Obesity Paradox: Pulmonary Complications Rather than Mortality after Transcatheter Aortic Valve Implantation?

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Research Article

Keywords: Aortic stenosis, TAVI, Body mass index, intubation time

Posted Date: June 2nd, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-575463/v1>

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Abstract

Background: Transcatheter aortic valve implantation (TAVI) for symptomatic aortic stenosis (AS) is considered a minimally invasive procedure. Body mass index (BMI) has been rarely evaluated for pulmonary complications after TAVI. This study aimed to assess the influence of BMI on the pulmonary complications and other related outcomes after TAVI.

Methods: The clinical data of 109 patients who underwent TAVI in our hospital from May 2018 to April 2021 were retrospectively analyzed. Patients were divided into three groups according to BMI: normal weight (BMI $<24.0\text{kg/m}^2$, $n=54$), overweight (BMI $24.0\text{--}27.9\text{kg/m}^2$, $n=41$) and obesity (BMI $>28\text{kg/m}^2$, $n=14$) and two groups according to vascular access: through femoral artery route (TF-TAVI) ($n=94$) and through the transapical route (TA-TAVI) ($n=15$). Procedure endpoints, procedure success, and adverse outcomes were evaluated according to the Valve Academic Research Consortium (VARC)-2 definitions.

Results: Obese patients had higher proportion of older ($p < 0.01$) and previous percutaneous coronary intervention patients ($p < 0.01$) and higher percentage of diabetes mellitus ($p = 0.016$) and frailty ($p = 0.024$), lower level of glomerular filtration rate ($p < 0.01$). Procedure success was found similar between the three groups. 30-day all-cause mortality of patients with normal weight, overweight, and obesity was 3.7% (2/54) vs 4.9% (2/41) vs 7.1% (1/14), respectively. In the multivariable analysis, overweight and obese patients exhibited similar overall mortality (overweight vs normal, $p = 0.550$ and obese vs normal, $p = 0.763$) and similar intubation time compared to normal weight patients (9.3 ± 5.2 hours vs 9.0 ± 6.2 hours vs 8.8 ± 4.3 hours in obesity, overweight, and normal weight patients, respectively, $p = 0.699$). Although obese patients had lower PaO₂/FiO₂ than the normal weight patients at baseline, transitional extubation and postextubation 12th hour ($p=0.046$, 0.036 , 0.047 respectively), there was no difference at postextubation 24th hour, postextubation 48th hour and postextubation 72th hour ($p = 0.778$, 0.866 , 0.886 respectively). Chronic lung disease (OR=7.986, $p=0.001$) rather than obesity (OR=1.967, $p=0.132$) or overweight (OR=3.046, $p=0.081$) affected postoperative PaO₂/FiO₂ after TAVI.

Conclusions: We did not find the existence of an obesity paradox after TAVI. BMI showed no effect on the postoperative intubation time. Patients with a higher BMI should be treated equally and do not need to deliberately extend the intubation time for TAVI.

Introduction

Aortic stenosis (AS) is one of the most common degenerative valvular heart diseases ^{1,2}. With years of gradual development, multiple factors including genetic susceptibility, anatomical changes and lifestyle seem to contribute to valvular development into a clinically related stage of obstruction. Due to impaired cardiac function, patients with AS experience a high disease burden and a poor prognosis ³. There is no doubt that the prevalence of severe AS develops with age, bothering about 4% of the population over the age of 75 years ^{4,5}. The traditional treatment has been surgical aortic valve replacement (SAVR), which

involves cardiopulmonary bypass (CPB) and a sternotomy. However, depending on individual comorbidities, this process may pose a high risk to some patients ⁶.

Transcatheter aortic valve implantation (TAVI), an interventional method that implants the valve via the transfemoral artery percutaneously (TF-TAVI) or directly via the transapical route (TA-TAVI), has turned into a worth-considering method for inoperable or high-risk surgical patients with severe AS ^{7,8}. Although the TAVI technique has been greatly improved, patients undergoing TAVI are older and also have unique associated comorbidities ⁹.

Early extubation is associated with a good prognosis because prolonged intubation will increase infection risk which subsequently result in respiratory failure ^{10,11}. However, the risk factors for prolonged intubation are not fully clear. Previous research indicates that overweight or obese patients are more likely to ventilate longer than normal weight patients after acute thoracic aortic dissection (ATAD) surgery ¹². Weight loss is reported related to a significant improvement in pulmonary function ¹³. Obesity has also been considered as a predictor of postoperative hypoxemia ^{14,15}.

Obesity is also considered a important and modifiable risk factor for cardiovascular morbidity and mortality and has been associated with greater mortality in the general population and cardiovascular disease (CVD) patients ^{16,17}. Despite their adverse effect on general health, overweight and obesity showed protective effect in a variety of cardiovascular interventions ¹⁸⁻²⁰. This discrepancy was also appeared in severe AS patients undergoing TAVI ^{18,21-27}.

This study aims to explore whether obesity also affects the ventilation time and whether there is an "obesity paradox" in the prognosis of patients after TAVI, in order to obtain information that will help clinical practice.

Subjects And Methods

1. The research subjects

We examined consecutive patients with severe symptomatic aortic stenosis (AS) that underwent transcatheter aortic valve implantation (TAVI) during May 2018 to April 2021 at our institute, who were considered inoperable or too high-risk for a traditional surgical aortic valve replacement ⁶. The medical staff measured the height and weight of all the patients on admission. Patients were classified into three groups: normal weight if BMI was $<24 \text{ kg/m}^2$, overweight if BMI $24-27.9 \text{ kg/m}^2$ and obese if BMI $\geq 28 \text{ kg/m}^2$ according to the most commonly used body mass index (BMI) classification system for adults in China ²⁸. Patients were also classified into two groups according to vascular access: through femoral artery route (TF-TAVI) and through the transapical route (TA-TAVI). We decided which method was best for the patients according to current guidelines ⁶ and made the decision by the local heart team composed of cardiac surgeons and cardiologists. Device endpoints, success rate and related adverse

events were recorded according to the Valve Academic Research Consortium (VARC)-2 definitions²⁹. Patients matching one or more of the following pathological characteristics were excluded: improper aortic valve size; thrombosis in the left ventricle; active endocarditis; high risk of coronary ostia obstruction; plaque in the ascending aorta or aortic arch with active thrombus.

2. Criteria

We recorded and defined the related cardiovascular risk factors as follows. Hypertension as a systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg³⁰. Diabetes mellitus as fasting blood glucose ≥ 7 mmol/L or a previous diagnosis³¹. Stroke by a clinical diagnosis or CT scan³². Hypoxaemia as an oxygen saturation $< 90\%$ by pulse oximetry or available arterial oxygen < 60 mmHg^{33,34}. Frailty was evaluated based on serum albumin, gait speed, grip strength, and number of independent activities of daily living.

We obtained informed consent from all study subjects. Patient anonymity was preserved. The study was carried out in accordance with the ethics of the 1975 Declaration of Helsinki with later amendments.

3. Procedural characteristics

All procedures were performed under general anesthesia. TF-TAVI (VitaFlow® Transcatheter Aortic Valve, Micro Port, Shanghai, China in 94 patients) was performed by percutaneous access through the femoral artery, while TA-TAVI was carried out via a small left anterior thoracotomy (J-Valve, JC Medical, China in 15 patients). In both types of surgery, 100 I.E./kg body weight of heparin were used for anticoagulation, which was subsequently antagonized by protamine at a ratio of 1:1. The detailed procedure can be seen in Supplementary Material.

4. Statistical analysis

All data were collected and showed as mean $\pm$ standard deviation (SD) for continuous variables and as number (percentage) of patients for categorical variables. For categorical data, the Chi-squared test was applied to evaluate the differences. Kruskal-Wallis H test was performed for abnormally distributed values with or without homogeneity of variance. Logistic regression analysis was conducted to seek the potential risk factors of overall mortality and hypoxemia. The factors for multivariate analysis were incorporated according to the results of univariate analysis and professional knowledge. Survival was used by the Kaplan-Meier method. $P < 0.05$ was considered statistically significant.

Results

1. Baseline Patient Characteristics

109 patients underwent transcatheter aortic valve implantation (TAVI) at our institute. 54 patients had normal weight (49.5%) with body mass index (BMI) of 22.4 ± 1.7 , 41 patients were overweight (37.6%) with BMI of 27.1 ± 1.4 , and 14 patients were obese (12.9%) with BMI of 34.9 ± 5.0 . Transfemoral approach was used in 86.2% of the cases (94 cases), transapical approach in 13.8% of the cases (15 cases). Table 1 shows the baseline clinical characteristics and pre-procedural imaging details of the study patients. Several baseline characteristics were different between groups: obese patients showed higher proportion of older ($p < 0.01$) and previous percutaneous coronary intervention patients ($p < 0.01$) and higher prevalence of diabetes mellitus ($p = 0.016$) and frailty ($p = 0.024$), lower level of glomerular filtration rate ($p < 0.01$). Aortic valve gradients and left ventricular ejection fraction showed similar between all groups.

Table 1
Baseline Patient Characteristics

Variable	BMI (kg/m ²)				p-value (normal vs 25+)
	Overall(n = 109)	18.5–24.(n = 54)	25-29.9(n = 41)	≥ 30(n = 14)	
Age (years)	72.0 ± 8.8	72.6 ± 9.4	74.4 ± 7.3	76.4 ± 8.4	< 0.01
Men	67 (61.5%)	35 (64.8%)	26 (63.4%)	6 (42.9%)	0.306
Body mass index (kg/m2)	26.8 ± 5.7	22.4 ± 1.7	27.1 ± 1.4	34.9 ± 5.0	< 0.01
New York Heart Association class III or IV	87 (79.8%)	40(74.1%)	35(85.4%)	12(85.7%)	0.334
Hypertension	94(86.2%)	45(83.3%)	36(87.8%)	13(92.9%)	0.611
Diabetes mellitus	37 (33.9)	13 (24.1%)	15 (36.6%)	9 (64.3%)	0.016
Previous myocardial infarction	16 (14.7%)	6 (11.1%)	6 (14.6%)	4 (28.6%)	0.258
Previous coronary artery bypass graft	18 (16.5%)	6 (11.1%)	8 (19.5%)	4 (28.6%)	0.236
Previous percutaneous coronary intervention	28(25.7%)	9 (16.7%)	10 (24.4%)	9(64.3%)	< 0.01
Previous valve surgery	5 (4.6%)	2 (3.7%)	2 (4.9%)	1 (7.1%)	0.826
Peripheral artery disease	36 (33.0%)	16 (29.6%)	16 (39.0%)	4 (28.6%)	0.610
Previous stroke/transient ischemic attack	18 (16.5%)	8 (14.8%)	7 (17.1%)	3 (21.4%)	0.824
Chronic lung disease ^a	37 (33.9%)	15 (27.8%)	16 (39.0%)	6 (42.9%)	0.403
Glomerular filtration rate (mL/min/m ²)	55.9 ± 25.5	61.1 ± 18.1	53.4 ± 20.4	50.1 ± 31.0	< 0.01

Values are mean ± SD or n (%).

^a Interstitial lung disease or chronic obstructive pulmonary disease or asthma.

^b Assessed based on serum albumin, gait speed, grip strength, and number of independent activities of daily living. Suggested criteria for the diagnosis of frailty included 5-min walking time, grip strength, BMI < 20 kg/m² and/or weight loss of 5 kg/year, serum albumin < 3.5 g/dL, and cognitive impairment or dementia.

	BMI (kg/m ²)				
Previous pacemaker	14 (12.8%)	6 (11.1%)	6 (14.6%)	2 (14.3%)	0.925
Atrial fibrillation	27 (24.8%)	11 (20.1%)	12 (29.3%)	4 (28.6%)	0.557
Frailty ^b	31 (28.4%)	11 (20.1%)	12 (29.3%)	8 (57.1%)	0.024
Ejection fraction (%)	56.8 ± 14.9	55.9 ± 15.8	57.2 ± 14.5	58.1 ± 13.1	0.060
Aortic valve area (cm ²)	0.63 ± 0.16	0.62 ± 0.15	0.64 ± 0.16	0.66 ± 0.16	0.910
Aortic valve mean gradient (mm Hg)	45.4 ± 13.6	46.4 ± 13.0	43.8 ± 14.0	46.4 ± 13.8	0.226
Aortic valve maximal gradient (mm Hg)	76.2 ± 21.4	77.7 ± 21.0	73.8 ± 21.3	77.4 ± 21.8	0.160
CT mean annulus diameter (mm)	24.3 ± 2.7	24.2 ± 2.6	24.5 ± 2.6	24.1 ± 2.6	0.890
Values are mean ± SD or n (%).					
^a Interstitial lung disease or chronic obstructive pulmonary disease or asthma.					
^b Assessed based on serum albumin, gait speed, grip strength, and number of independent activities of daily living. Suggested criteria for the diagnosis of frailty included 5-min walking time, grip strength, BMI < 20 kg/m ² and/or weight loss of 5 kg/year, serum albumin < 3.5 g/dL, and cognitive impairment or dementia.					

2. Procedural details

Procedural details are shown in Table 2. Procedure success was similar between three BMI groups (94.4% vs 97.6% vs 92.9% for the normal weight, overweight and obese patients, respectively; p=0.555).

Table 2
Procedural Details

	BMI(kg/m2)			
Variable	18.0-24.9(n = 54)	25-29.9(n = 41)	≥ 30 (n = 14)	p-value
Implanted valve :				
VitaFlow® ^a	46 (85.2%)	36 (87.8%)	12 (85.7%)	0.338
J-Valve ^b	8 (44.4%)	5 (43.9%)	2 (42.9%)	
Implanted valve size (mm):				
21(VitaFlow®)	16 (29.6%)	12 (29.3%)	2 (14.3%)	0.567
24(VitaFlow®)	30 (55.6%)	19 (46.3%)	7 (50.0%)	
27(VitaFlow®)	8 (14.8%)	10 (24.4%)	4 (28.6%)	
30(VitaFlow®)	0 (0.0%)	0 (0.0%)	1 (7.1%)	
Vascular access:				
Transfemoral	46 (85.2%)	36 (87.8%)	12 (85.7%)	0.338
Transapical	8 (14.8%)	5 (12.2%)	2 (14.3%)	
Device success	51 (94.4%)	40 (97.6%)	13 (92.9%)	0.555
2nd valve	2 (3.7%)	2 (4.9%)	1 (7.1%)	0.826
Postdilatation	6 (11.1%)	5 (12.2%)	2 (14.3%)	1.000
Valve embolization	1 (1.9%)	0 (0.0%)	0 (0.0%)	1.000
Fluoroscopy time (min.)	17.7 ± 11.2	15.7 ± 6.8	16.7 ± 9.1	0.560
Total contrast used (ml)	86.9 ± 49.5	88.3 ± 44.5	91.6 ± 44.5	0.452
TEE postprocedural PVL:				
None/trace	41 (75.9%)	31 (75.6%)	11 (78.6%)	0.563
Mild	12 (22.2%)	10 (24.4%)	2 (14.3%)	
Values are mean ± SD or n (%).				
^a VitaFlow®Transcatheter Aortic Valve, Micro Port®ShangHai®China.				
^b J-Valve Transcatheter Aortic Valve, JC Medical,China.				
Abbreviations: PVL, perivalvular leak; TEE, transesophageal echocardiography				

		BMI(kg/m ²)		
Moderate	1(1.9%)	0 (0.0%)	1 (7.1%)	
Severe	0	0	0	
Postprocedural aortic valve gradient (mm Hg)	8.4 ± 4.8	9.7 ± 5.2	8.2 ± 5.3	0.343
Values are mean ± SD or n (%).				
^a VitaFlow®Transcatheter Aortic Valve, Micro Port, ShangHai, China.				
^b J-Valve Transcatheter Aortic Valve, JC Medical, China.				
Abbreviations: PVL, perivalvular leak; TEE, transesophageal echocardiography				

3. 30-day outcomes and 35-month mortality

30-day all-cause mortality was 3.7% (2/54, 1 case died of concurrent liver and kidney failure, another case died of postoperative cerebral hemorrhage due to combined nephrotic syndrome and coagulation dysfunction) vs 4.9% (2/41, died of acute renal failure) vs 7.1% (1/14, died of postoperative right coronary artery blockage) in normal weight, overweight, and obese patients, respectively. These 5 cases were all in-hospital deaths. 30-day complications are shown in Table 3.

Table 3
Clinical 30 days Outcome

Variable	BMI (kg/m ²)			
	Overall(n = 109)	18.5–24.9(n = 54)	25-29.9 (n = 41)	≥ 30 (n = 14)
Mortality	5 (4.6%)	2 (3.7%)	2 (4.9%)	1 (7.1%)
Cerebrovascular accident/transient ischemic attack	3 (2.8%)	1 (1.9%)	2 (4.9%)	0
Myocardial infarction	2 (1.8%)	0	1 (2.4%)	1 (7.1%)
Respiratory failure	7 (6.4%)	3 (5.6%)	2 (4.9%)	2 (14.3%)
Cardiogenic shock	3 (2.8%)	2 (3.7%)	1 (2.4%)	0
Cardiac tamponade	1 (0.9%)	1 (1.9%)	0	0
Major bleeding	2 (1.8%)	1 (1.9%)	1 (2.4%)	0
Major vascular complications	4 (3.7%)	2 (3.7%)	1 (2.4%)	1 (7.1%)
Minor vascular complications	8 (7.3%)	4 (7.4%)	3 (7.3%)	1 (7.1%)
New permanent pacemaker implantation	7 (6.4%)	3 (5.6%)	3 (7.3%)	1 (7.1%)
Acute kidney injury stage 3	13 (11.9%)	6 (11.1%)	6 (14.6%)	1 (7.1%)
New York Heart Association functional class	1.83 ± 0.7	1.82 ± 0.8	1.77 ± 0.8	1.79 ± 0.7
Values are mean ± SD or n (%).				

In addition to the 5 in-hospital deaths, 104 patients were discharged alive and followed up. 35-month mortality was 9.3% (5/54) for normal weight patients, 9.8% (4/41) for overweight patients, and 7.1% (1/14) for obese patients (p=0.836). The mean follow-up period was 18.65±9.36 months (range: 0-35 months). Survival curve of the normal weight, overweight and obese group was shown in Figure 1: The three groups of survival curve has been studied and showed no significant differences between them, p=0.836.

In the univariate model, obese patients had decreased overall mortality compared to normal BMI patients (Hazard Ratio [HR]=0.864, 95% Confidence Interval [CI] 0.321-0.910; p 0.028) (Table 4). However, in the multivariable analysis, mortality among all BMI groups was similar (HR=1.075 and 1.065, 95% CI 0.875-1.985 and 0.896-1.998; p=0.550 and 0.763 for the overweight and obese vs the normal weight group, respectively) (Table 4). In the univariable model, BMI, age, glomerular filtration rate, atrial fibrillation, frailty, ejection fraction, aortic valve mean gradient and alternative access were found independently associated with 35-month all-cause mortality in this study (Table 4). In a second multivariable model, we

found diabetes mellitus, glomerular filtration rate and frailty rather than higher BMI was related to overall mortality (Table 4).

4. **Pulmonary complications**

Overweight and obese patients also had similar intubation time compared to normal weight patients (8.8 ± 4.3 hours vs 9.0 ± 6.2 hours vs 9.3 ± 5.2 hours in normal weight, overweight, and obesity patients, respectively, $p=0.699$). Although obese patients have lower $\text{PaO}_2/\text{FiO}_2$ than the normal weight patients at baseline, transitional extubation and postextubation 12th hour ($p = 0.046, 0.036, 0.047$ respectively), there is no difference of $\text{PaO}_2/\text{FiO}_2$ at postextubation 24th hour, postextubation 48th hour and postextubation 72th hour ($p = 0.778, 0.866, 0.886$ respectively). (Table 5)

Chronic lung disease ($\text{OR}=7.986, p=0.001$) rather than obesity ($\text{OR}=1.967, p=0.132$) or overweight ($\text{OR}=3.046, p=0.081$) affects $\text{PaO}_2/\text{FiO}_2$ after TAVI. (Table 6)

Table 4
Univariate and Multivariate Cox Proportional Hazard Analysis of Overall Mortality

	Univariate analysis			Multivariate analysis		
	Hazard	Confidence		Hazard	Confidence	
Variable	ratio	interval	p-value	ratio	interval	p-value
BMI (categorical):						
Overweight vs normal	1.428	0.255–8.002	0.559	1.075	0.875–1.985	0.550
Obese vs normal	0.864	0.321–0.910	0.028	1.065	0.896–1.998	0.763
BMI ^a (kg/m ²)	0.959	0.922–0.968	0.032			
Age (years)	3.119	1.192–5.106	0.043	1.168	0.993–1.867	0.323
Gender	1.032	0.988–1.996	0.788	0.855	0.733–1.457	0.534
Diabetes mellitus	0.932	0.329–2.503	0.779	3.930	1.995–4.885	0.034
Chronic lung disease	1.986	0.392–2.831	0.409	1.306	0.156–1.887	0.460
Coronary artery disease	1.988	0.959–2.887	0.569	1.004	0.566–1.661	0.660
Previous myocardial infarction	0.925	0.780–2.944	0.099			
Previous coronary artery bypass graft or valve surgery	0.317	0.102–0.980	0.328			
Previous stroke/transient ischemic attack	0.878	0.884–1.488	0.587			
Glomerular filtration rate (mL/min/m ²)	0.898	0.877–1.219	< 0.001	3.006	1.876–3.301	0.046

Covariates included in the multivariate analysis: BMI categories, age, gender, diabetes mellitus, chronic lung disease, coronary artery disease, glomerular filtration rate, atrial fibrillation, frailty, ejection fraction, aortic valve mean gradient, valve type, and alternative access.

^aBMI as linear variable; hazard ratio per 1 kg/m² increment.

Abbreviations: BMI, body mass index.

	Univariate analysis			Multivariate analysis		
	Hazard	Confidence		Hazard	Confidence	
Atrial fibrillation	1.318	1.259– 2.916	0.04	1.558	0.885– 2.432	0.12
Frailty	3.125	2.035– 3.152	< 0.001	3.825	1.968– 4.730	0.003
Ejection fraction	0.958	0.881– 0.976	0.01	1.678	0.807– 1.806	0.063
Aortic valve mean gradient (mm Hg)	1.798	1.195– 1.989	0.004	1.806	1.606– 1.965	0.122
Aortic valve area (cm ²)	1.006	0.625– 1.986	0.763			
Valve type: VitaFlow [®] /J-Valve	1.160	0.914– 1.246	0.108	1.803	0.875– 1.954	0.098
Alternative access (Transfemoral/Transapical)	2.940	1.338– 2.957	< 0.001	1.551	1.022– 1.997	0.088
Covariates included in the multivariate analysis: BMI categories, age, gender, diabetes mellitus, chronic lung disease, coronary artery disease, glomerular filtration rate, atrial fibrillation, frailty, ejection fraction, aortic valve mean gradient, valve type, and alternative access.						
^a BMI as linear variable; hazard ratio per 1 kg/m ² increment.						
Abbreviations: BMI, body mass index.						

Table 5
Pulmonary complications

Variable	BMI (kg/m ²)				p-value
	Overall(n = 109)	18.5–24.9(n = 54)	25-29.9 (n = 41)	≥ 30 (n = 14)	
Intubation time (hours)	9.1 ± 6.9	8.8 ± 4.3	9.0 ± 6.2	9.3 ± 5.2	0.699
Baseline PaO ₂ /FiO ₂ (mmHg)	446.67 ± 50.95	450.95 ± 47.14	403.81 ± 83.33	377.62 ± 74.29	0.046
Transitional extubation, PaO ₂ /FiO ₂ (mmHg)	386.67 ± 67.88	424.24 ± 57.27	363.64 ± 67.88	298.79 ± 63.03	0.036
Postextubation 12th hour, PaO ₂ /FiO ₂ (mmHg)	417.58 ± 55.15	441.82 ± 63.03	409.09 ± 32.12	333.33 ± 46.97	0.047
Postextubation 24th hour, PaO ₂ /FiO ₂ (mmHg)	418.18 ± 64.24	426.67 ± 30.91	401.82 ± 56.36	420.30 ± 61.21	0.778
Postextubation 48th hour, PaO ₂ /FiO ₂ (mmHg)	426.06 ± 36.06	449.70 ± 62.12	381.82 ± 26.06	424.24 ± 47.88	0.866
Postextubation 72th hour, PaO ₂ /FiO ₂ (mmHg)	393.67 ± 46.06	410.91 ± 46.06	401.82 ± 32.12	389.39 ± 40.91	0.886
Values are mean ± SD.					

Table 6
Logistic regression of hypoxemia

Variable	Odds ratio	95% Confidence interval	Overall p-value
BMI (kg/m ²)			
BMI < 25	1.000		
BMI ≥ 25	3.046	1.678–13.985	0.081
BMI ≥ 30	1.967	0.369–10.876	0.132
Chronic lung disease			
No	1.000		
Yes	7.986	3.580-40.338	0.001 ^a
Abbreviations: BMI, body mass index.			
^a Statistically significant.			

Discussion

In this study, we found different baseline characteristics of obese patients undergoing transcatheter aortic valve implantation (TAVI): higher proportion of female and higher prevalence of diabetes mellitus, coronary artery disease, chronic lung disease and frailty and lower estimated glomerular filtration rate (GFR). However, similar procedural complications rate and device success were found between all body mass index (BMI) groups.

Obesity paradox in the univariate model

In the general population, as BMI increases above 30 kg/m², the risk of developing cardiovascular disease (CVD) increases, and the risk of mortality is higher³⁵. Nonetheless, it is often observed that obese individuals with chronic diseases have a reduced risk of mortality compared to non-obese individuals with similar disease characteristics. This positive effect of increased BMI following these interventions has been called the “obesity paradox”. This paradox effect has been described in many different disease categories, including CVD, diabetes mellitus, and chronic kidney disease³⁶⁻³⁸. The “obesity paradox” has been reported mainly in patients with heart failure, acute coronary syndrome and following percutaneous and surgical coronary interventions^{[18-20][36][38]}. Some studies have explained this protective effect that the soluble TNF- α receptor produced in adipose tissue neutralize the adverse effects of TNF- α on the mortality of patients with chronic inflammatory diseases such as CVD³⁹. In addition, higher lipoproteins in the circulation may also bind and reduce the role of lipopolysaccharides in stimulating the release of inflammatory cytokines³⁸.

There is also evidence for the obesity paradox in high-risk groups after TAVI^{21,26}. Konigstein et al. reported that after adjusting baseline characteristics, increased BMI was independently related to the improvement in survival after TAVI²¹. The conclusion of the data analysis from the large FRANCE 2 Registry including 3,072 patients was also consistent with the obesity paradox after TAVI²⁶. In our univariate model, obesity was found to be closely related to increased survival rates, which was also in line with the obesity paradox.

Disappearance of obesity paradox in the multivariate model

However, in the multivariate model, after adjusting for different baseline characteristics including diabetes mellitus, glomerular filtration rate and frailty, the overall mortality rate showed similar between three BMI groups. That means in contradiction to these previous studies, according to our multivariable model, there is no obesity paradox after TAVI and overall mid-term survival rates are similar among all BMI groups (Fig 1). Previous studies have explained this discrepancy because baseline frailty factor was not included in their research and analysis models. The updated VARC-2 document defined frailty as slowness, weakness, exhaustion, wasting and malnutrition, inactivity, and loss of independence and

emphasized that frailty is the most important feature in current risk models ²⁹, which was found to be a strong predictor of mortality and adverse effects after cardiac surgery and TAVI ⁴⁰⁻⁴². Indeed, in this study, frailty was found to be a strong predictor of overall mortality in both the uni- and multi-variable models (HR 3.825; p = 0.003; Table 4). Meanwhile, frailty was found to be present in 57.1% of obese patients vs 20.1% of normal weight patients (p=0.024), which might be a possible confounder of resisting the occurrence of the obesity paradox. In addition, obese patients in this research were significantly older, had less GFR and higher previous percutaneous coronary intervention, diabetes mellitus prevalence, which are also possible confounding factors might provides an explanation for the disappearance of protective effect of obesity on mortality in this study.

Obesity paradox of pulmonary complications

Many studies have consistently found that obese patients are more likely to develop severe hypoxemia after surgery because lung compliance declines particularly significantly in obese patients. Due to their abnormal BMI, obese patients may have some clinical features that require special management during the perioperative period, such as higher doses of medications, greater tidal volume, and higher airway pressure to ensure adequate postoperative ventilation. Therefore, the dyspnea of obese people has increased significantly. In addition, it has been shown that respiratory resistance increases in obesity and that the mechanism of ARDS may be attributed to the imbalance of anti-inflammatory and pro-inflammatory cytokines, as well as oxidants and anti-oxidants ⁴³⁻⁴⁶. Most obese patients suffer from chronic and excessive inflammation and oxidative stress ^{43,44}. When pro-inflammatory signaling pathways are significantly upregulated, obese patients are prone to produce more abnormal cytokine products and acute-phase reactants. Furthermore, induction of pro-inflammatory cytokines and mediators has been proved to increase with weight gain ^{45,46}. In addition, obesity can increase oxidative stress and reactive oxygen products, which may lead to direct damage to the cellular membranes, monocytes cellular adhesion, and the release of chemotactic factors and vasoactive substances. The above situations are especially obvious when undergoing cardiopulmonary bypass. However, in this study, although obese patients had lower PaO₂/FiO₂ than the normal weight patients at pre- and early postoperative time (baseline, transitional extubation and postextubation 12th hour), obesity did not cause a significant effect on severe postoperative hypoxemia and longer intubation time in our multiple regression model. One explanation for this divergence may be that patients with TAVI without cardiopulmonary bypass had not markedly activated the above-mentioned signalling pathways.

Limitations

Selection bias could occur because this study was based on a retrospective single-centre, which might have limited the conclusions. Furthermore, the differences of a longer-term prognosis of patients is needed. Moreover, the administration of TAVI patients should be time-consuming and a more

comprehensive evaluation of the prognostic value of BMI as a predictor of clinical results after TAVI is needed.

Conclusion

We did not find an “mortality obesity paradox” after TAVI. Obese patients in this study were significantly older, had less GFR and higher previous percutaneous coronary intervention, diabetes mellitus and frailty prevalence, which may explain the discrepancy between our results and previous reports that claimed a protective effect for increased BMI after TAVI.

While, we may be able to find an “pulmonary complications obesity paradox”: obese patients had experienced lower $\text{PaO}_2/\text{FiO}_2$ in the early postoperative period but avoided longer intubation time following TAVI. Patients with a higher BMI should be treated equally for TAVI, and do not need to deliberately extend the intubation time.

Abbreviations

TAVI: transcatheter aortic valve implantation; PVL: perivalvular leak; TEE: transesophageal echocardiography

Declarations

Ethical Approval and Consent to participate:

The present study was approved by the ethics committee of Fujian Medical University, China and adhered to the tenets of the Declaration of Helsinki.

Consent for publication:

Not applicable

Availability of Data and Materials:

Data sharing not applicable to this article as no data sets were generated or analyzed during the current study.

Funding:

The funding information is not applicable

Competing interests

All authors declare that they have no competing interests.

Author Contributions

Zeng-Rong Luo designed the study. Zeng-Rong Luo and Han-Fan Qiu collected and analyzed data together. Zeng-Rong Luo drafted the article and submitted the manuscript. Liang-Wan Chen supervised this study. All authors read the final version of this article and approved for publication.

Acknowledgement

We highly acknowledge the contribution by the participating doctors: Liang-Liang Yan, Xue-Shan Huang, Dong-Shan Liao, Xiao-Fu Dai, Dao-Zhong Chen, Feng Lin, Qi-Min Wang.

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Figures

Figure 1

Survival curve of the normal weight, overweight and obese group was shown in Figure 1: The three groups of survival curve has been studied and showed no significant differences between them, $p=0.836$.

Supplementary Files

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