Original Article

The effect of weight loss on the outcome after coronary artery bypass grafting in obese patients

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ABSTRACT

The role of body mass index (BMI) in the setting of coronary artery bypass graft (CABG) surgery has been a focus of past studies. However, the effects of postoperative weight loss in patients after CABG is yet to be known. We performed a retrospective study of 899 patients who underwent CABG at our institution. Perioperative patient information was collected from an onsite electronic record system. Patients were grouped into four BMI categories: normal controls, overweight, obese and morbidly obese. Based on the postoperative BMI changes, patients were then grouped into three categories: gainers, no change and losers. Statistical analyses were performed using analysis of variance and linear regression to establish an association among the data. Hazard ratios (HR) and cumulative survival were obtained by the Cox-Mantel and Kaplan-Meier analyses, respectively. The normal controls exhibited a markedly higher mortality postoperatively, at 27.9%, especially when compared with the obese individuals (16.1%). Patients who lost weight faced a significantly increased risk of mortality than those who experienced no changes or gained weight after surgery. This trend was especially salient among the obese patients, who more than tripled their mortality risk (HR = 3.24) versus individuals who gained weight, and more than doubled their risk (HR = 2.87) versus those who had no changes. We conclude that obesity confers a survival advantage in the setting of the CABG surgery. Weight loss among all BMI categories of patients studied results in an adverse effect on postoperative survival.

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INTRODUCTION

With the prevalence of overweight and obese individuals estimated at 68%, the significance of obesity in the United States has become a focus of increasing attention.[1,2] Resulting morbidity that includes hypertension, diabetes and coronary artery disease is reflected in 9.1% of all healthcare dollars that are devoted to the problem.[3] The study of effects of overweight and obesity has been extensive in the setting of coronary artery bypass graft surgery (CABG); however, their role has not been fully clarified with respect to postoperative mortality.[4-9]

Many of the studies have pointed toward an "obesity paradox," which is illustrated by the finding that obese and overweight individuals are not subject to higher mortality rates after revascularization procedures, and may in fact benefit from their body habitus.[2,10-13] The association of weight loss with mortality is well known, and has been demonstrated by a number of statistical approaches. Both intentional and unintentional loss have been noted to be risk factors for increased mortality.[14,15] Indeed, it has been shown that, over time, the lowest risk of death was present in persons with the least change in their body weight.[16] While patient weight and concomitant morbidities have received much

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of the investigators' attention, little is known about the effects of weight loss on mortality after CABG surgery. This study aims to determine the effect of postoperative weight changes in patients who have undergone CABG.

MATERIALS AND METHODS

Patient Population

This study was performed with the approval of the Institutional Review Board at the VA Western NY Healthcare System. All patients were retrospectively reviewed through an electronic medical record system at our institution. The study period covered surgeries performed between January 2001 and December 2009. It consisted of 899 consecutive isolated CABG operations. As part of standard practice of care, clinical data were collected in a concurrent fashion. These included baseline demographics, procedure data, risk factors, perioperative outcomes, deaths and follow-up. Postoperative data included duration of intensive care unit (ICU) stay, length of intubation and all complications that were categorized into arrhythmia, urinary tract infection, pleural effusion, pneumonia, cerebrovascular accident or an aggregate event. Patients were placed into four groups based on their body mass index (BMI):[17] normal (≤25 kg/m^2), overweight (25.1–29.9 kg/m^2), obese (30–34.9 kg/m^2) and morbidly obese (≥35 kg/m^2). Two sets of BMI data were then evaluated. These consisted of the patient's preoperative BMI and the second set reflected the BMI at first annual postoperative follow-up visit. Based on the resulting difference, the patients were subsequently placed into three groups that reflected their postoperative BMI changes: gainers (≥5% BMI gain), no change (<5% BMI loss or gain) and losers (≥5% BMI loss).

Operative Techniques

Patients were placed under general anesthesia and intubated. Left internal mammary artery and harvested saphenous vein conduits were used together or separately. The veins were harvested via open or endoscopic techniques. On or off-pump procedures were used. With on-pump surgeries, cold blood cardioplegia was used to maintain asystole. The number of grafts during a single procedure varied from 1 to 8 bypass grafts. Postsurgically, the patients were taken to the surgical ICU where they were extubated within 24 h of the procedure.

Statistical Analyses

Statistical analyses were performed using NCSS 2007 version 07.1.20 (NCSS, Kaysville, UT, USA). Continuous variables were compared using logistic regression. Categorical variables were compared with analysis of variance and cross-tabulation matching. Cox-Mantel hazard ratios (HR) were used in determination of risk. Cumulative survival was calculated using Kaplan-Meier analysis. A *P*-value of <0.05 was considered statistically significant. Some of the patient data that were not available for the study were supplemented in the following fashion: for a missing categorical variable, a value signifying a negative result, or 0, was used. In the case of a continuous variable, a median value of the particular category was applied to the missing data.

RESULTS

A total of 1052 patients who had CABG surgery over the 10-year interval were considered for the study, two patients with missing follow-up BMI were omitted, and 151 were excluded due to the existence of concomitant procedures like aortic valve replacement, closure of pericardial defects, vein patch angioplasty or radiofrequency ablation. Finally, 899 patients were included in the study.

Baseline study population demographics are summarized in Table 1, with stratification based on the four BMI groups. Among the patients studied, patients whose BMI is above 25 kg/m^2 [Figure 1] experienced the lowest mortality. The morbidly obese, along with the overweight and the obese patients, were similar to one another in terms of survival. Conversely, the normal patients saw their long-term survival diminish after the CABG surgery. The morbidly obese patients

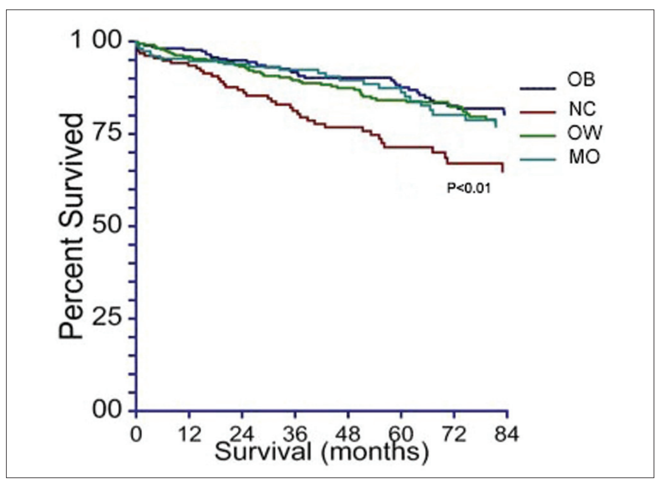

Figure 1: Survival curve stratified by body mass index categories from the nonparametric survival analysis. OB = obese; NC = normal control; OW = overweight; MO = morbidly obese

Table 1: Demographics, Mean and SD, of 899 patients stratified by body mass index (BMI) groups

BMI (kg/m²)	≤25.0	25.1–30.0	30.1–35.0	>35.0	*P*-value
n	154	328	267	150	
Age	66.4 (0.7)	67.0 (0.5)	64.0 (0.6)	62.8 (0.8)	0.00
Grafts	3.5 (0.1)	3.5 (0.1)	3.4 (0.1)	3.5 (0.1)	0.70
LV ejection fraction	46.8 (1.0)	49.7 (0.7)	50.0 (0.7)	49.9 (1.0)	0.04
Creatinine	1.2 (0.04)	1.2 (0.03)	1.3 (0.03)	1.3 (0.04)	0.73
Preoperative HCT	37.6 (0.4)	38.9 (0.3)	39.4 (0.3)	39.1 (0.4)	0.01
Preoperative PLT	225.8 (4.9)	215.3 (3.3)	211.6 (3.7)	216.9 (4.9)	0.14
FEV_1	69.2 (1.3)	74.1 (0.9)	74.8 (1.0)	71.4 (1.3)	0.00
CPB	129.8 (7.6)	124.5 (5.3)	129.0 (5.7)	142.1 (7.5)	0.30
AXC	103.2 (6.0)	101.5 (4.2)	106.9 (4.6)	113.2 (6.0)	0.43
PRBC	2.5 (0.2)	2.1 (0.1)	2.3 (0.1)	2.1 (0.2)	0.44
FFP	0.1 (0.1)	7.0 (0.0)	0.1 (0.0)	5.3 (0.1)	0.47
PLT	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)	0.0 (0.0)	0.63
CSS	617.9 (21.6)	605.9 (14.8)	647.6 (16.4)	741.6 (21.9)	0.00
CTD	689.8 (19.5)	699.8 (13.4)	662.3 (14.8)	681.3 (19.8)	0.31
Postoperative HCT	27.7 (0.3)	27.5 (0.2)	27.7 (0.3)	27.3 (0.3)	0.63
Postoperative PLT	106.3 (3.3)	112.1 (2.3)	125.3 (2.5)	123.8 (3.3)	0.00
LOS (days)	8.5 (0.8)	7.1 (0.5)	8.2 (0.6)	7.9 (0.8)	0.40
Ventilator (h)	35.5 (12.4)	22.2 (8.5)	38.0 (9.4)	25.4 (12.5)	0.59
ICU LOS (days)	3.7 (0.6)	3.1 (0.4)	4.1 (0.5)	3.1 (0.7)	0.48
Age at death	70.7 (0.8)	71.8 (0.5)	68.9 (0.6)	67.8 (0.8)	0.00
Mortality	43 (27.9)	60 (18.3)	43 (16.1)	29 (19.3)	0.03

LV - Left ventricle; HCT - Hematocrit; PLT - Platelets; CSS - Cell saver volume; FEV_1 - Forced expiratory volume in 1 second; CBP - Cardiopulmonary bypass; AXC - Aortic cross-clamp; PRBC - Packed red blood cells; FFP - Fresh frozen plasma; CTD - Chest tube drainage; LOS - Length of stay; ICU - Intensive care unit

presented for CABG surgery at a significantly earlier age than normal patients. Yet, their age at the time of death [Figure 2] is virtually indistinguishable in the survival analysis. Despite undergoing the surgery with a higher percentage of comorbidities, such as advanced congestive heart failure (NYHA class III), hypertension and status as current smokers [Table 2], the morbidly obese patients showed a survival advantage. Although having undergone surgery later in their life, the normal patients did not experience a subsequent change in survival; rather, their age at the time of death matches that of the other groups [Figure 2] in the survival analysis.

Preoperative and postoperative morbidities are listed in Table 2 according to BMI grouping. Normal patients were observed with lower preoperative hematocrit and postoperative platelet count than the other groups. They were also subject to a greater number of urgent surgeries, while majority of the obese and morbidly obese underwent CABG electively. Postoperatively, the morbidly obese and obese patients also suffered atrial fibrillation in greater numbers than the normal patients. However, fewer morbidly obese patients presented with chronic obstructive pulmonary disease and diabetes mellitus prior to the procedure.

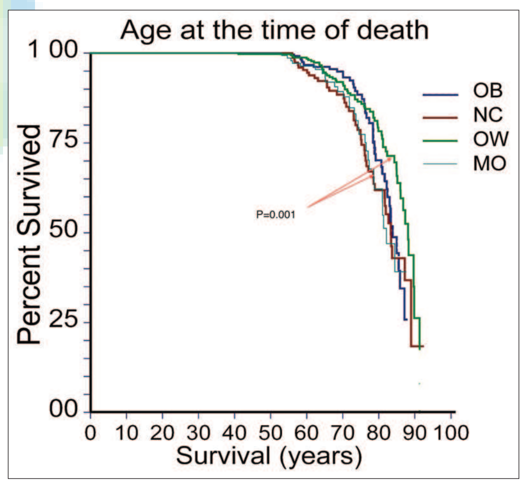

Figure 2: Survival curve indicating the age at the time of death. Stratification by body mass index categories from the nonparametric survival analysis. OB = obese; NC = normal control; OW = overweight; MO = morbidly obese.

Given the observation of the significant survival disadvantages of individuals with normal BMI in the CABG setting, the role of weight loss postoperatively was then investigated. Patients who have lost weight in excess of 5% of their preoperative BMI had significantly lower survival than the ones who had no change or had gained weight [Figure 3]. Individuals who lost weight after their CABG surgery (losers) had a pronouncedly higher mortality risk versus the gainers. Indeed, losers more than doubled their risk (HR = 2.66 [1.87–3.78],

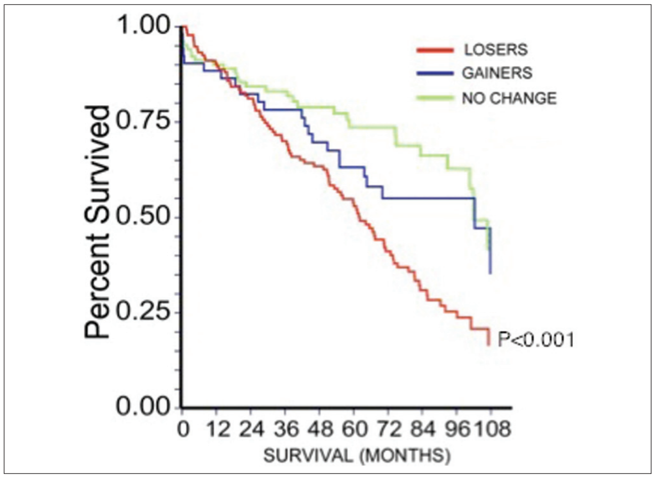

Figure 3: Survival curve stratified by postoperative body mass index (BMI) change categories. Loser: ≥5% BMI decrease; gainer: ≥5% BMI increase; no change: <5% BMI increase or decrease

$P < 0.01$) when compared with the gainers, and tripled their risk (HR = 3.13 [2.26–4.35], $P < 0.005$) when compared with the no change category. Reduction of the covariate influence with propensity score matching produced similar results. The HR for losers versus the other categories once again indicates toward this BMI change category as having the greatest mortality risk. Most pronouncedly, losers saw their risk double versus no change (HR = 2.15 [1.50–3.08], $P < 0.05$), highlighting the significance of weight loss in post-CABG patients. Additionally, the loser group had a 52% increase in mortality when compared with the gainer group (HR = 1.52 [1.07–2.78], $P < 0.05$).

Among all the BMI categories, losers were uniformly subjected to higher mortality. Figure 4 illustrates this

Table 2: Characteristics of study patients (Mean and SD)

BMI (kg/m^2)	≤25.0	25.1–30.0	30.1–35.0	>35.0	*P*-value
n	154	328	267	150	
Change in 1 year					0.60
Gainers	39 (25.3)	78 (23.8)	54 (20.2)	31 (20.7)	
Losers	44 (28.6)	110 (33.5)	80 (30.0)	51 (34.0)	
No change	71 (46.0)	140 (42.7)	133 (49.8)	68 (45.3)	
Redo					0.78
Performed	5 (3.2)	12 (3.7)	10 (3.7)	3 (2.0)	
Not performed	149 (96.8)	316 (96.3)	257 (96.3)	147 (98.0)	
Urgency					0.01
Elective	72 (46.8)	183 (55.8)	163 (61.0)	100 (66.7)	
Urgent	78 (50.6)	135 (41.2)	94 (35.2)	46 (30.7)	
Emergent	4 (2.6)	10 (3.0)	10 (3.7)	4 (2.7)	
CCS classification scale					0.24
1	22 (14.7)	23 (7.0)	24 (9.0)	15 (10.0)	
2	28 (18.2)	58 (17.7)	43 (16.1)	23 (15.3)	
3	37 (24.0)	99 (30.2)	92 (34.5)	42 (28.0)	
4	67 (43.5)	148 (45.1)	108 (40.4)	70 (46.7)	
NYHA classification scale					0.01
I	49 (31.8)	101 (30.8)	57 (21.3)	26 (17.3)	
II	32 (20.8)	77 (23.5)	69 (25.8)	42 (28.0)	
III	51 (33.1)	113 (34.5)	116 (43.4)	68 (45.3)	
IV	22 (14.3)	37 (11.3)	25 (9.4)	14 (9.3)	
MI prior to procedure					0.10
No	83 (53.9)	198 (60.4)	157 (58.8)	84 (56.0)	
>1 month prior	64 (41.6)	126 (38.4)	108 (40.4)	61 (40.7)	
<1 month prior	7 (4.5)	4 (1.2)	2 (0.7)	5 (3.3)	
HTN					0.01
No	41 (26.6)	54 (16.5)	44 (16.5)	18 (12.0)	
Yes	113 (73.4)	274 (83.5)	223 (83.5)	132 (88.0)	
Smoking					0.01
Never	23 (14.9)	48 (14.6)	49 (18.4)	25 (16.7)	
Current	59 (38.3)	164 (50.0)	131 (49.1)	85 (56.7)	
Quit <1 month ago	6 (3.9)	19 (5.8)	9 (3.4)	4 (2.7)	
Quit >1 month ago	65 (42.2)	88 (26.8)	75 (28.1)	32 (21.3)	
Other tobacco use	1 (0.6)	9 (2.7)	3 (1.1)	4 (2.7)	

(*Continued*)

Table 2: (Continued)

BMI (kg/m²)	≤25.0	25.1–30.0	30.1–35.0	>35.0	*P*-value
Functional status					0.30
No limitations	141 (91.6)	312 (95.1)	252 (94.4)	140 (93.3)	
Some limitations	13 (8.4)	13 (4.0)	13 (4.9)	10 (6.7)	
Significant limitations	0 (0.0)	3 (0.9)	2 (0.7)	0 (0.0)	
PCI					0.54
Never	131 (85.6)	279 (85.1)	229 (85.8)	131 (87.3)	
>1 month prior	19 (12.4)	47 (14.3)	36 (13.5)	19 (12.7)	
<1 month prior	3 (2.0)	2 (0.6)	1 (0.4)	0 (0.0)	
Perioperative	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	
COPD					0.03
Yes	106 (68.8)	262 (79.9)	209 (78.3)	109 (72.7)	
No	48 (31.2)	66 (20.1)	58 (21.7)	41 (27.3)	
DM					0.00
Yes	109 (70.8)	204 (62.4)	142 (53.2)	45 (30.0)	
No	45 (29.2)	123 (37.6)	125 (46.8)	105 (70.0)	
CHF					0.05
Yes	124 (80.5)	271 (82.6)	218 (81.6)	108 (72.0)	
No	30 (19.5)	57 (17.4)	49 (18.4)	42 (28.0)	
Carotid occlusion					0.59
<70%	138 (89.6)	286 (87.2)	237 (88.8)	137 (91.3)	
>70%	16 (10.4)	42 (12.8)	30 (11.2)	13 (8.7)	
IABP					0.20
No	128 (83.1)	285 (86.9)	234 (87.6)	137 (91.3)	
Yes	26 (16.9)	43 (13.1)	33 (12.4)	13 (8.7)	
Postoperative events					
CVA					0.38
No	149 (96.8)	321 (97.9)	263 (98.5)	149 (99.3)	
Yes	5 (3.2)	7 (2.1)	4 (1.5)	1 (0.7)	
MI					0.50
No	152 (98.7)	326 (99.4)	265 (99.3)	147 (98.0)	
Yes	2 (1.3)	2 (0.6)	2 (0.7)	3 (2.0)	
Pneumonia					0.12
No	149 (96.8)	321 (97.9)	252 (94.4)	146 (97.3)	
Yes	5 (3.2)	7 (2.1)	15 (5.6)	4 (2.7)	
Pleural effusion					0.94
No	151 (98.1)	319 (97.3)	261 (97.8)	146 (97.3)	
Yes	3 (1.9)	9 (2.7)	6 (2.2)	4 (2.7)	
UTI					0.58
No	152 (98.7)	326 (99.4)	263 (98.5)	147 (98.0)	
Yes	2 (1.3)	2 (0.6)	4 (1.5)	3 (2.0)	
Atrial fibrillation					0.02
No	142 (92.2)	278 (84.8)	233 (87.3)	120 (80.0)	
Yes	12 (7.8)	50 (15.2)	34 (12.7)	30 (20.0)	
Presence of any postoperative event					0.06
No	107 (69.5)	235 (71.6)	179 (67.0)	89 (59.3)	
Yes	47 (30.5)	93 (28.4)	88 (33.0)	61 (40.7)	

CCS - Canadian Cardiovascular Society; NYHA - New York Heart Association; MI - Myocardial infarction; HTN - Hypertension; Other Tobacco Use - Pipe, chewing tobacco; PCI - Percutaneous coronary intervention; COPD - Chronic obstructive pulmonary disease; DM - Diabetes mellitus; CHF - Congestive heart failure; IABP - Intraaortic balloon pump; CVA - Cerebrovascular accident; UTI - Urinary tract infection

trend, with the loser category having an elevated mortality risk versus gainers regardless of whether the initial BMI category was morbidly obese, obese, overweight or normal. Most notable were the obese patients among whom postoperative weight loss markedly increased the mortality risk. When compared with obese patients who gained weight postoperatively, their (obese group patients) mortality risk more than tripled (HR = 3.24), and when compared with obese patients who incurred no changes in their weight, their

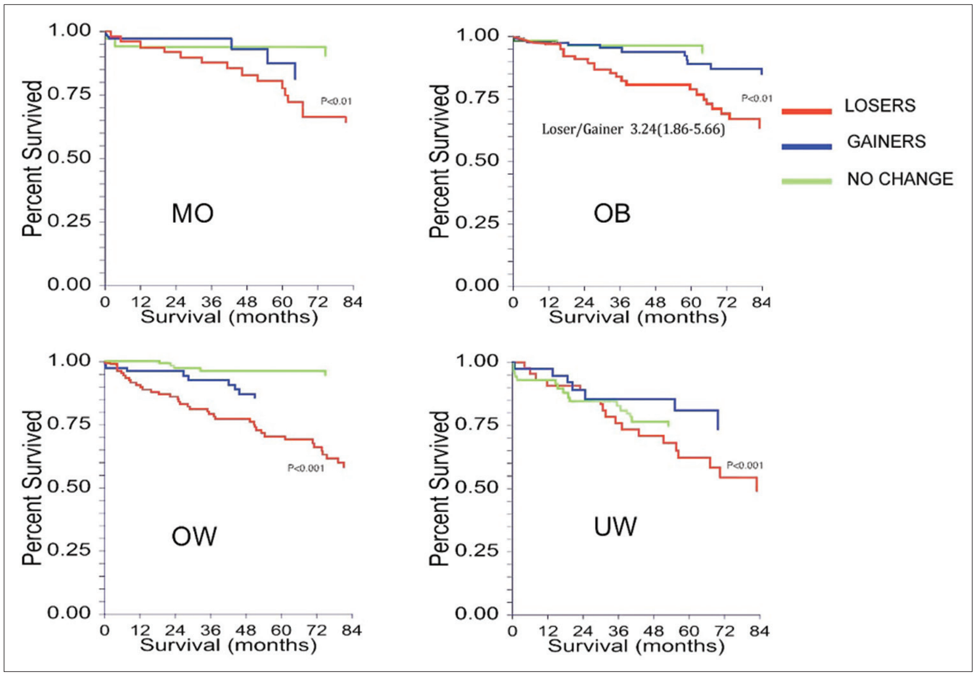

Figure 4: Survival curves from the propensity score matching analysis. The graphs show survival in each category based on BMI and stratified by postoperative BMI change categories. MO: morbidly obese, OB = obese; OW = overweight; UW = underweight; losers: ≥5% BMI decrease; gainers: ≥5% BMI increase; no change: <5% BMI increase or decrease

risk was more than doubled (HR = 2.87). However, postoperative weight gain among the obese did not demonstrate an increase in mortality risk.

Patients whose CABG surgeries were performed urgently and emergently exhibited similar survival trends to the entire studied population. Individuals in the loser category fared the worst, with pronounced mortality risk versus the no change group (HR = 3.43 [2.46–4.80], $P < 0.0001$).

DISCUSSION

This study was a retrospective analysis of data collected over a 9-year-period from individuals undergoing an isolated CABG surgery at a single institution. We have found that preoperative BMI status and postoperative BMI changes have a significant impact on mortality. Like other investigators, we have been able to witness the "obesity paradox" in our CABG population. Patients with a BMI of <25 kg/m^2 had a pronouncedly higher mortality than those with higher body weight.[8,10-13,18,19] Conversely, patients in the obese category exhibited the lowest mortality of the studied population. This overall effect on mortality has been also noted in individuals with coronary artery diseases (CAD), where obesity has not been established as a risk factor for increased mortality.

More specifically, Oreopoulos and colleagues[7] reported on a neutral to beneficial effect of overweight and obesity in postcoronary revascularization (PCI and CABG) patients. Interestingly, while patients with higher BMI benefited from lower postoperative mortality, they were subject to a reversal of this trend in terms of postoperative morbidity. Increased body weight was associated with a larger incidence of postoperative pneumonia, atrial fibrillation and composite events. This differs from what other investigators have observed, noting either no influence of higher body weight on postoperative morbidity[19] or only noting increased morbidity among the obese.[20]

Although modest weight loss in the range of 5–10% would be expected to result in significant improvement in the comorbid conditions,[21,22] weight loss has been associated with an increase in mortality in overweight and obese patients with CAD.[14,15,23] However, to the best of our knowledge, an explicit postoperative analysis of weight loss in CABG patients has not been previously carried out. Our analysis indicates a significant effect of postoperative weight loss on mortality. Individuals whose BMI decreased by ≥5% following a CABG surgery experienced a profoundly higher mortality than those who gained or saw no change in their postoperative weight. In the entire patient population studied, the Cox-Mantel HR propensity score matching analysis highlighted the fact that postoperative weight loss, regardless of initial weight category, carried a profound mortality risk. Preoperative weight resulting in BMI >25 kg/m^2 did not confer a survival benefit in the setting of weight loss following the CABG surgery. Obese patients were subject to the same decreases in survival and increases in mortality risk as others when weight loss occurred. Likewise, the urgency with which the CABG surgeries were carried out reflected the same trends with weight change.

Nutritional status exists along a continuum from poor to optimum nutrition, and is determined by the balance between nutrient intake, metabolic rate and physiologic demand. Nutritional status plays a critical role in surgical patients and has been directly related to postoperative outcome. Whether a patient who had CABG would lose or gain weight after CABG remains unpredicted. Potential causes for weight gain include decreased ambulation, water retention and better nutrition. On the other hand, possible causes for weight loss include surgical stress, following healthier diet and diuresis secondary to improved cardiac function. This implies that weight loss does not essentially mean healthier lifestyle or better outcome, and weight loss has been correlated to adverse postoperative outcomes.[24] Causes of weight loss were not addressed in our study, but this is likely an area of interest for future studies.

Possible explanations for increased morbidity in the morbid obesity patients include inadequate protection of thick myocardium caused by hypertension, higher postoperative ventilatory complications due to preexisting sleep apnea as evidenced by higher preoperative hematocrit,[25] excess adipose tissue predisposing to higher incidence of wound infection and delayed healing,[26] higher incidence of arrhythmia contributing to longer rewarming time and longer bypass time[5] and, finally, deleterious effects of hyperglycemia and hyperlipidemia on graft patency.[27] On the other hand, possible explanations for increased mortality with postoperative weight loss include decreased resistance to infection and decreased overall fitness. In fact, weight loss may be a manifestation of a complicated postoperative period. In other words, pronounced metabolic stress with neurohormonal and cytokine activation may cause weight loss and increased mortality.[28] Similarly, Higgins and colleagues[29] from the Framingham study group conducted a longitudinal study on 2500 patients over a period of 20 years, where they demonstrated higher cardiovascular mortality in those who had the highest reduction in BMI.

Limitations

Although a retrospective design is usually discouraged when a prospective study is feasible, a retrospective study can still serve useful purposes as it can help to focus the study question, clarify the hypothesis, determine an appropriate sample size and identify feasibility issues for a future prospective study. Here, the retrospective nature of our study dictates that some confounding factors may not have been considered.[30] The demographic and socioeconomic makeup of our patient population was not incorporated into the analysis. African American ethnicity,[31] reliance on Medicaid[32] and poverty[33] have all been reported as contributors to decreased survival after CABG. A negative impact on mortality was also seen in postoperative depressive states[34] and hyperglycemic states.[35] Conversely, improved survival is known in patients with AB blood group,[36] intraoperative use of volatile anesthetics[37] and the application of double internal thoracic artery grafts.[38] None of these factors were reflected in our calculations, yet, individually or as a group, their presence may have resulted in an imbalanced study sample that had the potential to impact the mortality outcomes. The presence of undiagnosed disease before the CABG procedure may also be important which may have later contributed to the weight loss and death.[39] Also, the obese and morbidly obese patients were on average 2.4 and 3.6 years younger, respectively, than the normal controls at surgery. This difference could have been responsible for our observation of the "obesity paradox," which may simply be an effect of patient age. The use of all-cause mortality as the end point may also impact the results, as stratification of the causes of death was performed. Also, while the BMI is most widely used in epidemiological studies to reflect the status of obesity, it is well known for its inability to differentiate between lean and fat body mass and central and peripheral obesity. The categorization scheme of BMI has also been of concern as it has been suggested that morbidity and mortality inference can be affected with such grouping.[40,41]

CONCLUSIONS

The serious health risks of obesity must be considered in general, and especially after a CABG procedure. There is a negative effect on overall health, particularly coronary health. The results of our study should be interpreted within this context. We were able to demonstrate that a significant risk of mortality is conferred by a reduction in BMI in excess of 5% in patients who undergo

CABG surgery. This is reflected in decreased survival associated with the postoperative weight loss. The obesity paradox remains an interesting finding that is not yet fully understood, and this clearly highlights the need for further studies.

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