



The impact of obesity on early mortality after coronary artery bypass grafting

Uticaj gojaznosti na rani mortalitet nakon koronarne *bypass* hirurgije

Nada Čemerlić-Adjić*[†], Katica Pavlović*[†], Marija Jevtić*^{†‡}, Radmila Velicki*^{†‡},
Saša Kostovski*, Lazar Velicki*[†]

*Institute of Cardiovascular Diseases of Vojvodina, Sremska Kamenica, Serbia;

[†]Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia; [‡]Institute of Public

Health of Vojvodina, Novi Sad, Serbia

Abstract

Background/Aim. It had been suggested that elevated body mass index (BMI) is a beneficial and preventive factor when it comes to the outcome for patients undergoing coronary artery bypass grafting (CABG). At the same time, obesity is strongly associated with coronary artery disease development. The aim of this study was to determine the significance of the obesity paradox in patients referred for CABG and to examine if a relationship exists between obesity and early coronary surgery outcome. **Methods.** This study compared 791 patients who had undergone isolated CABG over one year period (year 2010). The average age of patients was 62.33 ± 8.12 years and involved 568 (71.8%) male and 223 (28.2%) female patients, while the mean logistic EuroSCORE was 3.42%. The patients were categorized into three distinct groups based on their BMI: I – BMI < 24.9 kg/m²; II – BMI 25–30 kg/m²; III – BMI > 30 kg/m². Regression analysis was conducted to determine whether BMI was an independent predictor of early mortality after CABG. **Results.** The majority of the cohort could be categorized as overweight (49%) or obese (30%). There was no association between BMI and gender ($p = 0.398$). The overall early mortality was 2.15% (1.85% in the group I, 2.06% in the group II and 2.51% in the group III; $p = 0.869$). Univariate analysis showed that obesity cannot be regarded as an independent risk factor for early mortality following CABG (odds ratio 1.021, 95% confidence interval 0.910–1.145, $p = 0.724$). Duration of in-hospital period following the surgery was comparable within the BMI groups ($p = 0.502$). **Conclusion.** Compared to non-obese patients, overweight and obese individuals have similar early mortality rate following CABG. This study can substantiate the presence of obesity paradox only in terms that elevated BMI patients have comparable outcome with non-obese. Further research is needed to delineate potential underlying mechanisms that set off obesity to protective factor for coronary surgery.

Key words:

obesity; body mass index; myocardial revascularization; postoperative period; mortality.

Apstrakt

Uvod/Cilj. U ranijim radovima nagovešteno je da povišen indeks telesne mase (ITM) može biti koristan i da se može smatrati preventivnim faktorom kada se radi o ishodu operacije kod bolesnika koji se podvrgavaju koronarnoj *bypass* hirurgiji. Istovremeno, gojaznost se dovodi u vezu sa nastankom i razvojem koronarne bolesti. Cilj ove studije bio je utvrđivanje značaja paradoksa gojaznosti kod bolesnika koji su upućeni na hiruršku revascularizaciju miokarda, kao i ispitivanje uticaja gojaznosti na rani ishod koronarne hirurgije. **Metode.** Studijom je obuhvaćen 791 bolesnik podvrgnut izolovanoj koronarnoj hirurgiji tokom jednogodišnjeg perioda (2010. godina). Prosečno životno doba 568 (71,8%) bolesnika muškog pola i 223 (28,2%) bolesnika ženskog pola iznosilo je $62,33 \pm 8,12$ godina, dok je prosečna vrednost logističkog EuroSCORE iznosila 3,42%. Bolesnici su bili svrstani u tri grupe shodno njihovom ITM: I – ITM < 24,9 kg/m²; II – ITM 25-30 kg/m²; III – ITM > 30 kg/m². Regresiona analiza korišćena je kako bi se ispitalo da li je ITM nezavisni prediktor ranog mortaliteta nakon koronarne hirurgije. **Rezultati.** Većina bolesnika imala je prekomernu telesnu masu (49%) ili su bili gojazni (30%). Nije postojala povezanost između ITM i pola ($p = 0,398$). Prosečna rana smrtnost iznosila je 2,15% (1,85% u grupi I, 2,06% u grupi II i 2,51% u grupi III; $p = 0,869$). Univarijantna analiza pokazala je da se gojaznost ne može smatrati nezavisnim faktorom rizika od ranog mortaliteta nakon koronarne hirurgije (unakrsni odnos 1,021; 95% interval poverenja 0,910–1,145; $p = 0,724$). Dužina postoperativnog bolničkog perioda bila je uporediva među ITM grupama ($p = 0,502$). **Zaključak.** U poređenju sa negočajnim bolesnicima, bolesnici sa prekomernom telesnom masom i gojazni imaju sličnu stopu ranog mortaliteta nakon koronarne hirurgije. Ova studija može potvrditi prisustvo paradoksa gojaznosti samo u smislu da bolesnici sa povišenim ITM imaju uporediv ishod operacije sa negočajnim bolesnicima. Dalja istraživanja su neophodna kako bi se odredili mehanizmi koji utiču na to da gojaznost postane protektivni faktor za koronarnu hirurgiju.

Ključne reči:

gojaznost; telesna masa, indeks; miokard, revascularizacija; postoperativni period; mortalitet.

Introduction

Obesity has been increasing in epidemic proportions in both adults and children¹. Obesity is commonly regarded as a risk factor in development of different forms of cardiovascular diseases (CVD) such as coronary artery disease (CAD), heart failure, stroke, endothelial dysfunction, systolic and diastolic dysfunction and atrial fibrillation^{2,3}. The prevalence of obesity is on the rise and consequently larger population of obese patients are considered for some form of revascularization procedure including coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI).

Although long-term longitudinal studies have associated obesity with excess rates of cardiovascular morbidity and mortality, limited data exist on links between coronary artery revascularization and obesity⁴. Because obesity is considered to be a risk factor for CAD development, a conclusion is often drawn that obese patients should have poorer outcomes than non-obese patients. Surprisingly, several recent studies suggested that higher body mass index (BMI) is of benefit when it comes to lowering the mortality rate after heart surgery^{2,3,5,6}.

Obesity is usually defined through BMI that is easily calculated⁷. BMI's lack of ability to differentiate body fat and lean mass is sometimes viewed as its weakness in improving clinical outcome prediction for overweight and obese patients⁸⁻¹⁰.

There is a considerable disagreement regarding the influence of obesity on prognosis after heart surgery, with some major systems of classification indicating that obesity is associated with the poor outcome¹¹⁻¹⁴. Despite the positive correlation between higher BMI and CAD development, many studies suggest better outcome and prognosis in obese patients with CAD and in patients undergoing revascularization (PCI and CABG)¹⁵⁻¹⁹. The obesity paradox is a term that describes the favourable short and long-term results after CABG in overweight and obese patients. Romero-Corral et al.¹⁸, in their systemic review comprised of more than a quarter of a million patients, described the association between lower total and cardiovascular mortality and BMI status of patients with CAD in the sense that overweight and obese patients have a reduced risk as compared to underweight and normal weight individuals. According to these studies, a dual nature of obesity is evident. On the other hand, several studies found that obese patients have a higher incidence of morbidity and mortality after CABG¹⁵. It has been shown that obese patients are referred to surgery at a younger age and, in addition, with a higher frequency of comorbidities such as hypertension and diabetes mellitus.

The underlying mechanism that could explain obesity paradox remains elusive. It has been speculated that several factors – hormonal, inflammation, nutritional, and metabolic – might be involved in developing protective effect in population with elevated BMI and CAD²⁰. Adipose tissue is increasingly being recognized as an active endocrine organ; however, the effects of “adipokines” on coronary arteries and atherosclerosis are not fully understood and the exact nature of this association is yet to be defined.

The aim of this study was to determine the significance of the obesity paradox in patients referred for CABG and to examine if a relationship exists between obesity and early coronary surgery outcome.

Methods

This prospective study included all the patients submitted to isolated CABG during a year period. Patients undergoing additional procedures in conjunction with CABG were excluded from this study. The resulting cohort consisted of 791 patients. The hospital Ethical Committee approved the study protocol and waived the requirement of informed consent before the commencement of data acquisition.

The National Heart, Lung, and Blood Institute and the World Health Organization as mentioned have adopted a weight classification for BMI that is calculated by dividing a patient's weight in kilograms by that patient's height in meters squared⁷. According to this classification, a BMI < 18.5 kg/m² was considered underweight, a BMI of 18.5 to 24.9 kg/m² was considered normal, a BMI of 25 to 30 kg/m² was considered overweight, and a BMI > 30 kg/m² was considered obese. Since the number of patients with BMI of less than 18.5 kg/m² was too small and the fact that there was no mortality, this subgroup was appended to the 18.5–24.9 kg/m² BMI group creating unified < 25 kg/m² group. A patient's BMI was calculated in the same hospitalization as the operative treatment.

Several groups of risk factors were examined: demographic – age, sex; comorbidities – chronic obstructive pulmonary disease (COPD), peripheral vascular disease, previous stroke, unstable angina, recent myocardial infarction (0–90 days prior the surgery), ejection fraction of the left ventricle and diabetes mellitus; surgical parameters: logistic EuroSCORE²¹, aortic cross-clamping time, extracorporeal circulation time, number of distal coronary anastomoses and number of postoperative days. Surgical outcome defined as early mortality included 30-day mortality or mortality during the same hospitalization as the operation (status of every patient was verified by telephone on the 30th postoperative day).

The results are reported as mean ± standard deviation (SD) for quantitative variables and are summarized by absolute frequencies and percentages for categorical variables. Assessments of the continuous variables were performed using one-way analysis of variance (ANOVA). The χ^2 analyses were used to assess categorical variables and outcomes the Mann-Whitney test was used for non-parametric comparison. Multivariate logistic regression models for assessing the relation between BMI (as the classified form) and early mortality rate and presence of confounders were established, and associations are expressed as odds ratios (OR) with 95% confidence intervals (CI). The significance level for all analyses was $\alpha = 0.05$. Statistical analysis was performed using SPSS 13.0 for Windows (SPSS, Chicago, IL).

Results

This study compared 791 patients who had undergone isolated CABG over one year period (year 2010). The aver-

age was 62.33 ± 8.12 years and involved 568 (71.8%) male and 223 (28.2%) female patients, while the mean logistic EuroSCORE was 3.42%.

Baseline patient characteristics and comorbidities are listed in Table 1. Of 791 patients, 629 (79.52%) were over-

and the lowest prevalence in the high BMI ($\geq 30 \text{ kg/m}^2$) group] and renal failure [the highest prevalence in the low BMI ($< 18.4 \text{ kg/m}^2$) group and the lowest prevalence in patients with BMI ($\geq 25 \text{ kg/m}^2$)]. The patients with higher BMI tended to be younger and there was an overall trend

Table 1

Baseline patient characteristics, comorbidities and surgical parameters

Parameter	BMI (kg/m^2) (number of patients)				p
	≤ 18.4 (n = 7)	18.5–24.9 (n = 155)	25–29.9 (n = 390)	≥ 30 (n = 239)	
Age, years, ($\bar{x} \pm \text{SD}$)	61.00 ± 7.09	63.63 ± 8.22	63.00 ± 7.88	60.46 ± 8.20	< 0.0001
Female, n (%)	3 (42.9)	44 (28.4)	101 (25.9)	75 (31.4)	0.398
COPD, n (%)	1 (14.3)	8 (5.2)	25 (6.4)	22 (9.2)	0.344
PVD, n (%)	4 (57.1)	43 (27.7)	91 (23.3)	39 (16.3)	0.005
Previous stroke, n (%)	0 (0%)	3 (1.9)	10 (2.6)	8 (3.3)	0.812
Serum creatinine $>200 \mu\text{mol/L}$, n (%)	1 (14.3)	2 (1.3)	1 (0.3)	1 (0.4)	< 0.0001
Unstable angina, n (%)	1 (14.3)	42 (27.1)	86 (22.1)	54 (22.6)	0.578
Ejection fraction, n (%)	52.86 ± 12.95	51.42 ± 10.40	54.18 ± 8.70	53.09 ± 9.41	0.02
Recent MI, n (%)	3 (42.9)	35 (22.6)	69 (17.7)	49 (20.5)	0.233
Urgent surgery, n (%)	0 (0)	3 (1.9)	7 (1.8)	5 (2.1)	0.976
Logistic EuroSCORE, ($\bar{x} \pm \text{SD}$)	3.39 ± 1.35	4.15 ± 5.08	3.28 ± 3.51	3.18 ± 4.33	0.107
IDDM, n (%)	0 (0)	19 (12.3)	32 (8.2)	27 (11.3)	0.317
NIDDM (%)	3 (42.9)	36 (23.2)	104 (26.7)	78 (32.6)	0.144
Ao-X (min), ($\bar{x} \pm \text{SD}$)	64.57 ± 28.11	58.37 ± 23.53	56.13 ± 30.46	55.72 ± 24.93	0.666
ECC time (min), ($\bar{x} \pm \text{SD}$)	80.86 ± 38.37	70.17 ± 27.57	67.36 ± 33.47	66.06 ± 26.25	0.379
No. of distal anastomoses, ($\bar{x} \pm \text{SD}$)	2.71 ± 0.76	2.65 ± 0.93	2.63 ± 0.93	2.55 ± 0.82	0.630
Postoperative days, ($\bar{x} \pm \text{SD}$)	8.29 ± 1.11	9.41 ± 4.94	10.03 ± 7.88	10.43 ± 7.03	0.502
30-day mortality, n (%)	0 (0)	3 (1.93)	8 (2.05)	6 (2.51)	0.869

BMI – body mass index, COPD – chronic obstructive pulmonary disease; PVD – peripheral vascular disease; MI – myocardial infarction; IDDM – insulin dependent diabetes mellitus; NIDDM – non-insulin dependent diabetes mellitus; Ao-X – aortic cross clamp; ECC – extracorporeal circulation.

weight or obese, 155 (19.60%) were of normal weight, and 7 (0.88%) underweight (Figure 1). There were more men than women in all the BMI groups. The prevalence of comorbidities was comparable between the BMI groups ($p > 0.05$) except for the peripheral vascular disease [the highest prevalence in the low BMI ($< 18.4 \text{ kg/m}^2$) group

toward lower mean age through increasing BMI group. Obese patients are submitted to coronary surgery on average 3 years earlier than normal weight or overweight population ($p < 0.0001$).

Surgical parameters and early mortality are summarized in Table 1. The mean BMI of the patients with early mortality was 28.14 ± 4.04 as compared to the patients with no mortality 28.12 ± 4.10 ($p = 0.629$) (Figure 2). There was no significant difference in aortic cross-clamp time, extracorporeal time, number of distal coronary anastomoses and

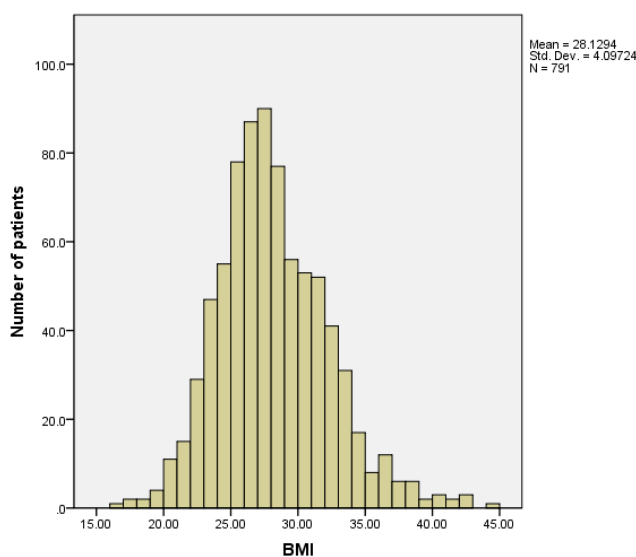


Fig. 1 – Number of patients in relation to a body mass index (BMI) value.

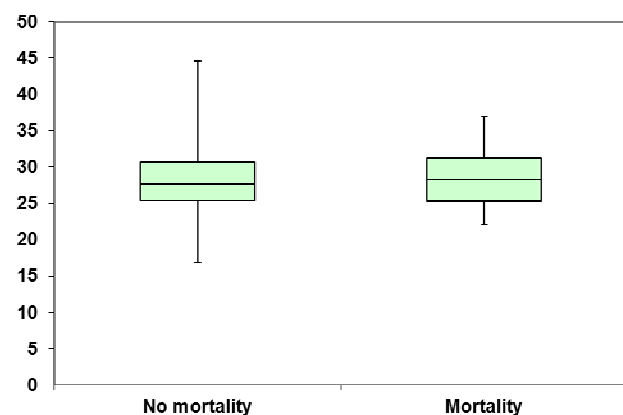


Fig. 2 – Box plot of the body mass index (BMI) values between the groups of patients in terms of mortality ($p = 0.629$).

number of postoperative days ($p > 0.05$). The average number of distal coronary anastomoses decreased as the value of BMI increased leading to decreased aortic cross-clamping time and subsequently extracorporeal time. This correlation did not reach the level of statistical significance. The average number of postoperative days increased in correlation with BMI value but, again, failed to reach the level of statistical significance ($p = 0.502$).

We conducted uni- and multivariate analyses to determine whether there was a relationship between early mortality and BMI. Regression analysis failed to designate BMI as an independent predictor of early mortality (OR = 1.021, 95% CI 0.910–1.145, $p = 0.724$). Table 2 demonstrates this relationship in univariate and multivariate analyses.

conclusions regarding the influence of BMI on early post-CABG mortality.

Several studies found that low BMI patients are at a higher risk^{15, 27}. These studies showed that patients in the underweight group experienced greatest mortality and other complications after CABG. It was suggested that a low BMI might be a marker for multiple risk factors such as peripheral vascular disease, cerebrovascular disease, and smoking history. In our study, we had only 7 patients designated as underweight with no mortality in this group and, therefore, no clinical implications. A low BMI might also be a marker for more advanced heart disease²⁸.

Wigfield et al.²³ evaluated the effect of severe obesity (BMI > 40 kg/m²) on the outcome of cardiac surgery and found that extreme obesity is not associated with an in-

Table 2

BMI (kg/m ²)	Univariate analysis			Multivariate analysis*		
	OR	95% CI	<i>p</i>	OR	95% CI	<i>p</i>
≤ 24.9	Reference			Reference		
25–29.9	1.061	0.278–4.053	0.931	1.720	0.388–7.635	0.476
≥ 30	1.305	0.321–5.296	0.710	2.824	0.598–13.346	0.190

BMI – body mass index; OR – odds ratio; CI – confidence interval.

*Adjusted for age, peripheral vascular disease, serum creatinine > 200 μmol/L and ejection fraction.

Discussion

There is a direct association between BMI and the incidence of CAD, however, once CAD is expressed, the association among BMI and prognosis becomes more complex²². Cardiac surgeons recognize obesity as a risk factor for perioperative adverse outcomes following CABG. Specifically, BMI greater than 30 are thought to be associated with excess of surgical risks²³. Data regarding the influence of BMI on CABG outcome and prognosis are conflicting. Instead, increased incidence of complications such as sternal and superficial wound infection, saphenous vein harvest site infection and dysrhythmias was observed^{24–26}.

The results of this research indicate that obesity alone is not associated with early mortality after isolated CABG. The author's hypothesis that patients with an obese BMI are at greater risk of mortality after CABG was not substantiated. There is a strong relationship between the age of the patients undergoing CABG and the BMI value ($p < 0.0001$) in terms that the patients with high BMI are referred to CABG at younger age; a known effect of accelerated progression of atherosclerosis in obese population with clinical manifestation appearing a decade earlier than in normal weight population. It should be noted that for every 1% above ideal BMI values, the risk for CAD increases by 3.3% for women and by 3.6% for men¹². The overall mortality for the entire group of our patients, regardless the BMI value, was 2.15% which is somewhat different from the other authors^{17, 19, 24}. In the same time, the average BMI value of our patients was 28.13 kg/m² which is significantly lower than in other studies^{26, 27}. These sample or population differences as well as the analytical approach and study design may give rise to different

creased mortality after cardiac surgery. In our research, the number of patients with extreme BMI values (> 40 kg/m²) was too small, only 9 of them, and we, also, did not find any association between high BMI values and early mortality. In contrast, Prabhakar et al.²⁹ used a very large database of 559,004 patients undergoing CABG to show an increased operative risk for moderately obese (BMI 35–39.9) and extremely obese (BMI > 40) patients (OR 1.21, 95% CI 1.1–1.3; OR 1.58, 95% CI 1.4–1.7, respectively).

In a propensity-matched analysis of 6,068 consecutive patients undergoing primary CABG at a single centre from 1991 to 2003, two propensity models were derived comparing all small patients with normal-sized persons and all obese patients with normal-sized persons³⁰. Mortality was observed to be higher in very obese patients (BMI ≥ 36 kg/m²) than in normal-sized individuals, but a worse survival rate was not observed among moderately obese patients (BMI 32–36 kg/m²). This statement is in concordance with our results. Since most of our patients were categorized as overweight and moderately obese with a negligible percentage of severely and morbidly obese patients, BMI had no significant influence on early mortality following CABG.

The study by Reeves et al.³¹ demonstrated that obese patients may be less likely to be selected for CABG and that, in general, obese patients undergoing CABG may have less high-risk features in particular less severe CAD and left ventricle dysfunction compared with lean patients, even when adjusting for these confounding factors. They demonstrated that underweight patients had a higher risk of perioperative complications, whereas the perioperative prognosis was not adversely affected by overweight and obesity.

Several studies tried to examine the effect of revascularization strategy and level of obesity on short- and long-term results. These attempts brought even more confusion in the field. Investigators from the Bypass Angioplasty Revascularization Investigation (BARI) trial had found that an increased BMI is associated with a worse long-term outcome after CABG but not after percutaneous coronary intervention (PCI)³². In contrast, the Arterial Revascularization Therapies Study (ARTS) which included a large cohort of patients who had multi-vessel CAD and underwent surgical or percutaneous revascularization, found that BMI had no effect on the 3-year outcome on those who underwent stenting⁴. “Conversely, among patients who underwent CABG, those who were overweight or obese had a significantly better outcome than did those who had a normal BMI with regard to survival without major adverse cardiac or cerebrovascular events, mainly due to lower rates of repeat revascularization procedures”⁴.

A recent meta-analysis investigated the effect of obesity on short- and long-term mortality post-coronary revascularization¹⁷. The analysis included 22 cohort publications, reporting results in 10 post-PCI and 12 post-CABG populations. “Compared to individuals with non-elevated BMI levels, obese patients undergoing PCI had lower short- (OR 0.63; 95% 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”¹⁷. The authors concluded that the mortality rate after CABG did not differ significantly between the BMI groups. Finally, the results also suggest that a potentially protective relationship between obesity and mortality is absent in longer follow-up times or increasing severity of obesity.

In the era of risk stratification and informed consent, universally applied assessment of surgical risks may not adequately aim to evaluate obesity as a predictor in various scoring systems²³. Based on the EuroSCORE model the BMI appears not to be considered as a potential risk factor^{33,34}. The STS scoring system includes low BSA as an independent risk factor (OR 0.91 per 1 unit). Florath et al.²⁸ attempted to modify the EuroSCORE algorithm by adding the risk factor ‘BMI < 24’ (with a coefficient established in their

study) that lead to an increased c-index to 0.75 (0.67–0.82). They concluded that the prediction of the EuroSCORE algorithm could be improved by including the risk factor ‘small BMI’.

The obesity paradox does appear to exist for high BMI patients with established CAD in whom prognosis appears to be generally equal-to or even superior to low or normal BMI patients^{35,36}. This paradox needs to be further evaluated and outcome integrated into modern risk scoring systems. It may be that the mortality after CABG is increased for patients with an extreme BMI in either the low or the high range¹⁵. A consensus of whether small BMI or high BMI is associated with an increased risk is required in order to be integrated into the outcome prediction model.

Several limitations of this study are currently noted. The study evaluated only the short-term outcome. A longer follow-up period may have detected additional events influencing the final results. The study offers no data on the number of other comorbid conditions and potentially confounding factors such as fitness, neurologic disease, cancer, HIV status, smoking history, pulmonary hypertension, heart failure status, pre-surgical weight loss history, alcohol/illicit drug abuse, cardioprotective medication use, markers of inflammation, and clotting factors. Adiposity was assessed through BMI including no waist circumference, nor waist-to-hip ratio.

Conclusion

Whether obesity directly affects the outcome and prognosis of CABG is still the subject of considerable debate. Although the authors found no relationship between obesity and early postoperative mortality, it remains advisable for patients to reduce their weight to normal range. Obesity is a well-known risk factor for developing numerous cardiovascular diseases. Obesity can also be considered a predictor of elevated risk of postoperative complications. Further research is required to study the impact of obesity on the intermediate and long-term outcomes in patients after CABG.

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