Am J Cardiovasc Dis 2026;16(3):185-193
www.AJCD.us /ISSN:2160-200X/AJCD0166972

Original Article

Protective effect of overweight status in aortic valve surgery: revisiting the obesity paradox

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Received June 21, 2025; Accepted June 9, 2026; Epub June 15, 2026; Published June 30, 2026

Abstract: Objectives: To investigate the relationship between body mass index (BMI) and postoperative mortality in patients undergoing aortic valve surgery, with an emphasis on exploring the presence and limits of the "obesity paradox", the phenomenon wherein overweight and mildly obese patients may experience lower mortality despite obesity's general association with adverse health outcomes. Methods: The Nationwide Inpatient Sample (NIS) database was used to obtain data from adult patients who underwent aortic valve surgery between 2016 and 2020. BMI categories, as well as comorbidities, were identified using ICD-10 codes. Mortality rates across BMI categories were compared, and multivariate analysis was performed to adjust for comorbid conditions. This is a retrospective observational study. Results: We found 301,250 adult patients who underwent aortic valve surgery. Normal weight patients (n=226,490) had a mortality rate of 3.79%. Overweight (n=2,555) and obese (n=46,320) patients demonstrated significantly lower mortality rates of 1.17% (OR=0.30, 95% CI: 0.14-0.66; P=0.003) and 2.43% (OR=0.63, 95% CI: 0.55-0.73; P<0.001), respectively. Cachectic patients (n=835) had the highest mortality rate at 14.97% (OR=4.47, 95% CI: 2.87-6.96; P<0.001). Morbidly obese patients (n=25,450) had a mortality rate of 4.13%, which was not significantly different from normal-weight patients (OR=1.09, 95% CI: 0.94-1.26; P=0.23). These trends and statistical significance remained after multivariate logistic regression, accounting for demographics and comorbidities. Conclusions: The partial obesity paradox is true in patients undergoing aortic valve surgery, with the lowest mortality occurring in overweight patients, followed by obese patients, and with cachexia having the highest mortality out of all groups.

Keywords: Obesity paradox, aortic valve surgery, aortic valve replacement, aortic valve disease, body mass index

Introduction

Aortic valve disease is a broad term encompassing a spectrum of disorders that impair the proper functioning of the aortic valve, with the primary pathological forms being aortic stenosis (AS) and aortic regurgitation (AR) [1-3]. Aortic stenosis is the most prevalent valvular heart disease and is most commonly caused by age-related buildup of calcification on the valve that increases resistance and causes outflow obstruction [1]. Aortic regurgitation contrasts with the pathophysiology of stenosis, as it is an incompetent valve that allows regurgitant flow from the aorta back to the left ventricle during diastole [2]. Development of a diseased valve is impacted by a variety of risk factors, such as hypertension, smoking, hyperlipidemia, diabetes, and metabolic syndrome, alongside congenitally predisposing factors, most notably having a bicuspid valve or being male [4]. Markedly, a high body mass index (BMI) is an independent and causal risk factor for both the development and the severity of a diseased aortic valve [5, 6]. Obesity causes both structural and metabolic changes in the body that impact the heart; the increased stress on the heart accelerates atherosclerotic changes and leads to calcification, and increased circulating lipoproteins in obesity deposit in leaflet walls and causes an inflammatory-mediated diseased valve [6]. Transthoracic echocardiography remains the cornerstone of diagnosis and grading for both aortic stenosis and regurgitation, allowing for assessment of valve anatomy, function, and ventricular response [3, 7]. There are two main approaches for the correction of aortic valve pathology, surgical aortic valve

https://doi.org/10.62347/LTPQ4636

replacement (SAVR) and transcatheter aortic valve replacement (TAVR) [7-9]. Correction of aortic valve dysfunction is indicated when the severity of valve dysfunction results in clinical symptoms such as dyspnea, heart failure, and palpitations, as well as if structural heart changes occur or when there is impaired ventricular function that will result in a poor outcome if left uncorrected, such as an asymptomatic patient with a LVEF less than 50% [8]. Surgical intervention has been shown to decrease all-cause mortality by 45% compared with no intervention, a significant benefit that can substantially lengthen a patient's lifespan [9]. As with any surgery, the risks of a procedure must be weighed against the dangers of living with a pathology that is not corrected, but as the mortality of severe aortic valve disease is quite high without intervention (50% at 2 years in AS and 34% at 10 years in AR), a corrective surgery is often the logical way forward [10, 11].

Many variables have previously been identified that impact the mortality of aortic surgeries, with some of the greatest predictors of complications being diabetes, ventricular ectopy before surgery, decreased hemoglobin and hematocrit levels, longer bypass and aortic cross-clamp time, and chronic kidney disease, among others [7, 12]. Although a very elevated BMI has been observed to negatively contribute to the mortality of surgery, possibly due to factors such as impaired breathing mechanics, increased comorbidities, and infectious susceptibility, a trend has been observed in which being overweight can actually reduce mortality in aortic valve [12-15]. Previously observed in procedures like coronary artery bypass grafting, the so-called "obesity paradox" describes this phenomenon in which patients with a higher BMI experience outcomes after heart valve surgery that are equivalent to, or often better than, those of their normal-weight counterparts, despite obesity's known association with increased comorbidities and reduced life expectancy in general [14, 15]. It has been shown that patients with higher BMI undergoing valve surgery demonstrated similar or reduced rates of postoperative complications such as myocardial infarction, stroke, reoperation, acute kidney injury, dialysis, and bleeding [14]. The underlying mechanisms behind this abnormality are still only speculative, but some of the suggested mechanisms behind this protective effect include more aggressive medical care, patients already being on cardioprotective pharmacotherapy, and having an increased physiological reserve for recovery, but a definite link has not been established [14]. In addition, it is also observed that those who are underweight often have worse outcomes regarding all-cause mortality, which is true in both cardiac and non-cardiac surgeries [16, 17].

This study aims to further explore the impact of BMI on the mortality and outcomes of patients undergoing aortic valve replacement by retrospectively analyzing the BMI of patients using the Nationwide Inpatient Sample (NIS) database. Inclusions were all patients over the age of 18 who underwent aortic valve surgery. Exclusions were patients 18 years of age or older or patients without an ICD-10 code for aortic valve surgery.

Methods

Data source and study population

Patient data from 2016 to 2020 from the NIS database were analyzed for this study. To be included in data analysis, patients were required to be at least 18 years old, have a documented weight category available, and undergo surgery of the aortic valve. International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes were used to identify patients, using cachexia (ICD-10: R64) as a marker of malnourishment/underweight, overweight (ICD-10: E66.3) being synonymous with a BMI of 25-29.9, obesity (ICD-10: E66.9, E66.8, E66.0) being synonymous with a BMI of 30-34.9, and morbid obesity (ICD-10: E66.01, E66.2) being synonymous with a BMI of >35.

The observation indicators were all-cause inpatient mortality based on different weight categories. Multivariate analysis was performed to evaluate the independent cause of mortality in each weight category, adjusting for baseline characteristics and comorbidities.

Statistical analysis

Patient demographic, clinical, and hospital characteristics are reported as median (IQR) for continuous variables and proportions, 95%

confidence intervals for categorical variables. Logistic regression was performed to ascertain the odds of binary clinical outcomes relative to patient and hospital characteristics. All statistical models were adjusted for confounding variables. All analyses were conducted following the implementation of population discharge weights. All *p*-values were 2-sided, with a P<0.05 considered statistically significant. Data will be analyzed using STATA 17 (Stata Corporation, College Station, TX).

Results

A total of 301,250 patients who underwent an aortic valve surgery from 2016-2020 were included in the data collection for this study, with a median age of 67 (IQR 59-74), and males undergoing procedures at a rate 2.19× that of females (68.66% vs 31.34% respectively). **Table 1** summarizes the demographic characteristics of patients examined in this study. **Tables 2**-**5** shows mortality data based on gender and race across different weight categories.

In line with findings from studies examining what has been termed "the obesity paradox", a statistically significant inverse correlation was identified between being either overweight or obese and mortality, when compared to individuals with a normal BMI range. Among patients with a normal BMI (n=226,490) who underwent aortic valve surgery, the overall mortality rate was 3.79%. When examining those with a weight below a normal BMI, it was found that patients with cachexia (n=835) were found to have the most extreme deviation from normal weight mortality by far, with a mortality of 14.97% (OR=4.47, 95% CI: 2.87-6.96, P<0.001) for an absolute risk increase of 11.18% (**Figure 1**). Conversely, in those who were overweight (n=2,555) or obese (n=46,320), mortality rates were considerably lower when compared to a normal BMI, at 1.17% (OR=0.30, 95% CI: 0.14-0.66, P=0.003) and 2.43% (OR=0.63, 95% CI: 0.55-0.73, P<0.001) respectively (**Figure 1**). This demonstrates an absolute risk reduction of 2.62% among patients who are overweight and 1.35% among patients who are obese. However, when BMI was increased further into the range of morbid obesity, there was no longer an observably positive or statistically significant impact on mortality. In patients with morbid obesity (n=25,450), mortality was 4.13% (OR=1.09, 95% CI: 0.94-1.26, P=0.23) (**Figure 1**).

These associations between BMI categories and mortality persisted even after adjusting for a comprehensive set of covariates in multivariate logistic regression analysis. Specifically, odds ratios were adjusted for age, sex, race, and comorbid conditions, which included smoking, diabetes, hypertension, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), history of ST-elevation myocardial infarction (STEMI), non-STEMI, and prior myocardial infarction. After adjustment, overweight status remained independently associated with a significantly reduced odds of mortality (OR 0.34, 95% CI: 0.16-0.75, P=0.007), as did obesity (OR 0.67, 95% CI: 0.58-0.78, P<0.001). Patients classified as having cachexia still demonstrated markedly elevated mortality risk, with an adjusted OR of 3.82 (95% CI: 2.39-6.12, P<0.001). Morbid obesity was again not found to be significantly associated with increased or decreased odds of mortality following adjustment (OR 1.14, 95% CI: 0.97-1.33, P=0.107), consistent with the unadjusted mortality data.

A year-by-year analysis of postoperative mortality from 2016 to 2020 was also conducted across each BMI category to evaluate temporal trends. Among patients with a normal BMI, mortality rates remained relatively stable throughout the five years of data collection analyzed, fluctuating within a narrow range between 3.47% and 4.41%. In contrast, patients classified as cachectic exhibited marked variability in mortality over the same time frame, with annual rates ranging from 7.69% to as high as 27.50% (**Figure 2**). Overweight individuals demonstrated consistently lower mortality rates across all years, ranging from 0.00% to 2.88%, supporting the observed protective trend noted in aggregate analysis (**Figure 3**). Similarly, patients categorized as obese showed a narrow mortality range of 1.98% to 2.71% (**Figure 4**). By contrast, patients with morbid obesity experienced somewhat higher mortality rates, with a yearly range between 3.70% and 4.90%, approximating or slightly exceeding the mortality seen in individuals with normal BMI, which is again consistent with the unadjusted odds ratio (**Figure 5**).

Table 1. Baseline characteristics * showing significant findings of P<0.001 comparing cachexia, overweight, and obesity to normal weight patients

2016-2020	Aortic Valve Surgery	Normal Weight	Cachexia	Overweight	Obesity	Morbid Obesity
Total Population	301,250	226,490	835	2,555	46,320	25,450
Age (Median(IQR))	67 (59-74)	68 (59-75)	64 (54-74)	67 (60-74)	67 (59-74)	65 (57-71)
LOS (Median(IQR))	7 (5-12)	7 (5-12)	20 (12-31)	7 (5-10)	7 (5-10)	7 (6-13)
Total Charges $ (Median)	$211,601	$213,859	$447,033	$204,766	$197,830	$215,816
Mortality	3.61%	3.79%	14.97%*	1.17%*	2.43%*	4.13%
Gender						
Male	68.66%	70.38%	69.46%	72.80%	66.12%	57.36%
Female	31.34%	29.62%	30.54%	27.20%	33.88%	42.64%
Race						
White	81.79%	81.25%	71.60%	81.21%	83.79%	83.35%
Black	5.89%	5.82%	11.11%	5.25%	5.76%	6.70%
Hispanic	7.22%	7.32%	8.02%	8.08%	7.06%	6.53%
Asian/Pac Isl	2.01%	2.34%	3.09%	2.42%	0.90%	1.00%
Native American	0.45%	0.42%	0.62%	0.20%	0.50%	0.63%
Others	2.64%	2.85%	5.56%	2.84%	1.99%	1.79%

Morbid obesity mortality was not statistically different compared to that of normal-weight patients.

Table 2. Showing the mortality data of cachectic patients compared to others

Mortality	*p*-value	OR	95% C.I.	
			Lower	Upper
Cachexia	<0.001	3.82	2.39	6.12
Gender (Female)	<0.001	1.45	1.300	1.61
Race				
White	REF			
Black	<0.001	1.52	1.26	1.84
Hispanic	0.508	1.07	0.88	1.30
Asian/Pac Isl	0.292	1.19	0.86	1.63
Native American	0.087	1.72	0.92	3.20
Others	0.473	1.13	0.81	1.57

ORs (Odds ratios) of patients undergoing aortic valve surgery in cachectic patients compared to those with normal weight.

Table 3. Showing the mortality data for overweight patients compared to others

Mortality	*p*-value	OR	95% C.I.	
			Lower	Upper
Overweight	0.007	0.34	0.16	0.75
Gender (Female)	<0.001	1.45	1.31	1.61
Race				
White	REF			
Black	<0.001	1.53	1.27	1.85
Hispanic	0.487	1.07	0.88	1.30
Asian/Pac Isl	0.317	1.18	0.85	1.62
Native American	0.076	1.75	0.94	3.26
Others	0.624	1.09	0.78	1.52

ORs (Odds ratios) of patients undergoing aortic valve surgery in overweight patients compared to those of normal weight.

Discussion

This study was devised to examine how the weight of a patient may impact the mortality seen after aortic valve surgery. Drawing from a large sample set from the NIS database of over 300,000 patients between 2016 and 2020 who underwent surgery on their aortic valve, we found that weight is a significant, although somewhat unintuitive, predictor of mortality postoperatively. Cachexia was associated with the most significant increase in mortality risk post-aortic valve surgery, an over fourfold increase, with an absolute risk increase of 11% compared to normal-weight patients. Overweight and obese BMIs were associated with significantly lower mortality, about a 70% risk reduction and a 37% risk reduction, respectively, when compared to normal weight individuals. Deviating from this trend, morbid obesity showed a slight increase in mortality, although this difference was not found to be statistically significant from the normal weight mortality.

Table 4. Showing the mortality of obese patients compared to others

Mortality	*p*-value	OR	95% C.I.	
			Lower	Upper
Obesity	<0.001	0.67	0.58	0.78
Gender (Female)	<0.001	1.46	1.32	1.61
Race				
White	REF			
Black	<0.001	1.60	1.35	1.91
Hispanic	0.487	1.07	0.89	1.29
Asian/Pac Isl	0.482	1.12	0.81	1.54
Native American	0.078	1.69	0.94	3.04
Others	0.248	1.20	0.88	1.63

ORs (odds ratios) of patients undergoing aortic valve surgery in obese patients compared to those of normal weight.

Table 5. Showing the mortality of morbidly obese patients compared to others

Mortality	*p*-value	OR	95% C.I.	
			Lower	Upper
Morbid obesity	0.107	1.14	0.97	1.33
Gender (Female)	<0.001	1.42	1.29	1.57
Race				
White	REF			
Black	<0.001	1.47	1.22	1.76
Hispanic	0.504	1.06	0.89	1.28
Asian/Pac Isl	0.219	1.21	0.89	1.64
Native American	0.101	1.64	0.91	2.96
Others	0.738	1.06	0.77	1.46

ORs (Odds ratios) of patients undergoing aortic valve surgery in morbidly obese patients compared to those of normal weight.

Importantly, these associations found between BMI and surgical mortality remained statistically significant even after adjusting for multiple clinical and demographic covariates. In a multivariate logistic regression model accounting for age, gender, race, smoking status, diabetes, hypertension, COPD, chronic kidney disease, STEMI, non-STEMI, and prior MI, the protective effects of being overweight (OR 0.34, 95% CI: 0.16-0.75, P=0.007) and obese (OR 0.67, 95% CI: 0.58-0.78, P<0.001) persisted. Cachexia remained a strong independent predictor of elevated mortality (OR 3.82, 95% CI: 2.39-6.12, P<0.001), while morbid obesity continued to show no significant association with mortality (OR 1.14, 95% CI: 0.97-1.33, P= 0.107). These findings underscore the robustness of the relationship between body weight and surgical outcomes, independent of common confounding factors.

A temporal analysis of mortality from 2016 to 2020 across all BMI categories was also performed to assess the longitudinal consistency. While annual fluctuations were observed within individual weight groups, particularly in the cachectic cohort, where mortality ranged dramatically from 7.69% to 27.50%, these year-on-year changes did not reach statistical significance within any single year, likely due to a relatively small sample size. However, when data were aggregated over the entire five-year span, significant differences in mortality emerged across BMI categories, which reinforces the validity of the broader associations, and the overall trend supports a durable and reproducible relationship between BMI and postoperative outcomes.

The exact mechanisms behind some of the findings seen in this data are difficult to pinpoint, but several considerations should be considered. For example, in cachexic patients, there is not merely a low body weight, but a complex, catabolic condition characterized by skeletal muscle atrophy, systemic inflammation, and nutritional deficiencies. Cachexia has been indicated as independently associated with higher rates of postoperative complications, including infections, wound complications, respiratory failure, and increased mortality across a range of surgical populations [18]. The loss of muscle mass and function is a key driver, as it impairs overall mobility, a patient's respiratory mechanics, and immune competence [19]. Systemic inflammation, a hallmark of cachexia, further exacerbates catabolism and impairs the body's response to surgical injury. With a reduced ability to respond to metabolic stress, heal tissues, fight infections, and maintain organ function, a major surgery such as an aortic valve repair can be too much for an already metabolically taxed body to withstand, leading to poorer outcomes. Incorporating evaluations of nutritional status and muscle mass into preoperative assessments could help identify high-risk patients, and implementing targeted nutritional support preoperatively may mitigate risks and improve outcomes.

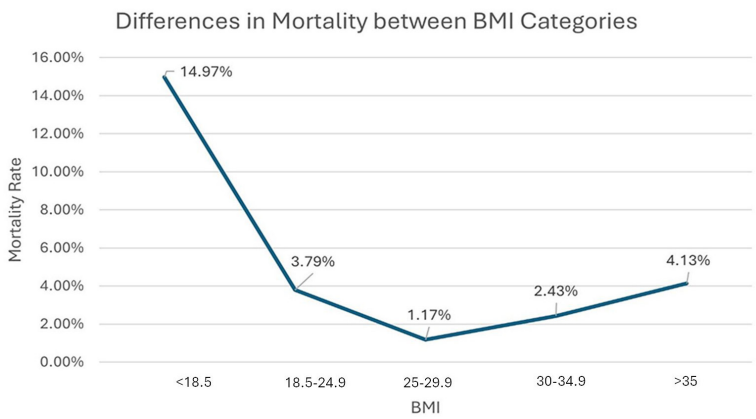

Figure 1. Having a BMI greater than the normal range of 18.5-24.9 had a statistically significant effect on post-surgery mortality.

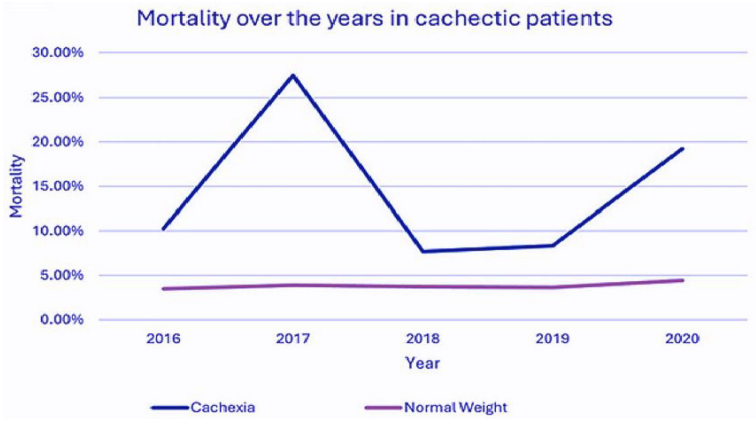

Figure 2. Year-on-year comparison of mortality in cachectic vs normal weight patients.

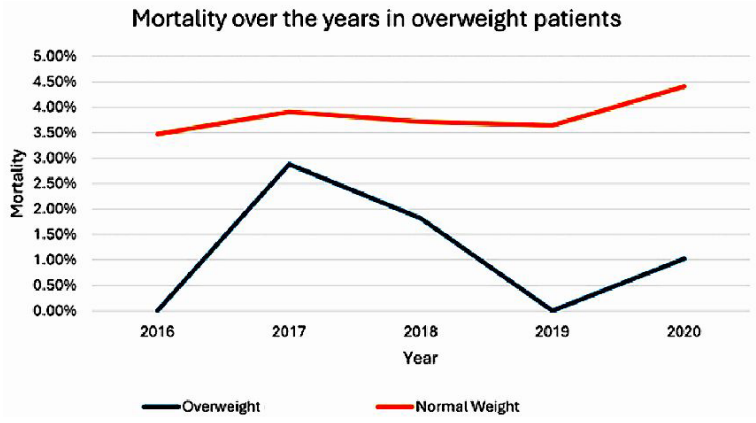

Figure 3. Year-on-year comparison of mortality in overweight vs normal weight patients.

Patients who are overweight or obese are noted to often experience improved outcomes relative to normal-weight individuals regarding mortality after aortic valve surgery, and our findings continue to support that observation. This is what has been previously deemed the "obesity paradox", where increased body mass may confer metabolic reserves that help withstand surgical stress in aortic valve surgery. These findings are nuanced, and may be influenced by factors such as fat distribution, comorbidities, and selection biases. Overweight and obese patients may receive closer surveillance due to their perceived risk of adverse surgical outcomes, they often have a broader range of pharmacotherapy that is cardioprotective, and they have a larger physiological reserve to draw from. Further research is needed to elucidate the underlying mechanisms and to determine how best to assess and manage risk in patients across the BMI spectrum undergoing aortic valve interventions.

Morbidly obese patients in this patient population did not have the same improvement in outcome as those with only a slight increase in BMI. This group may face more surgical complexity (e.g., airway difficulties, impaired wound healing, thromboembolic risk, etc.), reducing the protective effect that metabolic reserves have been proposed to confer. This contrasts with some studies that have shown the obesity paradox holds in patients with a BMI >25 [12]. Our data suggests there may be an upper limit to the beneficial effects of excess weight, in which the detrimental effects of BMI overcome the paradoxical protection it seems to offer.

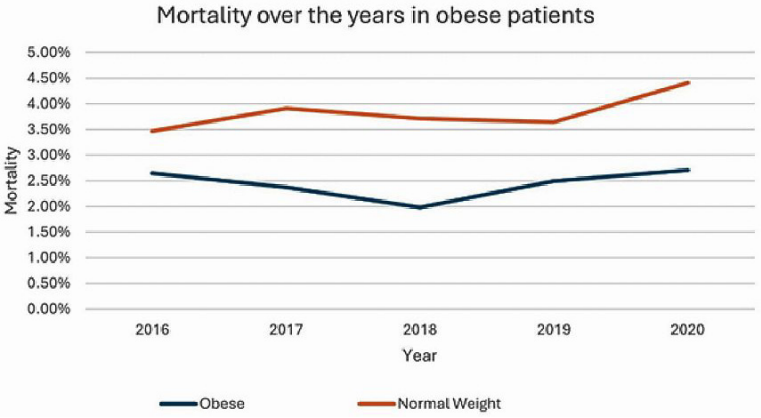

Figure 4. Year-on-year comparison of mortality in obese vs normal weight patients.

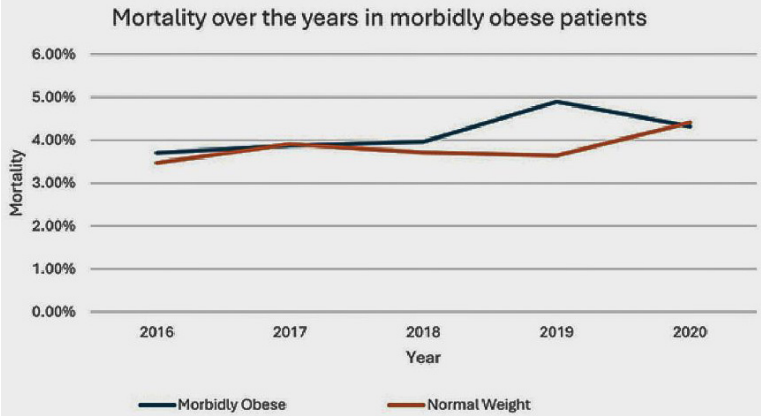

Figure 5. Year-on-year comparison of mortality in morbidly obese vs normal weight patients.

This study provides compelling evidence that BMI significantly influences postoperative mortality in patients undergoing aortic valve surgery and largely supports the presence of the aforementioned "obesity paradox". While cachexia was strongly associated with increased surgical mortality, which underscores the critical importance of nutritional and systemic health, patients in the overweight and obese categories exhibited statistically significantly lower mortality than those with a normal BMI. These findings suggest that modest excess body weight may offer a physiologic buffer against the metabolic and inflammatory stresses of surgery, possibly due to bolstered energy reserves, or as a result of preemptive cardioprotective therapies and heightened clinical monitoring. However, this protective effect appears to diminish at the end of the extreme BMI spectrum, as morbid obesity did not confer a significant survival advantage. The nonlinear relationship between BMI and surgical outcomes highlights the complexity of body composition's role in perioperative risk.

The mortality trends observed in this study may, in part, be explained by differences in physiological reserve, or the body's ability to withstand, adapt to, and recover from acute stressors, such as a major surgery [20]. Overweight and moderately obese individuals possess greater metabolic and nutritional reserves, including higher glycogen stores, adipose tissue, and, importantly, lean muscle mass. During the catabolic state induced by major surgery and the period of recovery that follows, these reserves can be accessed by the body to provide crucial nutritional components required for wound healing, immune responses, and maintenance of hemodynamic stability. In contrast, normal-weight individuals may have limited excess substrate availability, and cachectic patients, who are already in a chronic catabolic state, may lack the energetic and protein reserves required to meet the heightened metabolic demands of surgery. Cachexia often involves a loss of both fat and lean mass, impairing both energy provision and functional capacity. Moreover, muscle tissue serves as a key reservoir for amino acids essential for synthesizing acute-phase proteins, clotting factors, and immunoglobulins, which are all critical for postoperative recovery. The presence of adequate reserves in overweight and obese individuals may therefore buffer against postoperative complications that cause mortality such as infection, organ dysfunction, and delayed wound healing, while the absence of such reserves in cachectic individuals likely contributes to their significantly elevated mortality risk. This differential capaci-

ty to tolerate metabolic and inflammatory stress may represent a key mechanism underlying the observed non-linear relationship between BMI and surgical outcomes, the obesity paradox. It also highlights the importance of considering body composition in risk stratification, not just body weight, as the amount of lean muscle mass that is increased in overweight patients may be what is providing that mortality benefit as opposed to simply adipose tissue. These findings underline the need to re-evaluate traditional risk assumptions based only on BMI, and advocate for more individualized preoperative assessments. An analysis including a more detailed account of a patient's body composition beyond BMI that measures true muscle mass and fat distribution would be helpful in further narrowing down the mechanism behind the phenomenon. This would allow for better strategies moving forward that would optimize a patient's health before aortic valve surgery, improving outcomes and reducing mortality for all weight classifications.

Limitations

Our data used ICD-10 coding with its inherent limitations and accuracy. Furthermore, we only evaluated short-term inpatient mortality and not long-term mortality after discharge. This was a retrospective study needing confirmation in randomized prospective trials with more accurate measures of body composition and causes of mortality.

Conclusions

The partial obesity paradox is true in patients undergoing aortic valve surgery, with the lowest mortality occurring in overweight patients, followed by obese patients, and with cachexia having the highest mortality out of all groups.

Disclosure of conflict of interest

None.

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