

Original Article

Impact of obesity on outcomes of transcatheter aortic valve implantation in patients with aortic stenosis: a systematic review and meta-analysis of real-world data

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Abstract: Most recent large-scale global analyses on transcatheter aortic valve implantation (TAVI) for aortic stenosis (AS) showed favorable survival outcomes in patients with high body mass index (BMI). We performed a meta-analysis pooling all clinical studies to assess the validity of improved post-TAVI prognosis in obese patients. MEDLINE and Scopus were queried till January 2023 to identify studies comparing AS patients with BMI ≥ 30 kg/m², and BMI 18.5 to <25 undergoing TAVI. Data were analyzed using a random-effects model to derive odds ratios (ORs) for all outcomes, and hazard ratios (HRs) for long-term overall survival with 95% confidence intervals. The primary outcomes of interest included 30-day all-cause mortality and long-term overall survival while secondary outcomes consisted of myocardial infarction (MI), major bleeding, major vascular events and acute kidney injury (AKI). A total of 24 studies comprising 38,743 patients were included in this meta-analysis. All-cause mortality at 30-days was significantly reduced in patients with BMI >30 kg/m² (OR 0.71, $P < 0.0001$) vs. normal BMI. Every 1 kg/m² increase in BMI was associated with better overall survival (HR 0.96, $P < 0.0001$). Obese patients had greater long-term overall survival (HR 0.87, $P < 0.00001$) compared with non-obese patients. No significant differences in MI (OR 0.84, 95% CI 0.52-1.34), major bleeding (OR 0.94, 95% CI 0.72-1.21), major vascular events (OR 1.18, 95% CI 0.97-1.43) and AKI (OR 1.17, 95% CI 0.87-1.56) were observed between the two groups. Obese AS patients might have similar procedural complications, but reduced mortality, and increased overall survival in comparison with normal weight individuals.

Keywords: Obesity, transcatheter aortic valve implantation, aortic stenosis

Introduction

Aortic stenosis (AS) comprises the most frequent degenerative valvular heart disorders associated with significant disease burden owing to poor prognosis and reduced heart function [1-3]. The prevalence of severe AS increases with age, affecting around 4% of the elderly population (>75 years). Conventional surgical valve replacement, including cardiopulmonary bypass (C.B.P.) and sternotomy, has been the standard therapy. However, these techniques are met with post-operative complications such as stroke, acute respiratory distress syndrome, heart block and multisystem-organ failure in high-risk patients [4, 5]. The overall high complication rates associated with conventional treatments has led to the intro-

duction of alternate, minimally invasive techniques such as transcatheter aortic valve implantation (TAVI) which involves the implantation of a valve percutaneously via the transfemoral (TF) or transapical (TA) route [6]. TAVI is recommended and considered a viable option mainly for treatment in severe AS patients deemed to be inoperable or at high-risk for surgical aortic valve replacement (SAVR) [7, 8]. Furthermore, between 2011 and 2014, there was a 25-fold rise in the rate of obese individuals undergoing TAVI in the United States, highlighting the rapidly growing indications for the procedure in patient profiles ranging from low to high surgical risk groups [9, 10]. Obese individuals, particularly morbidly obese (MO) patients (Body mass index (BMI) ≥ 40 kg/m²), are under-represented in clinical trials, and there is a lack

of data regarding long-term results following TAVI in this specific population. MO patients present a distinct combination of complications, such as metabolic syndrome-related comorbidities, as well as respiratory and mobility issues, which may complicate their periprocedural recovery.

However, the validity of an “obesity paradox” in cardiovascular illness is still being contested, albeit this paradigm has lately been questioned in MO patients [11, 12]. Peri-procedural and long-term outcomes following TAVI in obese individuals have showcased contradictory results [13-15]. Single-center studies with small sample sizes, notably in the MO cohort, and a variety of BMI cutoff points utilized to determine patient groups further complicates the interpretation of these results [16]. Obesity is regarded as a significant and modifiable risk factor for cardiovascular morbidity and mortality, in both the general population as well as patients with cardiovascular disease (CVD) [17]. Despite their negative impact on overall health, intermediate and high-weight individuals proved to be protected throughout many cardiovascular procedures. This disparity was also discovered in individuals with severe AS who underwent TAVI [15, 18]. A previous meta-analysis conducted by Lv and colleagues [19] investigated the obesity paradox in patients undergoing TAVI. Since then, newer cohort studies with larger sample sizes comparing clinical outcomes in patients with vs. without obesity have shown inconsistent and conflicting results. A prospective cohort study [20] demonstrated no difference in overall-mortality between normal and obese patients, however, overweight patients had significantly lower mortality rates on multivariable analysis. Sharma and coworkers [13] evaluated the relationship between BMI and baseline and procedural characteristics from the Society of thoracic surgeons-American college of cardiology transcatheter valve therapy (STS/ACC TVT) Registry. They demonstrated overweight patients, and those with class I and class II obesity to have a decreased risk of one-year mortality compared with normal weight patients. Furthermore, among those with $BMI \leq 30 \text{ kg/m}^2$, each 1-kg/m^2 increase was associated with a 2% and 4% decrease in the risk of 30-day and one-year mortality, respectively; for $B.M.I. \geq 30 \text{ kg/m}^2$, a 1-kg/m^2 increase was associated with a 3%

increased risk of 30-day mortality but not with one-year mortality. These conflicting findings in recently published clinical data warrants the conduction of an updated meta-analysis to showcase a comprehensive clinical evaluation of TAVI in obese individuals, and to confirm the validity of the improved outcomes with its therapy.

Methods

Our meta-analysis was conducted in accordance to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guideline [21].

Data sources and search strategy

Two investigators (FY and AM) independently searched through the electronic databases PubMed (MEDLINE) and Scopus for relevant articles. All studies published from inception till January 2023 were reviewed. No restrictions were implemented based on geographical location, year of publication, publication type, and language of publication. The following keywords were used ‘body mass index’, ‘BMI’, ‘obesity’, ‘transcatheter aortic valve replacement’, ‘transcatheter aortic valve implantation’ and ‘TAVI’ alongside their MeSH (medical subject headings) terms incorporated with Boolean Operators “OR” and “AND”. The detailed search strategy utilized for each database is given in [Supplementary Table 1](#). Further, we manually searched through reference lists of review articles, pertinent editorials and original publications. Google scholar, medrxiv.org, and ClinicalTrials.gov were also searched to identify grey literature and preprints. We excluded case studies, reviews, conference abstracts, preclinical experiments and letters from this analysis.

Study selection and eligibility criteria

All relevant articles identified via systematic search were exported to EndNote X9 Reference Manager (Clarivate Analytics, Philadelphia, Pennsylvania) using which duplicates were removed among various online databases. Two independent investigators (FY and AM) performed initial screening of the remaining articles based on title and abstract to ensure they met the required eligibility criteria. Finally, full texts were evaluated for relevance. Any discrepancies were resolved by discussion with the

third investigator (FZ). The search was restricted to the following inclusion criteria: observational retrospective and prospective cohort studies of patients with aortic stenosis aged ≥ 18 years undergoing transcatheter aortic valve implantation, studies with an experimental group (obese patients) and a control group (normal patients), and studies that reported at least one of the outcomes of interest including 30-day all-cause mortality, long-term overall survival, myocardial infarction (MI), major bleeding, major vascular events, and acute kidney injury (AKI) as primary or secondary endpoints. Clinical outcomes and complications were recorded according to the Valve Academic Research Consortium-2 consensus definitions (VARC2) [22]. According to the definitions set by the World Health Organization (WHO), B.M.I. (kg/m^2) was categorized as underweight (<18.5), normal (18.5 to <25), overweight (25 to <30) and obese (≥ 30). In our study, the patients with $\text{B.M.I.} \geq 30 \text{ kg}/\text{m}^2$ were labeled as obese, and the patients with $25\text{--}30 \text{ kg}/\text{m}^2$ were labeled as overweight.

Data extraction and study quality assessment

Two investigators (FY and AM) independently extracted data from the shortlisted articles using pre-specified collection forms. In addition to the population, and study characteristics, data on primary and secondary outcomes were also extracted. The data extracted included: study data including first author's last name, publication year, country of origin; experimental data including study design, study period, follow-up duration, cut offs of B.M.I., type of TAVI procedure, primary (30-day all-cause mortality and long-term overall survival) and secondary outcomes (myocardial infarction, major bleeding, major vascular events, and acute kidney injury); demographic data including total sample size, number of patients in the experimental and control groups, and major patient characteristics comprising mean age, male/female percentage, comorbidities, and statistical data including outcome statistics for the estimate of relative risk (R.R.s), odds ratio (O.R.s), and hazard ratios (H.R.s) and statistical method. Long-term overall survival was defined as survival recorded across at least one-year follow-up. The quality of each non-randomized study was assessed using the Newcastle-Ottawa Quality Assessment Scale (N.O.S.) [23]. The N.O.S. uti-

lizes a star scoring system comprising of eight items divided into three domains; selection, comparability and outcome or exposure. Each study was assigned a score from 0 to 9. Studies scoring seven or above were considered to be of high quality and thus at a low risk of bias whereas those scoring five or less were considered to be of poor quality.

Statistical analysis

We performed the statistical analysis using Review Manager (RevMan) V.5.3 Cochrane Collaboration, London, United Kingdom. A random-effects model was utilized to pool odds ratios (O.R.s) with 95% confidence intervals (C.I.s) that served as the appropriate estimate for evaluation of 30-day mortality and procedural complications extrapolated from either the demographic data or directly reported in the original studies. It was our first priority to integrate the OR statistics derived from multivariate analysis because of the adequate eliminations for confounding factors. Regarding the long-term overall survival, we used hazard ratios (H.R.s) with 95% CI as the summarized estimates, because the H.R. was the only appropriate statistic compatible for both censoring and time to event analysis. Similarly, incorporating the multivariate H.R. statistics would be considered first. In instances of a lack of multivariate statistic reporting, the H.R. value was extrapolated using published survival data with the log-rank p value as proposed by Tierney and coworkers [24]. Publication bias was ascertained for all clinical outcomes by generating a funnel plot and confirming the bias by Egger's regression test. The Higgins I-squared (I^2) statistical model was used to assess heterogeneity in the clinical outcomes of the included studies whereby a value of $I^2=25\%$ – 50% was considered mild, 50% – 75% as moderate, and greater than 75% as severe heterogeneity [25]. A p value of <0.05 was considered as statistically significant.

Results

Study characteristics and baseline demographics

The PRISMA flow chart summarizes the search and study selection process in **Figure 1**. The initial search retrieved a total of 844 relevant articles. After reviewing the titles and abstracts,

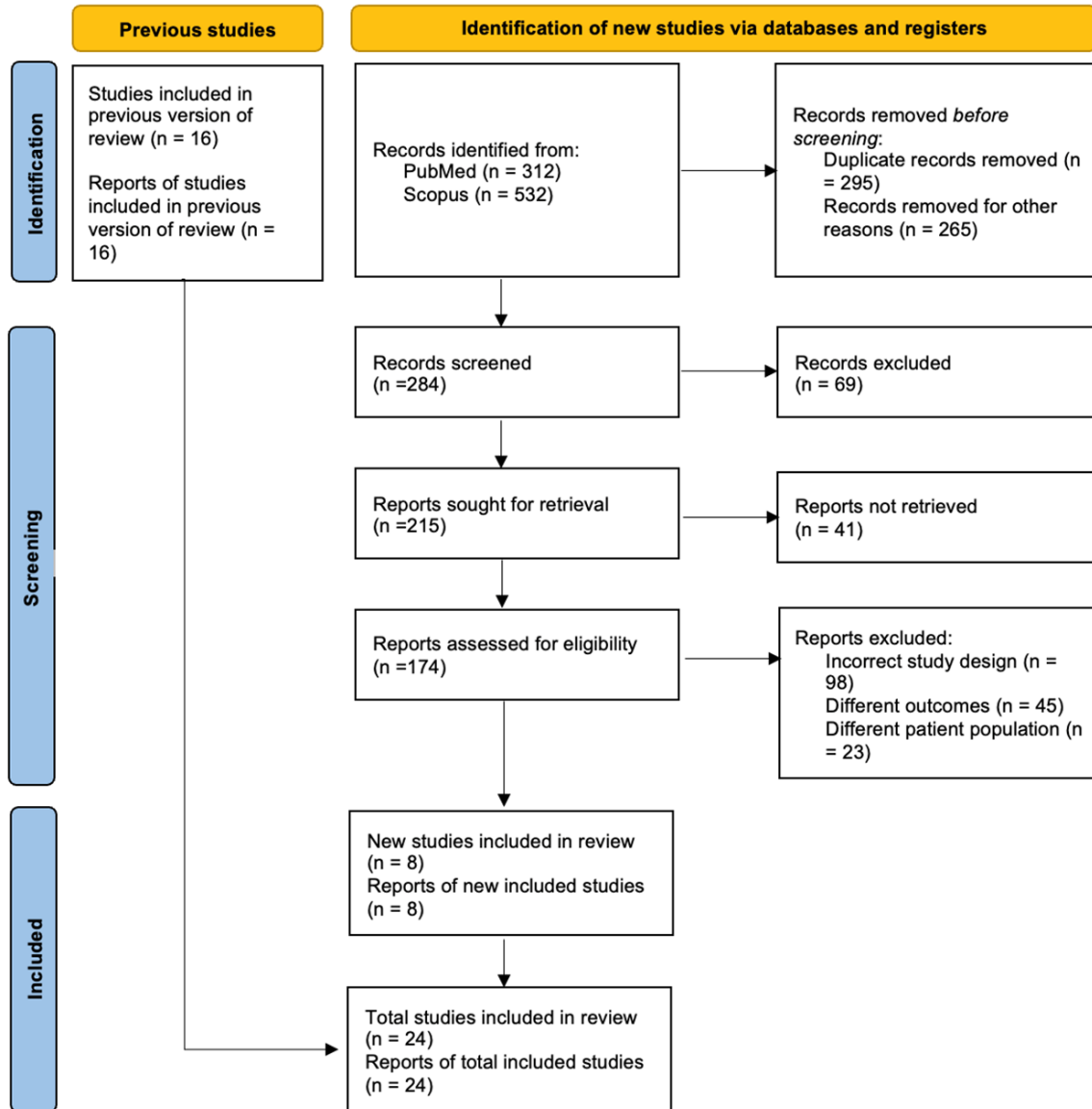


Figure 1. PRISMA flowchart diagram.

560 were removed due to duplication and irrelevance. From the finalized studies, 174 were assessed for eligibility on the basis of their full text. A total of 24 clinical studies were then included in this meta-analysis [13, 15-16, 20, 26-45]. From the included studies, n=10 reported the outcome of 30-day mortality, n=23 reported long-term overall survival as an outcome, and n=13 reported procedural complications. Six studies were prospective observational studies [15, 20, 27-29, 44] whereas 18 studies [13, 16, 26, 30-43, 45] were retrospective observational studies. A total of 38,743 patients who underwent TAVI were

included in our study. 47.7% of the included participants were male, and the mean age of the included patients was 82.1 years. The follow-up period of the eligible studies ranged from 30 days to three years. The baseline characteristics of the included studies are presented in **Table 1**.

Quality assessment and publication bias

According to the Newcastle Ottawa Scale, seven studies were assigned the score seven, 14 studies were assigned the score eight, and three studies were assigned the score nine. Overall, all of the included studies were of good

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Table 1. Baseline characteristics of included studies

Author, Year	Type of study	Country	Study Period	Sample size	Gender (male ratio)	Age (years)	Outcome reporting HR ^a /OR ^b	Type of TAVI procedure	Follow-up period, months	Outcomes reported
Abawi, 2017 [15]	Prospective observational	Netherlands	2008-2016	549			HR	Transfemoral, Transapical, Direct aortic	12	30-day mortality, long-term overall survival, procedural complication
Abramowitz, 2016 [26]	Retrospective observational	U.S.A.	2012-2015	805	484 (60.1%)	82.0 ± 8.8	H.R., OR	Transfemoral, Transapical, Transaortic, Subclavian	12	30-day mortality, long-term overall survival, procedural complication
Aung, 2013 [30]	Retrospective observational	U.K.	2007-2012	175	86 (49.1%)	83.0 ± 7.0	H.R.	Transfemoral, Transapical	12	Long-term overall survival
Beohar, 2014 [31]	Retrospective observational	U.S.A.	2007-2009	485	261 (53.8%)	N.A.	H.R.	Transfemoral, Transapical	12	Long-term overall survival
Boukhris, 2021 [43]	Retrospective observational	Canada	2009-2019	412			HR	Transfemoral, non-transfemoral	12	30-day mortality, long-term overall survival, procedural complication
Corcione, 2021 [27]	Prospective observational	Italy	2008-2018	3,705			HR	NA	NA	30-day mortality, long-term overall survival, procedural complication
Dvir, 2014 [32]	Retrospective observational	U.S.A.	2007-2009	1,108	603 (54.4%)	82.7 ± 7.2	H.R.	Transfemoral, Transapical	12	Long-term overall survival
Gonzalez-Ferreiro, 2017 [16]	Retrospective observational	Spain	2008-2015	770	332 (43.1%)	80.7 ± 6.3	H.R.	Transfemoral, Trans-axillary	36	Long-term overall survival, procedural complication
Iung, 2014 [33]	Retrospective observational	France	2010-2011	2,552	1288 (50.5%)	82.9 ± 7.2	OR	Transfemoral, Transapical, Subclavian	1	30-day mortality
Kamga, 2013 [29]	Prospective observational	Belgium	2009-2011	30	16 (53.3%)	86.0 ± 3.0	H.R.	Transfemoral	12	Long-term overall survival
Kische, 2016 [39]	Retrospective observational	Germany	2013-2015	172	100 (58.1%)	81.0 ± 5.5	OR	Transfemoral	12	30-day mortality, long-term overall survival
Koifman, 2016 [34]	Retrospective observational	U.S.A.	2007-2014	448	233 (52.0%)	82.9 ± 8.3	H.R.	Transfemoral	12	Long-term overall survival, procedural complication
Konigstein, 2015 [45]	Retrospective observational	Israel	2009-2013	409	173 (42.3%)	82.0 ± 5.7	H.R., OR	Transfemoral	12	30-day mortality, long-term overall survival, procedural complication
Marzo, 2021 [28]	Prospective observational	Italy	2014-2019	645			OR	Transfemoral	6	30-day mortality, long-term overall survival, procedural complication
Mok, 2013 [36]	Retrospective observational	Canada	2005-2009	319	147 (46.1%)	80.0 ± 8.0	H.R.	Transfemoral, Transapical, Transaortic	12	Long-term overall survival
Nieuwkerk, 2021 [41]	Prospective observational	U.S.A., Brazil, Israel, European countries	2007-2018	12,381			HR, OR	Transfemoral	12	30-day mortality, long-term overall survival
Quine, 2020 [20]	Prospective observational	U.S.A., Australia	2008-2019	634			HR	Transfemoral, Transapical, Subclavian, Direct aortic, Subclavian and Transfemoral	12	30-day mortality, long-term overall survival, procedural complication

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Salizzoni, 2016 [38]	Retrospective observational	Italy	2007-2012	1,904	757 (39.8%)	81.7 ± 6.2	H.R.	Transfemoral, Transapical, Transaortic, Trans axillary	24	Long-term overall survival
Seiffert, 2014 [37]	Retrospective observational	Germany	2008-2011	845	413 (48.9%)	80.9 ± 6.5	H.R.	Transfemoral, Transapical, Subclavian	12	Long-term overall survival
Sharma, 2020 [13]	Retrospective observational	U.S.A.	2011-2015	31,929			HR	Transfemoral, Transapical, Transaortic, Subclavian	12	30-day mortality, long-term overall survival, procedural complication
Tokarek, 2019 [35]	Retrospective observational	Finland	2008-2015	148			HR	Transfemoral, Transapical, Transaortic, Subclavian	12	30-day mortality, long-term overall survival, procedural complication
Van der Boon, 2013 [41]	Retrospective observational	Netherlands	2005-2011	940	506 (53.8%)	81.0 ± 7.0	H.R., OR	Transfemoral, Transaortic	12	30-day mortality, long-term overall survival, procedural complication
Yamamoto, 2013 [42]	Retrospective observational	France	2010-2011	3,072	1564 (50.9%)	82.8 ± 7.2	H.R., OR	Transfemoral, Transapical, Subclavian	12	30-day mortality, long-term overall survival, procedural complication
Yoon, 2016 [40]	Retrospective observational	Korea	2010-2014	848	396 (46.7%)	81.8 ± 6.6	H.R.	Transfemoral, Transapical, Transaortic, Subclavian	24	Long-term overall survival

a: Hazards ratio, b: Odds ratios.

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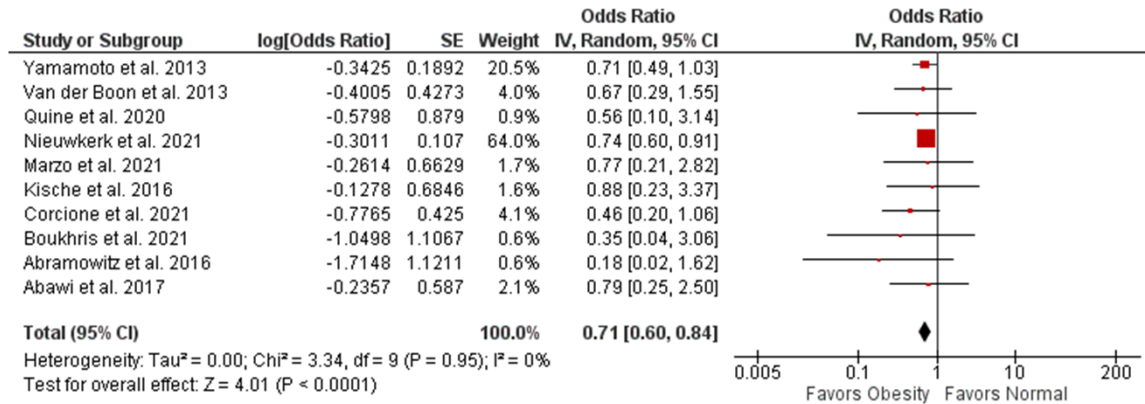


Figure 2. Forest plot of 30-day mortality and its association with obesity.

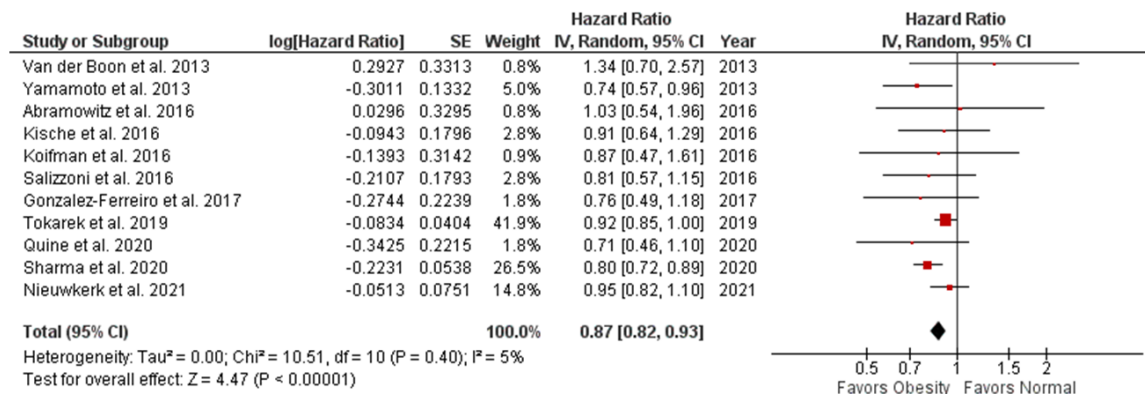


Figure 3. Forest plot of long-term overall survival and its association with obesity.

quality owing to their robust methodology as shown in [Supplementary Table 2](#). Funnel plots were created for 30-day mortality, A.K.I., major bleeding, vascular complications, and long-term overall survival as shown in [Supplementary Figures 1, 2, 3, 4, 5, 6](#). All of the aforementioned outcomes were subjected to some degree of asymmetry. Egger's regression test was used to confirm the risk of publication bias. Upon confirmation, only overall survival with 1 kg/m² increase in B.M.I. had some degree of publication bias as shown in [Supplementary Table 3](#).

30-day mortality

10 studies compared 30-day mortality between obese patients and normal patients. Upon analysis, a significant decrease could be observed in 30-day mortality among obese patients (OR 0.71, 95% CI 0.60-0.84, $P < 0.0001$; $I^2 = 0\%$) as shown in [Figure 2](#).

Long-term overall survival

11 studies compared the long-term overall survival between obese and normal patients, and their pooled estimates based on a random-effects model (HR 0.87, 95% CI 0.82-0.93, $P < 0.00001$; $I^2 = 5\%$) indicated that obesity could be predictive of better prognosis among TAVI patients ([Figure 3](#)). Comparably, a significant improvement could be seen for long-term overall survival with every 1 kg/m² increase in BMI (HR 0.96, 95% CI 0.94-0.98, $P < 0.0001$; $I^2 = 45\%$) ([Figure 4](#)).

Procedural complications

Seven studies reported an incidence of MI. No significant difference was observed between obese and normal patients in MI (OR 0.84, 95% CI 0.52-1.34, $P = 0.66$; $I^2 = 0\%$) as given in [Figure 5](#). Similarly, pooled data of 11 studies showed no significant difference for major bleeding (OR 0.94, 95% CI 0.72-1.21, $P = 0.02$; $I^2 = 54\%$) and

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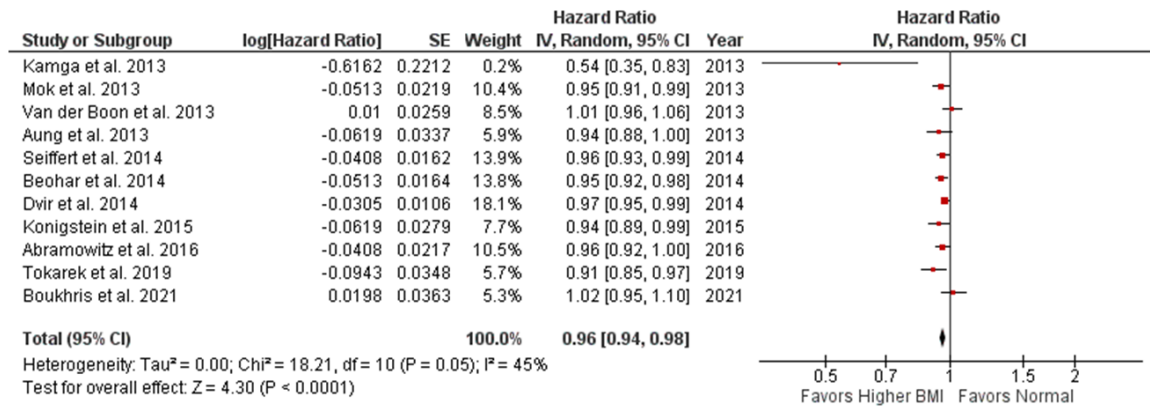


Figure 4. Forest plot of long-term overall survival and its association with B.M.I.

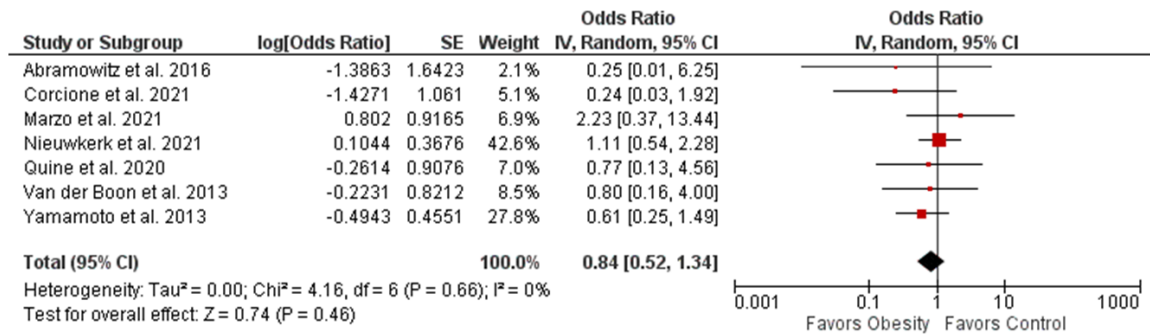


Figure 5. Forest plot of myocardial infarction and its association with obesity.

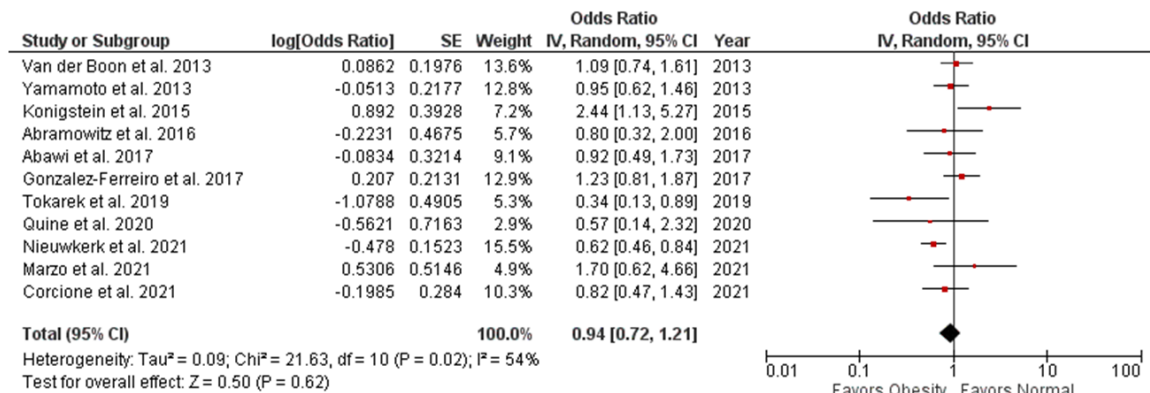


Figure 6. Forest plot of major bleeding and its association with obesity.

major vascular events (OR 1.18, 95% CI 0.97-1.43, P=0.51; I²=0%) (Figures 6 and 7). Moreover, analysis of 10 studies revealed no difference between obese and normal patients suffering from A.K.I. following TAVI (OR 1.17, 95% CI 0.87-1.56, P=0.12; I²=36%) as shown in Figure 8.

Discussion

Our meta-analysis evaluated the existence of the obesity paradox in clinical outcomes among patients undergoing TAVI. The results of our analysis revealed obesity to be significantly associated with reduced 30-day mortality, and

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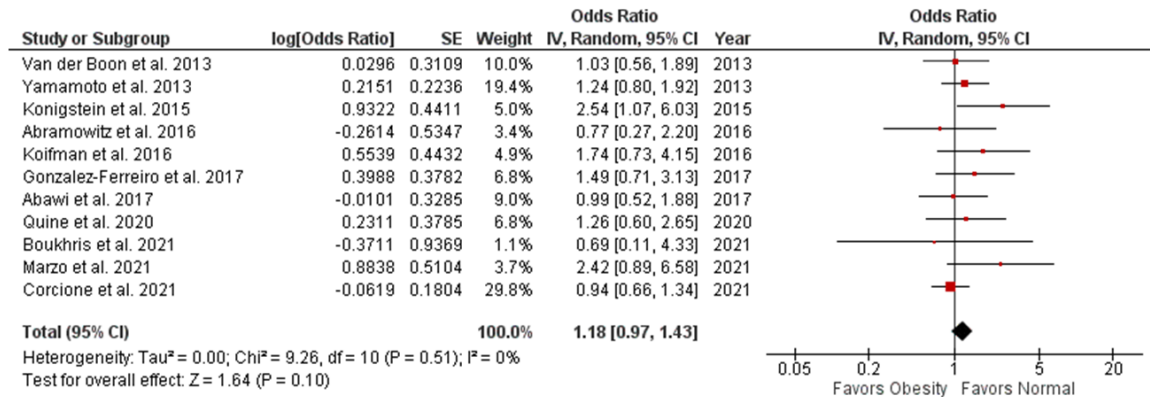


Figure 7. Forest plot of major vascular complications and its association with obesity.

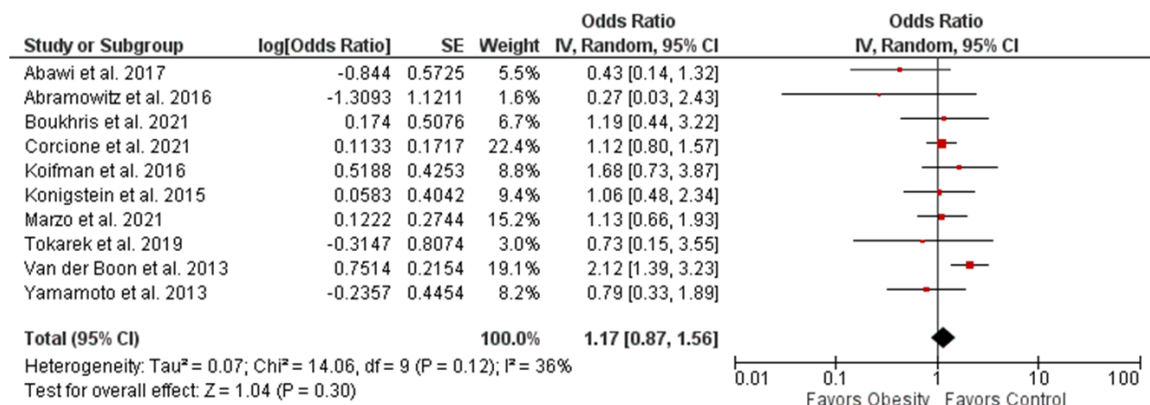


Figure 8. Forest plot of A.K.I. and its association with obesity.

better overall long-term survival with no significant differences in the incidence of MI, major bleeding, A.K.I. and major vascular events in either of the two groups. Obesity has a strong correlation with metabolic diseases, hypertension and dyslipidemia, making it a strong risk factor for the occurrence of major cardiovascular events. However, recent evidence has highlighted that obese individuals may have a better prognosis following cardiovascular surgical interventions. A meta-analysis of 26,842 heart failure patients conducted by Khan and coworkers [46] showed that obese individuals ($\text{BMI} \geq 30$ kg/m^2) receiving left ventricular assist device (LVAD) implantation had significantly improved short-term (≤ 1 year) survival rates when compared with non-obese patients. A retrospective study including 865 candidates undergoing aortic valve replacement for AS found that a BMI in the lower 30 s resulted in lower risks of 30-day and long-term mortality [47]. Furthermore, another investigation revealed significantly

reduced bleeding complications and incidence of stroke in obese patients compared with their counterpart ($P < 0.001$ and $P < 0.03$, respectively) [48].

The results of our analysis can be validated with findings from several other investigations. A meta-analysis of 12,330 patients conducted by Lv and coworkers [19] revealed a favorable prognosis in terms of 30-day and long-term mortality ($P = 0.024$ and $P < 0.001$, respectively) in obese individuals in comparison with non-obese patients. Furthermore, similar to our findings, they also observed that with every increase of 1 kg/m^2 in BMI the rates of 30-day mortality significantly reduced. Similarly, another investigation sought to analyze 221,000 patients from the National Inpatient Sample Database found obese ($P < 0.001$) and MO ($P < 0.001$) TAVI patients to be significantly associated with reduced in-hospital mortality when compared with normal-weight individuals [49],

further substantiating our results. Gupta and coworkers [50] assessed the obesity paradox in a total of 99,829 participants and ascertained the obese group to be significantly correlated with a lower risk of short and long-term mortality. However, unlike our results, they determined that obese patients were at significantly higher odds of developing AKI ($P=0.01$) compared to their normal-weight counterparts. It is important to emphasize that certain studies reported no significant differences in mortality rates across varying BMI categories [39, 41]. For example, Abramowitz and coworkers [26] included a total of 805 patients and upon multivariate analysis found mortality rates to be comparable in both the cohorts. However, most of these investigations were limited by their small sample sizes which may account for the discrepancies with our findings.

The incidence of AS is generally more prevalent in obese patients than in non-obese patient [51]. Several factors that may elucidate the reasoning behind positive surgical outcomes in obese patients undergoing interventions for cardiovascular diseases should be discussed. According to Hayashida and coworkers [52] major vascular complications, which included access site related injuries leading to death, blood transfusions or surgical interventions, were found to be predictors of 30-day mortality in patients who underwent TAVI ($P=0.049$). Perhaps having a higher body surface area (BSA) and a larger vasculature serves to protect obese patients in acquiring vascular injuries during procedures. Zafrir and coworkers [53] analyzed data from the heart failure long-term registry of the Heart Failure Association of the European Society of Cardiology and found a progressive inverse relationship between all-cause mortality and BSA levels. Although our analysis stated no significant differences in bleeding and major vascular complications between the two cohorts, this may be attributed to the limited number of studies reporting on these outcomes.

Furthermore, age should also be considered a vital confounder in establishing the relationship between B.M.I. and mortality in TAVI patients. Older patients tend to be weaker and leaner compared to younger individuals and are associated with several accompanying comorbidities [54]. A study of 7099 patients revealed

increasing age to be significantly associated with poor 30-day mortality outcomes in participants undergoing TAVI [55]. Obesity has become increasingly prevalent in the younger populations [56] and these individuals are also diagnosed earlier than their regular weight counterparts. Hence, it can be concluded that timely diagnosis, increased tolerance to surgical procedures and aggressive pharmacological intervention for several comorbidities may put obese patients at an advantage and likely result in fewer mortality rates, as observed in our analysis.

Moreover, adipokine physiology plays a crucial role in the improved survival rates of obese patients. An increased fat distribution in obesity offers a more extensive energy reserve to compensate for the increased catabolic demands in patients with cardiovascular disease [57]. Increased levels of adipocytes and lipoproteins might be beneficial as they bind to and neutralize bacterial toxin [58]. An elevated adiponectin level and a more rigorous catecholamine response to stress are also reported in patients with lower BMI [59] which may provide plausible reasonings for our results. Lastly, amongst the varying BMI categories reported in most studies, underweight patients carry the greatest risk of the mortality burden following TAVI. Studies suggest that cachexia is strongly interrelated with neuroendocrine and immunologic abnormalities [60] leading to adverse outcomes post-surgical procedures [61].

Body Mass Index (BMI) is widely utilized for assessing adiposity and categorizing individuals by weight classifications, encompassing underweight, normal weight, overweight, and obese categories. Nonetheless, its use as the sole measure of obesity has been questioned due to inherent limitations. BMI relies solely on weight and height, failing to distinguish between lean mass (muscle, bone) and fat mass. Moreover, BMI does not indicate fat distribution across the body, distinguishing between central (abdominal) and peripheral fat deposition [62]. Central obesity is particularly linked to heightened metabolic risks compared to peripheral fat. To address these limitations, alternative tools offer improved assessments of obesity. Waist circumference and waist-to-hip ratio measure abdominal fat distribution, which is metabolically active and strongly associated with obesity-related health risks [63].

Furthermore, advanced techniques such as dual-energy X-ray absorptiometry (DXA), bio-electrical impedance analysis (BIA), and underwater weighing provide more precise evaluations of body fat percentage and distribution than BMI [64]. These alternative measures contribute to a more comprehensive understanding of adiposity and its implications for health.

Our study comprises a few limitations that should be discussed. Firstly, most of the studies included in this analysis are retrospective, resulting in potential recall bias. Our meta-analysis could not conduct a subgroup analysis concerning factors such as TAVI access sites, race differences and severity of AS, as most investigators did not report on these parameters. Future investigations are encouraged to assess the impact of these factors to produce more concrete results. Secondly, our analysis comprised some studies that utilized univariate O.R.s to report their results, which might diminish the accuracy of our outcome. Lastly, since the incidence of comorbidities like hypertension, diabetes, and coronary heart disease is greater in obese patients compared to non-obese patients, it is imperative to adjust these factors when analyzing the overall effect of obesity on outcomes like mortality and complications associated with TAVI.

Conclusion

The results of this meta-analysis verify the concept of the 'obesity paradox' in the context of interventions such as TAVR in patients suffering from AS. Obesity and a high BMI significantly improved short and long-term overall mortality in patients of TAVI. However, no significant decrease was observed when analyzing complications of major bleeding, major vascular events, MI and AKI in the obese group.

Disclosure of conflict of interest

None.

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Impact of obesity on clinical outcomes of TAVR

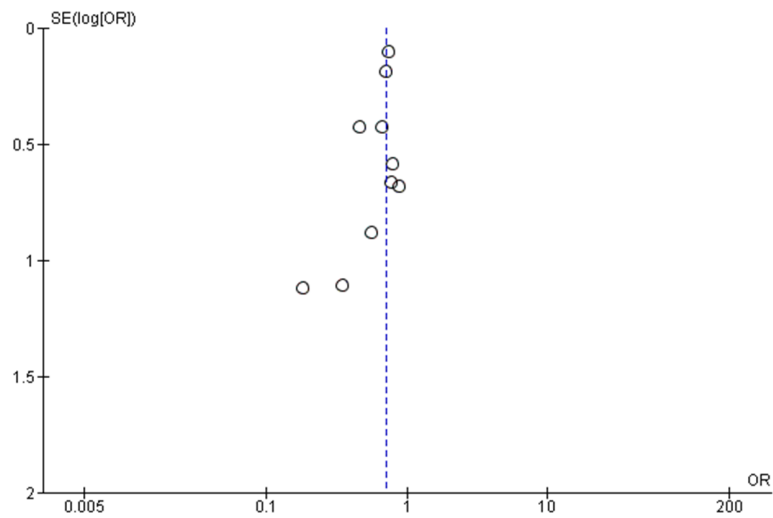
Supplementary Table 1. Detailed search strategy used in each database

PubMed	("BMI"[All Fields] OR "body mass index"[All Fields] OR "obesity"[All Fields]) AND ("TAVI"[All Fields] OR "TAVR"[All Fields] OR "transcatheter aortic valve implantation"[All Fields])
Scopus	("BMI" OR "body mass index" OR "obesity") AND ("TAVI" OR "TAVR" OR "transcatheter aortic valve implantation")

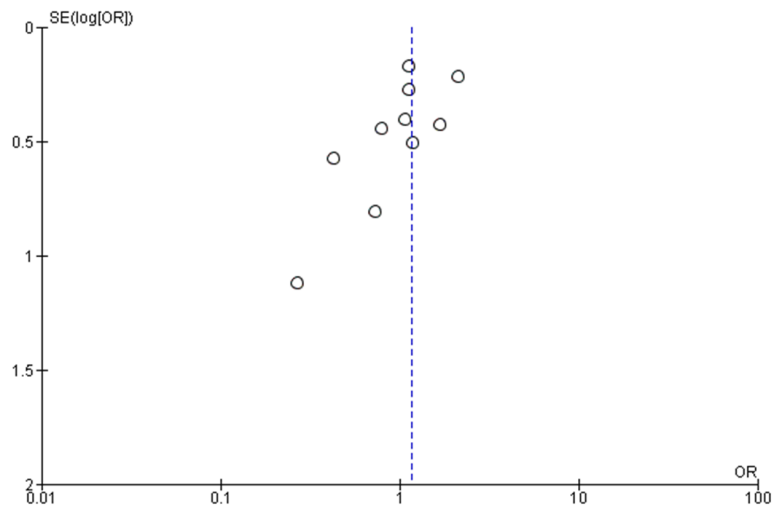
Supplementary Table 2. Newcastle-Ottawa Scale for observational studies

Study, Year	Selection				Comparability		Outcome			Total Score
	S1	S2	S3	S4	C		O1	O2	O3	
Abawi, 2017	*	*	*	*	*	*	*		*	8
Abramowitz, 2016	*	*	*	*	*		*		*	7
Astrid, 2021	*	*	*	*	*	*	*		*	8
Aung, 2013	*	*	*	*	*	*	*		*	8
Beohar, 2014	*	*	*	*	*	*	*		*	8
Boukhris, 2021	*	*	*	*	*		*		*	7
Corcione, 2021	*	*	*	*	*		*		*	7
Dvir, 2014	*	*	*	*	*	*	*		*	8
Gonzalez-Ferreiro, 2017	*	*	*	*	*	*	*	*	*	9
Iung, 2014	*	*	*	*	*		*		*	7
Kamga, 2013	*	*	*	*	*	*	*		*	8
Kische, 2016	*	*	*	*	*		*		*	7
Koifman, 2016	*	*	*	*	*	*	*		*	8
Konigstein, 2015	*	*	*	*	*	*	*		*	8
Marzo, 2021	*	*	*	*	*	*	*		*	8
Mok, 2013	*	*	*	*	*		*		*	7
Quine, 2020	*	*	*	*	*	*	*	*	*	9
Salizzoni, 2016	*	*	*	*	*	*	*		*	8
Seiffert, 2014	*	*	*	*	*	*	*		*	8
Sharma, 2020	*	*	*	*	*	*	*		*	8
Tokarek, 2019	*	*	*	*	*		*		*	7
Boon, 2013	*	*	*	*	*	*	*		*	8
Yamamoto, 2013	*	*	*	*	*	*	*		*	8
Yoon, 2016	*	*	*	*	*	*	*	*	*	9

Impact of obesity on clinical outcomes of TAVR

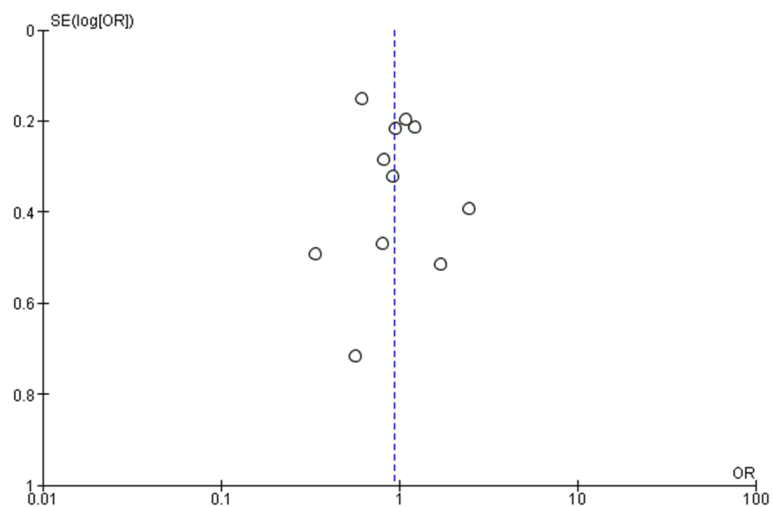


Supplementary Figure 1. 30-day mortality funnel plot.

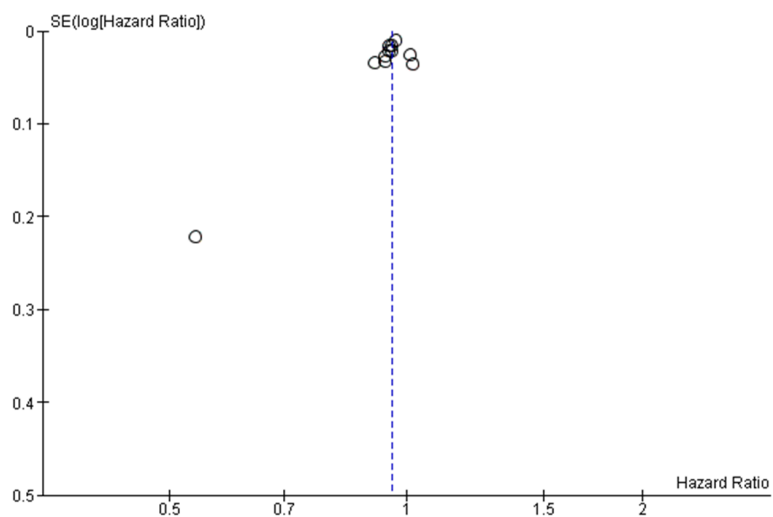


Supplementary Figure 2. Acute kidney injury funnel plot.

Impact of obesity on clinical outcomes of TAVR

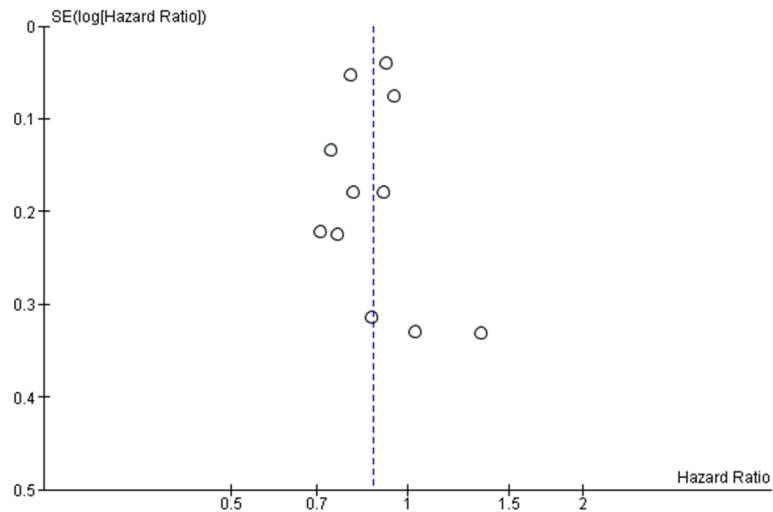


Supplementary Figure 3. Major bleeding funnel plot.

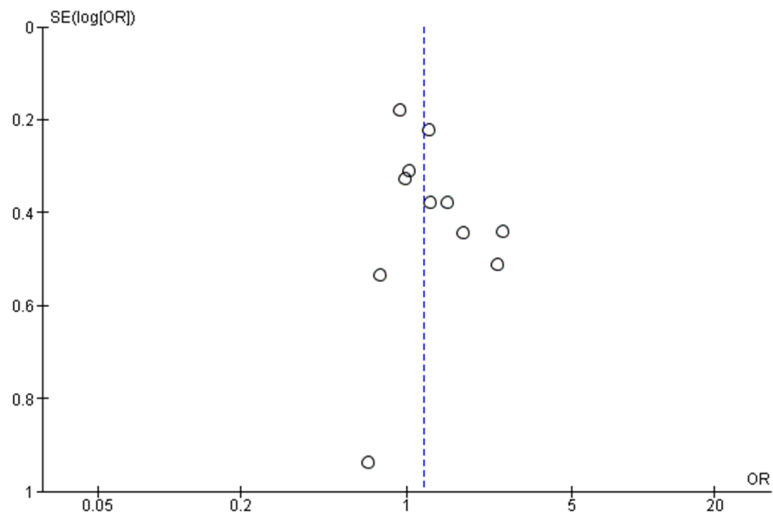


Supplementary Figure 4. Long-term overall survival associated with BMI funnel plot.

Impact of obesity on clinical outcomes of TAVR



Supplementary Figure 5. Long-term overall survival associated with obesity funnel plot.



Supplementary Figure 6. Vascular complications funnel plot.

Supplementary Table 3. Egger's regression test for publication bias

Outcome	Egger's P-value
30-day mortality	0.0844
Overall survival with BMI	0.0034
Overall survival with obesity	0.7471
Acute kidney injury	0.1092
Major bleeding	0.6286
Vascular complications	0.2350