Transcatheter Versus Surgical Aortic Valve Replacement on Hemodynamic and Left Ventricular Remodeling: A Meta-Analysis

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Research article

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Abstract

Background

Transcatheter aortic valve replacement (TAVR) has become the choice for the treatment of severe aortic stenosis (AS) patients at high surgical risk in clinical practice. This meta-analysis aimed to further investigate the effect of the relative hemodynamics and postoperative LV remodeling by TAVR and surgical aortic valve replacement (SAVR).

Methods

Relevant studies were identified via systematic searches of PubMed, Google Scholar, and the Cochrane database. Relevant data were pooled as weighted mean difference (WMD) or odds risk (OR), with their 95% confidence intervals (CI). A random-effect model or fixed effect model was utilized according to the results of the heterogeneity test.

Results

The results indicated that peak aortic pressure gradient (\(WMD = -3.86, 95\% CI (-6.63, -1.09), P = 0.006\)) and left ventricular ejection fraction (LVEF\%) (\(WMD = -0.66, 95\% CI (-1.31, -0.22), P = 0.045\)) were lower in the TAVR group compared with the SAVR group, but there was no significant difference between TAVR group and SAVR group in effective orifice area (EOA) (\(WMD = 0.05, 95\% CI (-0.19, 0.28), P = 0.697\)), left ventricular mass (LVM) (\(WMD = 5.24, 95\% CI (-10.33, 20.80), P = 0.509\)). Compared with SAVR group, the incidence of prosthesis-patient mismatch (PPM) was significantly lower in the TAVR group (\(OR = 0.37, 95\% CI (0.23, 0.61), P < 0.0001\)).

Conclusion

For patients with severe AS, TAVR could have better performance on the hemodynamics than after SAVR in terms of peak aortic pressure gradient, LVEF\%, and the incidence of PPM, TAVR was comparable to SAVR at LV remodeling.

Background

Aortic stenosis (AS) is one of the most common cardiac valve diseases and the prevalence of AS increases with the worldwide population aging[1]. The incidence of AS was average 0.2% in the 50–59 years cohort and it increases up to 9.8% in the 80–90 years cohort[2]. The natural history of AS is characterized by slow progression from years to decades, morbidity and mortality increase with the rapid development of clinical symptoms[3], which is often accompanied by left ventricular (LV) hypertrophy and remodeling[4].

Surgical aortic valve replacement (SAVR) is a recognized treatment for severe AS with LV dysfunction symptoms or objective consequences[5]. However, up to half of the patients who satisfied the guideline recommendations for SAVR were rejected or refused treatment due to age, weakness, comorbidities, or personal choice[6]. Transcatheter aortic valve replacement (TAVR) has been confirmed to be feasible in patients with AS[7]. TAVR as a potential alternative treatment method to general SAVR is suitable for forbidden or high-risk patients with SAVR[3]. A critical review qualitatively explored whether TAVR has equivalent or long-term benefits in improving hemodynamic and reversing LV remodeling[8]. A PARTNER 3 Trial by Pibarot et al concluded that transprosthetic gradients, valve areas, PPM, and LV mass regression were similar in the group of TAVR and SAVR[9]. Similarly, Little et al suggested that TAVR had better systolic valve performance, but had similar left ventricular remodeling compared with SAVR[10]. In contrast, Guimarães et al found that compared with SAVR, TAVR had better superior value hemodynamics performance and lower incidence of severe PPM[11]. Maeda et al also showed that the incidence of PPM in the SAVR group was higher than that in the TAVR group[12].

To further investigate the effect of the relative hemodynamics and postoperative LV remodeling by TAVR and SAVR. We performed a quantitative meta-analysis of AS patients undergoing TAVR and SAVR that involved assessments of peak aortic pressure gradient, effective orifice area (EOA), left ventricular ejection fraction (LVEF), left ventricular mass (LVM), and prosthesis-patient mismatch (PPM).

Methods
This meta-analysis was carried out following the Preferred Reporting Item for Systematic Review and Meta-analysis Protocols statement (PRISMA) [13].

Search strategy

In this meta-analysis, we searched PubMed, Google Scholar, and the Cochrane database for studies published before 8, 2020, describing outcomes of patients with AS treated with TAVI versus SAVR. We also screened references of all searched articles to identify relevant studies. All studies were published in English. The search terms included (“aortic stenosis”) AND (“transcatheter aortic valve replacement” OR “transcatheter aortic valve implantation” OR “TAVR”) AND (“surgical aortic valve replacement” OR “surgical AVR” OR “SAVR”) AND (((“hemodynamic”) OR (“left ventricular remodeling”)) OR (((“left ventricular ejection fraction” OR “LVEF”) OR (“left ventricular mass” OR “LVM”) OR (“peak aortic pressure gradient”) OR (“effective orifice area” OR “EOA”) OR (“prosthesis-patient mismatch” OR “PPM”))).

Study selection and criteria

Two authors (HongJu Wang and Heng Zhang) screened titles and abstracts and inclusions were verified by a third author. Disagreements were discussed and then reached a consensus. Studies were eligible if they satisfied: (1) patients with severe aortic stenosis; (2) patients were treated by TAVR or SAVR; (3) primary outcomes of hemodynamic and left ventricular remodeling data were reported: post-procedural values of peak aortic pressure gradient, LVEF, EOA, LVM and PPM after TAVI or SAVR; (4) observational studies. We excluded duplicated studies, case reports, reviews, meta-analyses, abstracts, and conferences.

Data extraction and study quality

Two authors (Heng Zhang, and Bi Tang) independently reviewed the full text of included studies and extracted all data. The extracted information contained the first author’s name, publication year, sampling, follow-up duration, mean value and SD values of peak aortic pressure gradient, EOA, LVEF%, and LV mass in TAVR and SAVR surgeries, and the cases of PPM. We assessed the quality of studies through Newcastle-Ottawa Quality Assessment Scale (NOS). The NOS ranging from 0 (minimum) to 9 (maximum) adapted for non-randomized controlled studies was used to assess the quality of the articles, which considers the quality of selection, comparability, and outcome. The studies were divided into the following categories: very good studies: 7-8 scores; good studies: 5-6 scores; satisfactory studies: 3-2 scores; unsatisfactory studies: 0-1 score [14].

Statistical analysis

The effect size was calculated with the weighted mean difference (WMD) and 95% confidence intervals (CI), or odds risk (OR). All analyses were performed using Stata14.0. We generated $I^2$ statistics and $Q$ tests to assess heterogeneity among studies, percentages of about 25% ($I^2=25$), 50% ($I^2=50$), and 75% ($I^2=75$) were defined as low, medium, and high heterogeneity, respectively. If heterogeneity existed among studies, a random-effects model was used, otherwise, a fixed-effect model was used. We applied forest plots to evaluate pooled estimates, Egger’s test to explore publication bias. Sensitivity analyses were performed to examine the robustness of positive results by removing individual studies one at a time. A $P$ value below 0.05 was considered statistically significant.

Results

As shown in Figure s1, the database search identified 283 records. After removal of duplicates, 161 records were screened including title and abstract, and then 42 records were selected for full-text reading following eligibility. Reviewed of the full-text studies resulted the exclusion of 26 studies and the inclusion of 16 studies in this meta-analysis.

Of the 16 studies included and baseline characteristics of these studies were summarized in Table s1. From these 16 studies, all 4868 participants were enrolled (2575 cases in the TAVR, 2293 cases in the SAVR). The quality assessment showed that all these studies were considered very good quality based on NOS ($\geq 7$ points).

A pooled analysis of 10 [9–11, 15–21] studies utilizing the random-effects model demonstrated that a statistically significant difference in post-procedural values of peak aortic pressure gradient in hemodynamic between the TAVR group and SAVR group ($WMD= -3.86$, 95% CI (-6.63, -1.09), $P = 0.006$). There was considerable between-study heterogeneity ($I^2 = 94.3\%$, $P < 0.0001$) (Fig. 1).
Sensitivity analysis showed that pooled effect changed slightly by omitting each study one at a time (Figure s2). According to the Egger test ($P = 0.138$), there was no evidence of publication bias.

A total of 13[9–12, 15–18, 20–24] studies for EOA were included in this meta-analysis. The random-effects model showed that there was no significant difference in post-procedural values of EOA between TAVR and SAVR ($WMD = 0.05, 95\%CI(-0.19,0.28), P = 0.697$), with considerable heterogeneity among studies ($I^2 = 98.9\%, P<0.0001$) (Fig. 2).

The result of pooled analysis 12[10, 11, 15–17, 19, 20, 22–26] studies by fixed-effect model revealed that compared with the SAVR group, the post-procedural values of LVEF in the TAVR group was significantly lower ($WMD=-0.66, 95\%CI(-1.31,-0.22), P = 0.045$), with slightly heterogeneity across these studies ($I^2 = 48.4\%, P = 0.030$) (Fig. 3). According to the sensitivity analysis, the result was robust as shown in Figure s3. The Egger test ($P = 0.055$) suggested that there was no obvious publication bias.

The pooled estimate for 4[10, 17, 20, 25] studies reported LVM was calculated applying the random-effects model. The results indicated that there was no significant difference in post-procedural values of LVM between TAVR and SAVR ($WMD = 5.24, 95\%CI(-10.33, 20.80), P = 0.509$), with considerable heterogeneity among studies ($I^2 = 89.5\%, P < 0.0001$) (Fig. 4).

A pooled analysis of 7[11, 12, 16, 18, 20–22] studies using random-effects model showed that TAVR was associated with reduced risk of PPM (OR = 0.37, 95\% CI(0.23, 0.61), $P < 0.0001$), with medium heterogeneity across studies ($I^2 = 73.5\%, P = 0.001$) (Fig. 5). In a sensitivity analysis, removing individual study one at a time did not change the overall results of this analysis and the result was robust (Figure s4). According to the Egger test ($P = 0.978$), little publication bias was discovered among the studies.

**Discussion**

The results of our meta-analysis suggested better performance in peak aortic pressure gradient, LVEF, and low incidence of PPM for patients who received TAVR than those who received SAVR. However, we found that there was no difference in EOA and LVM improvement after TAVR than after SAVR treatment for patients with AS. A critical review by Kim et al concluded that TAVR showed a low incidence of PPM compared to SAVR[8]. A recent meta-analysis by Takagi et al summarized for limited patients with reduced LVEF, TAVR might be related to the improvement of LVEF[27]. This was consistent with the findings of our analysis.

TAVR was associated with better hemodynamic results, with peak aortic pressure gradient and valve area changed. Although there was no statistical difference in valve area in this analysis. Several studies have reported similar hemodynamic results after TAVR. For example, Smith et al showed that the mean aortic-valve gradient in the TAVR group ($10.2 \pm 4.3\text{mmHg}$) was slightly superior to the SAVR group ($11.5 \pm 4.3\text{mmHg}$) and mean valve area ($1.59 \pm 0.48\text{cm}^2$ vs $1.44 \pm 0.47\text{cm}^2$)[28]. The PARTNER 2 cohort a randomized trial by Leno et al revealed that the improvement in gradients and aortic-valve areas at all time points was significantly greater after TAVR than SAVR[29]. Additionally, Reardon et al have indicated TAVR had lower gradients and large aortic-valve areas compared to SAVR[30]. In patients with severe AS, EF showed a slight improvement in the TAVR group, but it remained stable in the SAVR group[31]. A meta-analysis by Takagi et al suggested no difference in LVEF improvement after treatment of TAVR and SAVR[27]. However, two studies involving patients with low baselines LVEF ($< 50\%$) revealed greater improvement of LVEF in the TAVR group compared to SAVR. Compared with patients with low LVEF and low gradients, patients with low-LVEF and high-gradient severe AS received TAVI have better LVEF recovery and clinical outcomes[34]. Even though LVEF is widely utilized in clinical practice, it is an insensitive and often misguided indicator of left ventricular myocardial contractility[35]. Non-invasive imaging techniques designed to directly evaluate LV myocardial deformation (such as speckle-tracking echocardiography) have indeed shown a deterioration of myocardial contractility in patients with AS despite the appearance of normal LVEF; changes in myocardial perfusion and metabolism altered and the improvement of ischemia and fibrosis have been considered as possible explanations for this discovery[36, 37].

In the study by Kamperidis et al[23], the TAVR group had a significantly less frequent presence of PPM. PPM was independently related to forward low-flow status, which is more common in patients receiving sutureless bioprosthesis[38]. Some studies have thought that PPM is associated with survival after TAVR or SAVR, but this remains controversial. Chacko et al. and Ewe et al. have recommended that there was no relationship between PPM and survival after TAVR or SAVR, whereas Hahn et al. has suggested that PPM was a predictor of mortality for patients undergoing TAVR or SAVR[15, 17, 39].

Several limitations of this meta-analysis needed careful consideration. First, we used data from observational studies. This type of study was likely to the effect of unmeasured confounders, which may affect the accuracy of our results. Second, most of the patients...
undergoing follow-up echocardiography may be survivors with increases in LVEF and LVM, but follow-up data of LVEF and LVM were not available during follow-up in patients with LV function and LVH impairment. However, this type of bias in longitudinal could not be avoided. Third, there were no significant differences in hemodynamic profiles between two TAVI devices (balloon-expandable and self-expandable) [11], in our studies, due to the limited number of studies, there was not separately explored difference for self and balloon-expandable prosthesis. Lastly, only four studies qualified for analysis of LVM, the validity of the results needs further updating and exploring.

**Conclusion**

In summary, our study indicated that compared with SAVR, there was a significant decrease in the peak aortic pressure gradient, AVEF, and low incidence of PPM in the group of TAVR. Although there was no statistically significant difference in EOA and LVM between the two groups, EOA and LVM were improved after TAVR than after SAVR. For patients with severe AS, TAVR had between performance on the relative hemodynamics than after SAVR, TAVR was may comparable to SAVR at LV remodeling.

**Abbreviations**

AS: Aortic stenosis  
TAVR: Transcatheter aortic valve replacement  
SAVR: Surgical aortic valve replacement  
LVEF: Left ventricular ejection fraction  
LVM: Left ventricular mass  
EOA: Effective orifice area  
PPM: Prosthesis-patient mismatch  
LV: Left ventricular  
WMD: Weighted mean difference  
OR: Odds risk  
95% CI: 95% confidence intervals

**Declarations**

*Availability of data and materials*

All data generated or analysed during this study are included in this published article and data showed in table1.

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Not applicable

*Ethics approval and consent to participate:* This is a meta-analysis. A meta-analysis involves the pooling of data from already published trials. The ethics approval and inform consent are not applicable.

*Consent for publication:* Not applicable.

*Competing interest:* The authors reported that they have no conflict of interest.

*Authors Contributions*
Shili Wu designed the literature search and analysis. HongJu Wang, Heng Zhang, and Bi Tang searched the studies and performed the quality assessment of the results. Shili Wu, Ling Xuan, and JinJun Liu analyzed the data and interpreted the result. Shili Wu wrote the manuscript. Yanhua Zhu and SuYun Shao finalized the manuscript. All authors discussed and reviewed and approved the final manuscript.

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Tables

Table s1 Baseline characteristics of included studies.
| Authors (Year)          | Follow up | group | Sample size | peak aortic pressure gradient (mmHg) | EOA\((\text{cm}^2)\) | LVEF(%) | LV mass (g) | PPM | Quality score |
|------------------------|-----------|-------|-------------|--------------------------------------|-----------------------|---------|-------------|-----|---------------|
| Mohammad A et al (2010)| 30 day    | TAVR  | 56          | 18.5±7.2                             | 0.68±0.21             | 49.4±11 | 7           |     |               |
|                        |           | SAVR  | 36          | 23.45±10.4                           | 1.85±0.16             | 55.7±7.7 |            |     |               |
| Giannini et al (2011)  | 12 month  | TAVR  | 58          | 19.10±7.0                            | 1.67±0.57             | 54.8±7.3 | 7           | 8   |               |
|                        |           | SAVR  | 58          | 27.1±13.9                            | 1.37±0.45             | 52.8±7.4 | 21          |     |               |
| Fairbairn et al (2013) | 6 month   | TAVR  | 25          |                                      | 56±10                 | 7       | 120±38      | 7   |               |
|                        |           | SAVR  | 25          |                                      | 57±8                  | 114±42  |             |     |               |
| Hahn et al (2013)      | 2 year    | TAVR  | 344         | 19.0±8.2                             | 1.57±0.42             | 56.0±10.0 | 226.7±73.8 | 9   |               |
|                        |           | SAVR  | 326         | 20.5±9.8                             | 1.50±0.46             | 57.4±10.4 | 213.7±60.7 |     |               |
| Gavina et al (2014)    | 6 month   | TAVR  | 42          |                                      | 1.95±0.54             | 61.27±11.35 | 9       | 8   |               |
|                        |           | SAVR  | 45          |                                      | 1.50±0.42             | 61.28±8.98 |           |     |               |
| Finkelstein et al (2014)| 3 month   | TAVR  | 86          | 14.9±6.6                             | 1.88±0.46             | 21       | 8           |     |               |
|                        |           | SAVR  | 49          | 19.2±8.2                             | 1.71±0.81             | 12       |             |     |               |
| Kamperidis et al (2015)|          | TAVR  | 40          |                                      | 1.00±0.30             | 59.57±10.45 | 8       |     |               |
|                        |           | SAVR  | 40          |                                      | 0.76±0.22             | 63.50±12.63 |         |     |               |
| Musa et al (2016)      | 6 month   | TAVR  | 32          | 25±13                                | 55±11                 | 7        |             |     |               |
|                        |           | SAVR  | 40          | 32±18                                | 57±8                  |           |             |     |               |
| Little et al (2016)    | 1 year    | TAVR  | 389         | 17.0±6.3                             | 1.9±0.5               | 59.5±9.8 | 206.97±61.94 | 7   |               |
|                        |           | SAVR  | 353         | 22.8±12.7                            | 1.6±0.5               | 59.7±8.5 | 192.31±51.56 |     |               |
| G. Nucifora et al (2017)| 15 month  | TAVR  | 35          |                                      | 69±14                 | 9        |             |     |               |
|                        |           | SAVR  | 24          |                                      | 74±10                 |           |             |     |               |
| Douglas et al (2017)   | 5 year    | TAVR  | 321         | 19.0±11.2                            | 1.57±0.45             | 54.0±10.0 | 199.7±63.7 | 188 |               |
|                        |           | SAVR  | 313         | 19.2±9.85                            | 1.48±0.35             | 54.5±9.41 | 211.5±7.8  | 26  |               |
| Salina et al (2017)    | 1 year    | TAVR  | 40          | 25.9±14.0                            | 1.35±0.34             | 18       | 8           |     |               |
|                        |           | SAVR  | 69          | 34.0±14.2                            | 1.28±0.49             | 38       |             |     |               |
| Maeda et al (2018)     | 6 year    | TAVR  | 238         |                                      | 1.48±0.34             | 17       | 7           |     |               |
|                        |           | SAVR  | 85          |                                      | 1.70±0.39             | 21       |             |     |               |
| Guimarães et al (2019) | 1 year    | TAVR  | 357         | 23±12                                | 1.46±0.39             | 57±10    | 192         | 8   |               |
|                        |           | SAVR  | 357         | 29±12                                | 1.25±0.37             | 57±9     | 284         |     |               |
| Pibarot, et al (2020)  | 2 year    | TAVR  | 495         | 25.0±10.1                            | 1.72±0.37             | 7        |             |     |               |
|                        |           | SAVR  | 453         | 21.3±8.8                             | 1.76±0.42             |           |             |     |               |
| Maidman et al (2020)   | 30 day    | TAVR  | 17          | 1.9±0.8                               | 34.2±17.6             | 8        |             |     |               |
|                        |           | SAVR  | 20          | 1.7±0.2                               | 45.0±18.1             |           |             |     |               |
Note: TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; EOA, effective orifice area; LVEF, left ventricular ejection fraction; LV mass, left ventricular mass; PPM, prosthesis-patient mismatch.

Figures

Figure 1

Forest plot of peak aortic pressure gradient
Figure 2

Forest plot of EOA

| Study                          | ID       | WMD  (95% CI)       | Weight |
|-------------------------------|----------|---------------------|--------|
| Mohammad A et al (2010)       |          | -1.17 (-1.25, -1.09)| 7.92   |
| Giannini et al (2011)         |          | 0.30 (0.11, 0.49)   | 7.59   |
| Hahn et al (2013)             |          | 0.07 (0.00, 0.14)   | 7.93   |
| Gavina et al (2014)           |          | 0.45 (0.25, 0.65)   | 7.52   |
| Finkelstein et al (2014)      |          | 0.17 (-0.08, 0.42)  | 7.33   |
| Kamperidis et al (2015)       |          | 0.24 (0.12, 0.36)   | 7.83   |
| Little et al (2016)           |          | 0.30 (0.23, 0.37)   | 7.92   |
| Douglas et al (2017)          |          | 0.09 (0.03, 0.15)   | 7.94   |
| Saina et al (2017)            |          | 0.07 (-0.09, 0.23)  | 7.71   |
| Maeda et al (2018)            |          | -0.22 (-0.31, -0.13)| 7.88   |
| Guimarães et al (2019)        |          | 0.21 (0.15, 0.27)   | 7.95   |
| Pibarot, et al (2020)         |          | -0.04 (-0.09, 0.01) | 7.95   |
| Maidman et al (2020)          |          | 0.20 (-0.19, 0.59)  | 6.53   |
| Overall (I-squared = 98.9%, p = 0.000) | 0.05 (-0.19, 0.28) | 100.00 |

NOTE: Weights are from random effects analysis
Figure 3

Forest plot of LVEF
Figure 4

Forest plot of LVM
Figure 5

Forest plot of PPM

Supplementary Files

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