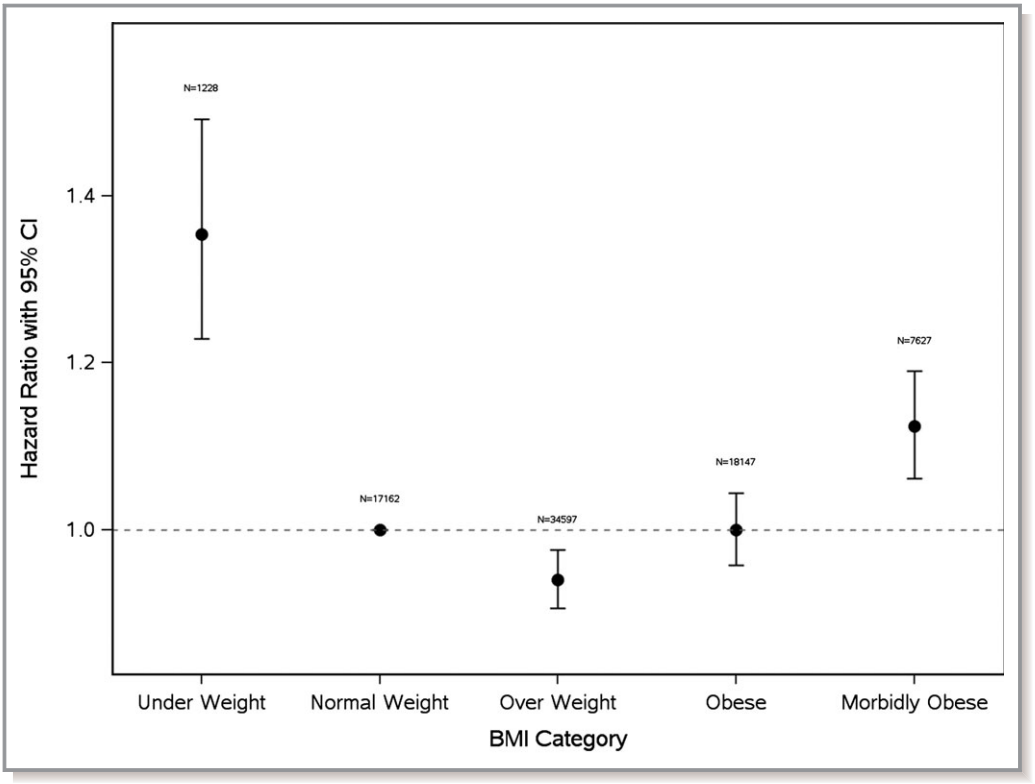

Figure 3. Hazard ratios for mortality with 95% confidence intervals by body mass index category, with reference to normal weight. BMI indicates body mass index.

(96.5% [95% CI, 95.4 to 97.7], 91.4% [95% CI, 89.6 to 93.2], and 75.9% [95% CI, 73.0 to 78.7]) (Table 4 and Figure 2). A reverse J-shaped relationship exists between BMI range and mortality (Figure 3), with their respective hazard ratios, using normal weight as the reference: underweight (1.35 [95% CI, 1.23 to 1.49]); overweight (0.94 [95% CI, 0.91 to 0.98]); obese (1.00 [95% CI, 0.96 to 1.04]); morbidly obese (1.12 [95% CI, 1.06 to 1.19]).

Factors related to the risk of death using bivariate (Table 5) and multivariate (Table 6) analyses are presented. Clinical considerations dictated the choice between co-linear variables, which included age, sex, diabetes, smoking history, PVD, COPD, dialysis, CVD, CHF, Elixhuaser index, surgery type, LOS, reoperation, blood transfusion, stroke in hospital, MI in hospital, dialysis within 1 year, stroke within 1 year, MI within 1 year.

In the bivariate analysis, BMI significantly influenced survival when each of the above variables were factored into the model, with reference to the normal weight group for all variables, except PVD, CVD, MI in hospital for morbidly obese group. For example, adjusting for age (eg, underweight comprised the oldest BMI group), BMI independently influenced mortality (hazard ratio for underweight group 1.62, CI 1.48 to 1.79). Even when adjusting for co-morbidities (Elixhauser index), BMI still affected mortality (hazard ratio for underweight group 1.39, CI 1.26 to 1.53). Similarly, considering the morbidly obese group was youngest, BMI still independently affected mortality.

Using multivariate analysis, the reverse J-curve relationship between BMI and mortality was confirmed (Figure 3). Underweight patients had a significantly higher risk of death (hazard ratio, 1.35, 95% CI, 1.23 to 1.49) compared with patients with normal weight, as did morbidly obese patients (hazard ratio, 1.12, 95% CI, 1.06 to 1.19). There was a survival advantage in the overweight group, and no difference in the obese group, compared with normal weight. The Elixhauser index was highly predictive of mortality, such that for each 1 point increase, there was a 22% increase in mortality rate. Age also impacted mortality, such that for every year of increase in age, the chance of death increased by 6%, taking BMI and all other factors relating to survival into account. However, BMI had an independent influence on mortality when adjusting for both age and risk score.

Discussion

Obesity is a well-recognized risk factor for the development of cardiovascular disease, and patients with high BMI are highly represented among the population presenting for cardiac surgery (77% of the total in the current study). However, we have confirmed, using a cohort study with large administrative

Table 5. Bivariate Cox Analysis

Variable	Value	Parameter Estimate	Hazard Ratio	95% Lower Confidence Limit	95% Upper Confidence Limit	*P* Value
Age at admission		0.073	1.076	1.074	1.078	<0.001
	Under weight	0.485	1.624	1.475	1.789	<0.001
	Over weight	−0.092	0.912	0.879	0.946	<0.001
	Obese	0.054	1.056	1.011	1.102	0.013
	Morbidly obese	0.320	1.377	1.303	1.456	<0.001
Sex (female)		0.202	1.224	1.184	1.266	<0.001
	Under weight	0.496	1.642	1.491	1.809	<0.001
	Over weight	−0.182	0.833	0.803	0.865	<0.001
	Obese	−0.171	0.843	0.808	0.879	<0.001
	Morbidly obese	−0.076	0.927	0.878	0.980	0.007
Diabetes		0.459	1.582	1.536	1.629	<0.001
	Under weight	0.533	1.705	1.548	1.877	<0.001
	Over weight	−0.200	0.819	0.789	0.849	<0.001
	Obese	−0.224	0.799	0.766	0.834	<0.001
	Morbidly obese	−0.161	0.852	0.806	0.900	<0.001
Smoking history		0.194	1.214	1.178	1.252	<0.001
	Under weight	0.531	1.701	1.545	1.874	<0.001
	Over weight	−0.208	0.812	0.782	0.843	<0.001
	Obese	−0.197	0.821	0.787	0.857	<0.001
	Morbidly obese	−0.084	0.919	0.870	0.971	0.003
PVD		0.831	2.296	2.216	2.380	<0.001
	Under weight	0.500	1.649	1.497	1.816	<0.001
	Over weight	−0.187	0.829	0.799	0.860	<0.001
	Obese	−0.171	0.843	0.808	0.880	<0.001
	Morbidly obese	−0.043	0.958	0.907	1.012	0.124
COPD		0.769	2.158	2.066	2.255	<0.001
	Under weight	0.477	1.612	1.463	1.775	<0.001
	Over weight	−0.195	0.823	0.793	0.854	<0.001
	Obese	−0.190	0.827	0.793	0.863	<0.001
	Morbidly obese	−0.099	0.905	0.857	0.957	<0.001
Dialysis		1.332	3.789	3.465	4.145	<0.001
	Under weight	0.506	1.658	1.506	1.827	<0.001
	Over weight	−0.185	0.831	0.801	0.863	<0.001
	Obese	−0.166	0.847	0.812	0.884	<0.001
	Morbidly obese	−0.051	0.950	0.899	1.004	0.069
Cerebrovascular disease		0.725	2.066	1.985	2.150	<0.001
	Under weight	0.525	1.691	1.535	1.862	<0.001
	Over weight	−0.186	0.830	0.800	0.861	<0.001
	Obese	−0.162	0.851	0.815	0.888	<0.001
	Morbidly obese	−0.044	0.957	0.906	1.011	0.118

Continued

Table 5. Continued

Variable	Value	Parameter Estimate	Hazard Ratio	95% Lower Confidence Limit	95% Upper Confidence Limit	*P* Value
CHF		1.464	4.321	4.035	4.628	<0.001
	Under weight	0.508	1.661	1.508	1.830	<0.001
	Over weight	−0.186	0.830	0.800	0.862	<0.001
	Obese	−0.165	0.848	0.813	0.885	<0.001
	Morbidly obese	−0.059	0.942	0.892	0.996	0.034
Elixhauser index		0.329	1.389	1.381	1.398	<0.001
	Under weight	0.329	1.390	1.262	1.531	<0.001
	Over weight	−0.166	0.847	0.816	0.879	<0.001
	Obese	−0.244	0.783	0.751	0.818	<0.001
	Morbidly obese	−0.333	0.717	0.678	0.758	<0.001
Surgery (CABG only)		−0.948	0.388	0.372	0.404	<0.001
	Under weight	0.492	1.636	1.485	1.802	<0.001
	Over weight	−0.191	0.826	0.796	0.857	<0.001
	Obese	−0.174	0.840	0.805	0.877	<0.001
	Morbidly obese	−0.063	0.939	0.889	0.992	0.026
Length of hospital stay, days		0.018	1.018	1.017	1.019	<0.001
	Under weight	0.517	1.677	1.522	1.846	<0.001
	Over weight	−0.177	0.838	0.808	0.870	<0.001
	Obese	−0.179	0.836	0.801	0.873	<0.001
	Morbidly obese	−0.077	0.926	0.877	0.978	0.006
Reoperation		0.816	2.262	1.991	2.569	<0.001
	Under weight	0.526	1.692	1.536	1.863	<0.001
	Over weight	−0.192	0.825	0.795	0.856	<0.001
	Obese	−0.172	0.842	0.807	0.878	<0.001
	Morbidly obese	−0.058	0.944	0.894	0.997	0.04
Blood transfusion	Red blood cell	0.653	1.921	1.852	1.993	<0.001
	Platelet	0.177	1.193	1.029	1.383	0.019
	Other	0.148	1.159	1.095	1.228	<0.001
	Under weight	0.443	1.557	1.414	1.715	<0.001
	Over weight	−0.110	0.897	0.864	0.931	<0.001
	Obese	−0.044	0.957	0.917	0.999	0.044
	Morbidly obese	0.085	1.088	1.030	1.150	0.003
Stroke in hospital		1.001	2.722	2.255	3.286	<0.001
	Under weight	0.533	1.704	1.547	1.877	<0.001
	Over weight	−0.194	0.823	0.794	0.854	<0.001
	Obese	−0.174	0.840	0.805	0.877	<0.001
	Morbidly obese	−0.061	0.941	0.891	0.994	0.03
MI in hospital		0.170	1.186	1.141	1.233	<0.001
	Under weight	0.525	1.690	1.534	1.861	<0.001
	Over weight	−0.190	0.827	0.797	0.858	<0.001
	Obese	−0.168	0.845	0.810	0.882	<0.001
	Morbidly obese	−0.053	0.948	0.898	1.002	0.059

Continued

Table 5. Continued

Variable	Value	Parameter Estimate	Hazard Ratio	95% Lower Confidence Limit	95% Upper Confidence Limit	*P* Value
Dialysis within 1 year of discharge		1.717	5.565	5.045	6.139	<0.001
	Under weight	0.502	1.652	1.500	1.819	<0.001
	Over weight	−0.188	0.829	0.799	0.860	<0.001
	Obese	−0.169	0.845	0.810	0.882	<0.001
	Morbidly obese	−0.061	0.941	0.890	0.994	0.029
Stroke within 1 year of discharge		1.255	3.507	3.052	4.031	<0.001
	Under weight	0.529	1.696	1.540	1.868	<0.001
	Over weight	−0.196	0.822	0.792	0.853	<0.001
	Obese	−0.175	0.839	0.804	0.876	<0.001
	Morbidly obese	−0.063	0.939	0.889	0.992	0.025
MI within 1 year of discharge		0.889	2.433	2.258	2.621	<0.001
	Under weight	0.535	1.707	1.550	1.880	<0.001
	Over weight	−0.192	0.825	0.796	0.857	<0.001
	Obese	−0.171	0.843	0.807	0.879	<0.001
	Morbidly obese	−0.058	0.944	0.894	0.997	0.04

Hazard ratios for mortality for each BMI category with respect to the Normal Weight group. For each comorbidity factor, overall hazard ratios are shown, followed by effect of BMI category adjusted for that factor. CABG indicates coronary artery bypass graft; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; PVD, peripheral vascular disease.

datasets and 5-year follow-up for survival analysis and mean follow-up of 7.8 years (±4 years) that overweight and obese patients who undergo cardiac surgery have a survival advantage over underweight, normal weight, and morbidly obese patients. A reverse J-shaped relationship was found relating BMI with mortality, such that BMI independently predicted survival when multiple confounders were considered.

At times of illness and stress, excess adiposity may confer an advantage.[17] Low BMI individuals may not have the reserve to tolerate the effects of weight loss as readily as obese individuals, potentially contributing towards high mortality.[18,19] The improved survival of obese patients could be attributed to high metabolic reserves and body fat.[20,21] This may be due to an increase in secretion of amino acids and dipokines, a decrease in the levels of B-type natriuretic peptide and in oxidative stress and inflammation.[22] Potential moderators of the relationship between obesity and mortality may include hormones and cytokines.[20,21,23,24] It can be argued that the observed reverse J-shaped relationship in our study can be due to reverse causation, since the underweight group could have been malnourished or cachectic and were older, with a high prevalence of comorbidities.[25–27] In order to adjust for important confounders, obesity could be considered as a time-varying exposure to account for changes in weight status over the lifespan.[28,29] However, no substantial change in mortality risk has been shown when excluding patients who had a history of cancer, or who died within the first 4 years of follow-up.[30–32] In the current study, bivariate and multivariate analyses demonstrated that effect modification due to age had an impact on results; however, when adjusting for age, there was still a significant relationship between BMI and mortality. Our findings may also be due to lead-time bias, since patients with high BMI tend to be treated sooner.[23,33]

This study demonstrated the lowest survival following cardiac surgery in the underweight group. As low BMI could represent a surrogate for serious underlying illness, we attributed a well-validated co-morbidity index to all patients. The Elixhauser index was developed on administrative data from California, and is designed to be used with large data sets.[15,16,34] The index includes 30 co-existing conditions using International Statistical Classification of Disease codes ICD-9 and ICD-10. Its performance has been shown in a recent systematic review to provide the best fit among various co-morbidity indices, especially when estimating mortality beyond 30 days.[35] Unsurprisingly, the Elixhauser index was highest in the underweight and morbidly obese groups. When including the Elixhauser index in our bivariate and multivariate models, low BMI remained the most significant independent predictor of mortality.

Our results correspond with findings that have examined BMI and mortality, in that moderate obesity provides a protective effect in patients who undergo cardiac surgery[20,21,23,36–38] and the general population.[1,39] However,

Table 6. Multivariate Cox Analysis

Variable	Parameter Estimate	Hazard Ratio	95% Lower Confidence Limit	95% Upper Confidence Limit	*P* Value
Under weight BMI	0.303	1.354	1.229	1.493	<0.001
Over weight BMI	−0.062	0.940	0.906	0.976	0.001
Obese BMI	−0.001	0.999	0.957	1.044	0.981
Morbidly obese BMI	0.117	1.124	1.061	1.190	<0.001
Age at admission	0.060	1.062	1.060	1.064	<0.001
Sex (female)	−0.100	0.905	0.873	0.937	<0.001
Diabetes	0.100	1.106	1.071	1.142	<0.001
Smoking history	0.251	1.286	1.245	1.328	<0.001
Peripheral vascular disease	0.307	1.360	1.309	1.412	<0.001
Chronic obstructive pulmonary disease	0.304	1.355	1.295	1.417	<0.001
Dialysis	0.656	1.926	1.745	2.126	<0.001
Cerebrovascular disease	0.178	1.195	1.146	1.246	<0.001
Congestive heart failure	0.409	1.506	1.402	1.618	<0.001
Elixhauser index	0.195	1.216	1.205	1.226	<0.001
Surgery type: CABG only	−0.186	0.830	0.794	0.868	<0.001
Length of hospital stay, days	0.009	1.009	1.008	1.010	<0.001
Red blood cell transfusion	0.183	1.201	1.156	1.248	<0.001
Platelet transfusion	0.045	1.046	0.902	1.212	0.555
Other transfusion	0.106	1.112	1.049	1.177	<0.001
Stroke in hospital	0.358	1.430	1.183	1.729	<0.001
Myocardial infarction in hospital	0.087	1.091	1.049	1.135	<0.001
Dialysis within 1 year of discharge	0.379	1.461	1.310	1.629	<0.001
Stroke within 1 year of discharge	0.566	1.761	1.531	2.026	<0.001
Myocardial infarction within 1 year of discharge	0.501	1.651	1.530	1.781	<0.001

Hazard ratios for factors with significant effect on mortality. Each line represents the effect of that factor on mortality, adjusting for all other factors in this model. BMI indicates body mass index; CABG, coronary artery bypass graft.

limitations in past studies include a short follow-up of 3 years or less,[33,36,38,40] a small sample, and limited numbers of deaths,[23,41–46] as well as not accounting for possible confounders, such as chronic illness and smoking.[21,47] Certain studies with relatively small sample sizes and short follow-up[45,46] found no significant association between non-morbid obesity and mortality for CABG patients. Benedetto et al retrospectively studied 13 963 patients over 5 years and found that, using propensity score matching, obesity did not contribute towards operative mortality, but was related to a decrease in late survival in patients undergoing CABG.[41] However, their analysis was not statistically significant because of the small number of morbidly obese patients (N=211).

Other studies with follow-up longer than 3 years[12,47] found similar patterns, with a reverse J- or U-shaped relationship between BMI and mortality. Gurm et al found a curvilinear relationship between BMI and 5-year mortality, with higher risk of death associated with BMI extremes in patients who had undergone CABG (N=1526).[12] Sarno et al investigated the impact of BMI on 7427 patients who had been treated by percutaneous coronary intervention (PCI), assessing 5-year mortality.[37] They found that the "obesity paradox" observed could have been due to a large proportion of elderly patients in the normal BMI group. However, as in our study, obese patients had a higher rate of risk factors compared with the normal BMI group. In contrast, morbidly obese patients were the youngest, constituted the largest group of smokers, and had the highest rates of diabetes. Also congruent with our findings, Hastie et al examined 4880 patients who had undergone PCI for CAD over 5 years, and observed a U-shaped relationship between BMI and mortality, with the highest mortality risk for the underweight group.[23] Similarly, Birkmeyer et al found that obesity was not associated with increased mortality (N=11 101 CABG patients) over 4 years.[48]

The main strengths of our study are the large sample, allowing for robust analyses among BMI categories (particularly underweight and morbidly obese patients), and the long follow-up (5 years). In addition, numerous potential confounding variables were adjusted for, revealing results that were attributable to BMI alone. In particular, although the baseline risk index differed between BMI groups, when this was factored into multivariate analysis, the difference in mortality attributed to BMI was independent of baseline risk index. Limitations include using retrospective data, determination of all-cause mortality only, lack of inclusion of ethnicity, and lack of data related to fitness or weight change before surgery. Additionally, a possible confounding relationship of socioeconomic status with BMI has yet to be studied in this population.

The importance of our findings lies in risk assessment of patients presenting for cardiac surgery and the allocation of resources. Moderate obesity cannot be presumed to predict complications after surgery, whereas underweight and normal weight patients (aggregate BMI <25) may consume additional health care resources. The economic effect of these findings remains to be studied. The validity of BMI as an accurate adiposity measure has been questioned, given muscle mass decline with age,[49,50] as it does not account for body composition or the location of adipose tissue.[51–53] Nevertheless, several studies have shown that the obesity paradox exists with any measure of adiposity.[24,51,54–56] The definition of the BMI categories in the current study are closely based on WHO and Health Canada guidelines (with the exception of "underweight" being considered as BMI <18.5 in these guidelines).[13,14] These definitions reflect relative levels of risk to health.[14] Following the results of this and other studies confirming an obesity paradox in various clinical situations, we suggest that traditional BMI categorization may need to be revisited.

In summary, although obesity is a well-recognized risk factor for cardiovascular disease, overweight and moderately obese patients showed improved outcomes following CABG and CABG/AVR with respect to patients with "normal" BMI. As outcomes were significantly worse for morbidly obese and underweight patients, focus should be placed on these populations in risk assessment, preparation, and resource allocation prior to cardiac surgery.

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Disclosures

None.

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