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Publication Date

2020

DOI

10.1177/2040622320933775

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Meta-analysis of right ventricular function in patients with aortic stenosis after transfemoral aortic valve replacement or surgical aortic valve replacement

Ther Adv Chronic Dis

2020, Vol. 11: 1–15

DOI: 10.1177/2040622320933775

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Abstract

Background: Right ventricular function (RVF) is an independent predictor of prognosis for patients undergoing aortic valve replacement: transcatheter aortic valve replacement (TAVR) or surgical aortic valve replacement (SAVR). The effect of transfemoral aortic valve replacement (TF-TAVR) on RVF is uncertain. We aimed to perform a meta-analysis of the effect of TF-TAVR on RVF in patients with aortic stenosis (AS) and compare the effect of TF-TAVR with SAVR.

Methods: We searched relevant studies from PubMed, Embase, Cochrane Library databases, and Web of Science. Furthermore, two reviewers (Wang AQ and Cao YS) extracted all relevant data, which were then double checked by another two reviewers (Zhang M and Qi GM). We used the forest plot to present results. Tricuspid annular plane systolic excursion (TAPSE) was the primary outcome.

Results: This meta-analysis included 11 studies. There were 353 patients who underwent TF-TAVR, and 358 patients who were subjected to SAVR. There was no significant difference in TAPSE at 1 week and 6 months as well as right ventricular ejection fraction (RVEF) at <2 weeks and 6 months after TF-TAVR. For the SAVR group, TAPSE at 1 week and 3 months as well as fractional area change (FAC) at 3 months post procedure were significantly aggravated, while RVEF did not change significantly. Moreover, TAPSE post-TF-TAVR was significantly improved as compared with post-SAVR. The ΔTAPSE, the difference between TAPSE post-procedure and TAPSE prior to procedure, was also significantly better in the TF-TAVR group than in the SAVR group.

Conclusion: RVF was maintained post TF-TAVR. For SAVR, discrepancy in the measured parameters exists, as reduced TAPSE indicates compromised longitudinal RVF, while insignificant changes in RVEF implicate maintained RVF post procedure. Collectively, our study suggests that the baseline RV dysfunction and the effect of TF-TAVR *versus* SAVR on longitudinal RVF may influence the selection of aortic valve intervention.

Keywords: aortic valve stenosis, AS, right ventricule, right ventricular function, SAVR, surgical aortic valve replacement, TAVI, TAVR, TF-TAVR, transcatheter aortic valve implantation, transcatheter aortic valve replacement, transfemoral-aortic valve replacement

Received: 11 November 2019; revised manuscript accepted: 12 May 2020.

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Introduction

Aortic stenosis (AS) is the most prevalent acquired valvular disorder, affecting up to 4% of the elderly population and associating with significant morbidity and mortality.[1–3] Surgical aortic valve replacement (SAVR) has been the conventional treatment of choice for patients with severe AS. Over the past decade, transcatheter aortic valve replacement (TAVR) has emerged as an effective alternative for patients at intermediate, high, or prohibitive risk of ongoing SAVR.[4–6] TAVR is extensively performed worldwide and reduced rates of mortality and re-hospitalization in operable patients when compared with optimal medical treatment.[4] In patients with severe AS and reduced left ventricular ejection fraction (LVEF), TAVR attains better recovery of EF than SAVR.[7]

Right ventricular dysfunction is a well-recognized adverse prognostic factor in patients with SAVR.[8] In addition, right ventricular function (RVF) may further deteriorate after SAVR.[9] The influence of RVF on TAVR and the effect of TAVR on RVF are currently uncertain. This is partly due to the complex geometry of right ventricle and the lack of a widely accepted and generally applicable index for measurement of RVF.[10] Furthermore, RV size and function are not routinely measured or reported with outcomes of TAVR.[11] Of all the possible access sites, transfemoral transcatheter aortic valve replacement (TF-TAVR) accounts for 96% of the TAVR cases.[12] A recent meta-analysis showed that TAPSE remained unchanged following the TF-TAVR, but reduced significantly after the transapical TAVR (TA-TAVR) at the time of hospital discharge.[13] The purpose of the current meta-analysis is to evaluate the effect of TF-TAVR as opposed to SAVR on RVF in patients with severe AS.

Methods

Data sources and search strategy

We searched the PubMed, Embase, the Web of Science and the Cochrane library for relevant articles published prior to February 14, 2020. The search strategy contained a mix of MeSH and free text terms for key concepts related to transcatheter aortic valve implantation, surgical aortic valve replacement, and RVF in patients with aortic valve stenosis. Searches were limited to the trials of human subjects, with no language restriction. The detailed search strategy is shown in the electronic database search hedges in Appendix 1.

Study selection and eligibility criteria

Two investigators (Wang AQ and Cao YS) independently searched and critically selected the articles to ensure eligibility. We utilized the following criteria: (a) the procedure was performed in the patients diagnosed as AS (defined as the aortic valve area $<1\,cm^2$ or the indexed aortic valve area $<0.06\,cm^2/m^2$), and only human studies were included; (b) intervention was TF-TAVR and/or SAVR; (c) the outcome was RVF as assessed by echocardiography, cardiac magnetic resonance imaging, or radionuclide angiocardiography. The measurements of RVF included tricuspid annular plane systolic excursion (TAPSE), right ventricular ejection fraction (RVEF), and fractional area change (FAC). The primary outcome was TAPSE, the secondary outcomes included RVEF and FAC. Studies were excluded if they met one of the following criteria: (a) duplicate publication, (b) case reports and animal studies, (c) correspondence and letter, (d) published as abstracts without specific data, (e) articles that did not match inclusion criteria, or (f) papers unrelated to the topic. There were no restrictions on follow-up period.

Data extraction and management

All selected articles were assessed by two reviewers (Wang AQ and Cao YS) for relevance and eligibility by scrutinizing titles and abstracts. Full texts were reviewed and data extracted in the relevant studies assessing RVF after aortic valve replacement. Methodological disagreements were resolved by a third reviewer (Zhang M). The patients' characteristics included the traits that may influence the outcome of procedure, such as age, sex, Society of Thoracic Surgeons Predicted Risk of Mortality, coronary artery bypass grafting, chronic obstructive pulmonary disease, and so forth.

Quality assessment

Two authors (Zhang LY and He TT) independently assessed the risk of bias of randomized controlled trials using the Cochrane Risk-of-Bias tool,[14] which assesses the sequence generation, allocation

concealment, masking, and incomplete outcome data. The risk of bias in cohort and case–control studies was assessed using the Newcastle–Ottawa scale, which evaluates sample representativeness and size, representativeness of the cases as compared with control group, comparability between pre- and post-procedure as well as post-TF-TAVR and post-SAVR, ascertainment of AVR, and thoroughness of descriptive statistics reporting. The studies were judged as high risk of bias when assessment score was lower than three points, and as low risk of bias when the score was higher than three points. Another co-author (Wang AQ) resolved disagreements.

Statistical analysis and data synthesis

Meta-analysis was performed using RevMan 5.3 according to the *Cochrane Handbook*. The forest plot, the standard way to illustrate results of individual studies and meta-analysis, was used to present the results in our analyses. We used means, standard deviations (SDs), and p values to present outcomes.

We used funnel plots to assess the publication bias. A funnel plot is a scatter plot of the effect estimates from individual studies against a measure of each study's size. For the effect estimate, the accuracy increases with the sample size. In addition, effect estimates of the small sample distribute at the bottom of the figure with a wide range; in contrast, the range of the big sample is narrow. A symmetrical distribution of the studies' effect estimates in the funnel plot would suggest the absence of publication bias.

For the studies that were included in this meta-analysis but did not report SDs in the texts, we calculated the SDs after determining the correlation coefficient from a similar study. The correlation coefficient in the experimental group was calculated according to the following formula[15]:

$$\mathrm{Corr_E} = \frac{\mathrm{SD_{E,baseline}}^2 + \mathrm{SD_{E,final}}^2 - \mathrm{SD_{E,change}}^2}{2 \times \mathrm{SD_{E,baseline}} \times \mathrm{SD_{E,final}}}$$

($\mathrm{Corr_E}$ = the correlation coefficient in the experimental group, E = experiment)

We then calculated $\mathrm{SD_{E,final}}$ using the following formula[15]:

$$\mathrm{SD_{E,final}} = \sqrt{\mathrm{SD_{E,baseline}}^2 + \mathrm{SD_{E,final}}^2 - \left(2 \times \mathrm{Corr} \times \mathrm{SD_{E,baseline}} \times \mathrm{SD_{E,final}}\right)}$$

The heterogeneity was assessed using Chi-square test ($p < 0.10$) and the I^2 value. When the study demonstrated heterogeneity using $I^2 > 50\%$, we selected the random-effects model. Otherwise, we chose the fixed-effects model. The vertical dashed line on the forest plot represents an invalid line. The size of each box is proportional to the weight of the trial result. Diamonds represent the 95% confidence interval for the pooled estimates of the effect. The dashed vertical line through the middle of the diamond is the mean estimate of the meta-analysis and provides a reference line for an individual study.

Results

Study selection

We initially found 1537 articles by systematic literature search. After removing duplicates (316), there were 1221 studies to be screened for title and abstract. After irrelevant studies, case reports, animal studies, response to letter, meeting abstracts, reviews and meta-analyses were removed, 87 articles were evaluated in full-text. Irrelevant, correspondence only, abstracts without relevant data, articles that did not meet inclusion criteria or papers unrelated to the topic were then excluded. Finally, 11 studies met the inclusion criteria and were included in this meta-analysis (Figure 1).[12,16–25]

The search for the meta-analysis was performed on February 14, 2020. Study descriptions and patient characteristics are summarized in Tables 1 and 2 as well as Supplemental Tables 1 and 2 online. The studies were published from 1990 to 2016. The age of all the patients who underwent TF-TAVR or SAVR ranged from 61 to 88 years old. There were 353 patients who underwent TF-TAVR; 358 patients underwent SAVR. All patient characteristics were collected.

The outcomes of RVF in the selected studies are shown in Tables 3 and 4. All trials' follow-up time included pre-procedure and post-procedure, and quantitative data were presented as mean ± SD. The longest follow-up time was 6 months after procedure. Echocardiogram was

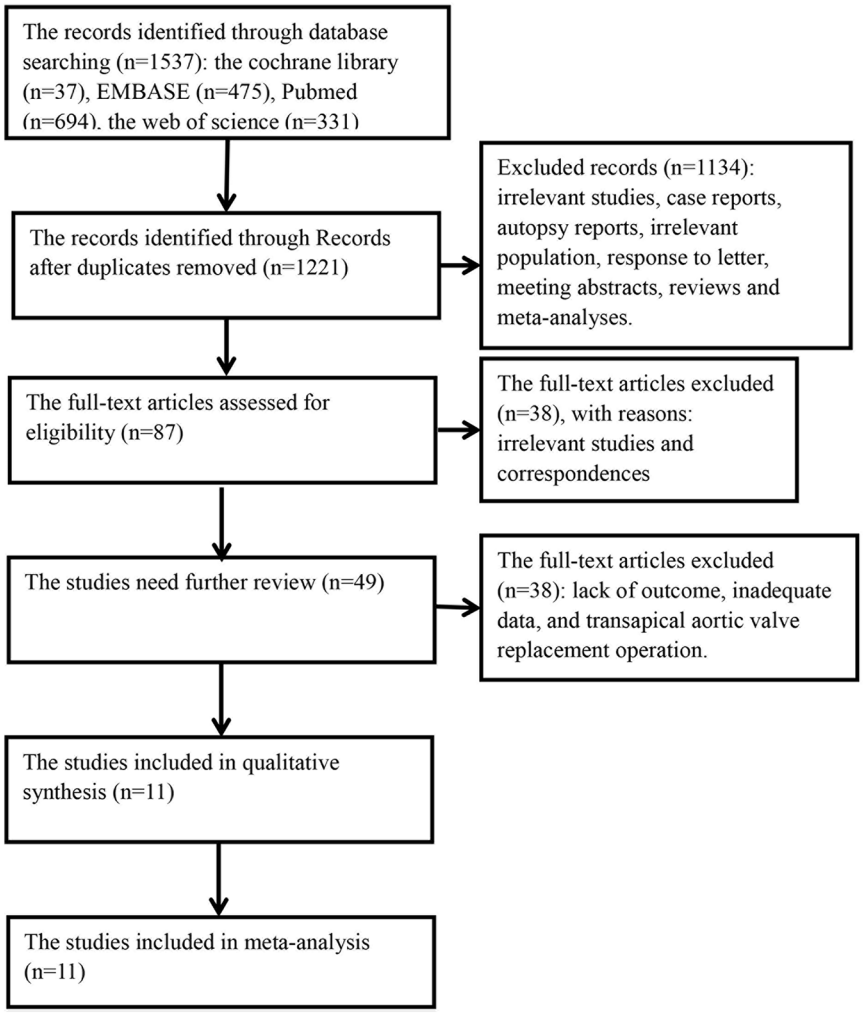

Figure 1. Flow diagram of literature search and study selection.

the most common method to measure RVF whereas three studies used cardiac magnetic resonance imaging and one used radionuclide angiocardiography.

Quality assessment

The quality of the included studies was assessed by the Cochrane Risk-of-Bias tool and shown in Supplemental Figure 1. Two trials[12,18] did not report allocation concealment, and it was unclear how the random sequence was generated and whether there were incomplete outcome data. The Newcastle–Ottawa score components for eight cohort studies are shown in Supplemental Table 3. Eight studies[16,17,19–24] were of high quality. All cohort studies[16,17,19–24] did not report the representativeness of the exposed cohort. Only two studies[17,21] followed up long enough (⩾6 months) to observe the outcomes. The Newcastle–Ottawa score components for case–control study are listed in Supplemental Table 4. The study was of high quality,[25] but it did not report the representativeness of the cases, selection of controls, and ascertainment of AVR.

Meta-analysis of RVF in patients with AS after TF-TAVR

The primary outcome. As compared with the TAPSE level pre-procedure, there were not significant differences in TAPSE at 1 week (including <8 days, 5–7 days, and 1 week; Figure 2) and 6 months (Figure 3) post TF-TAVR.

Table 1. Characteristics of transfemoral transcatheter aortic valve replacement studies.

Study	*n*	Patient selection	Age, years	Male	Pre-AVA, cm^2	Euro SCORE	STS score	STS mortality	NYHA			
									I	II	III	IV
Quick *et al.*[16]	74	Severe and symptomatic AS	80.5 ± 4.9	27	<1	21.2 ± 10.4	8.6 ± 4.9	NR	35		39	
Ayhan *et al.*[17]	50[a]	Severe calcified AS	78.1 ± 8.5	21	0.62 ± 0.17	22.2 ± 15.4	6.8 ± 5.0	NR	0	2	31	17
Okada *et al.*[18]	13	Severe AS	82.4 ± 4.3	6	NR	NR	NR	NR	NR	NR	NR	NR
Crouch *et al.*[19]	26	Severe AS	84.6 ± 5.6	17	NR	NR	7.7 ± 3.9	NR	2.5 ± 0.8			
Keyl *et al.*[20]	20	AS	83.0 ± 6.0	7	NR	11.9 ± 5.8	11.4 ± 9.4	NR	NR	NR	NR	NR
Musa *et al.*[21]	56[b]	Severe trileaflet degenerative AS	80.4 ± 6.6	32	0.60 ± 0.2	NR	NR	5.54 ± 3.41	NR	NR	NR	NR
Gronlykke *et al.*[12]	114[c]	Isolated severe AS	79.0 ± 5.1	64	NR	8.2 ± 4.1	3.0 ± 1.7	NR	5	54	53	2

Data presented as mean ± standard deviation, or number.
[a]Included two patients who underwent trans-subclavian artery transcatheter aortic valve replacement (TAVR).
[b]Included four patients who underwent trans-subclavian artery TAVR.
[c]Included three patients who underwent trans-subclavian artery TAVR, one patient who underwent trans-carotid artery TAVR and one patient who underwent direct trans-aortic TAVR.
AS, aortic stenosis; NR, not reported; NYHA, New York Heart Association; pre-AVA, pre-operation aortic valve area; STS, Society of Thoracic Surgery

Table 2. Characteristics of surgical aortic valve replacement studies.

Study	*n*	Patient selection	Age, years	Male	Pre-AVR, cm^2	Euro SCORE	STS score	STS mortality	NYHA			
									I	II	III	IV
Harpole and Jones[24]	11	AS	62 ± 15	NR	0.7 ± 0.2	NR	NR	NR	NR	NR	7	
Sandstede *et al.*[25]	14	AS	64 ± 10	12	0.7 ± 0.2	NR	NR	NR	NR	NR	NR	NR
Zhao *et al.*[22]	30	Symptomatic, severe AS	62 ± 11	19	NR	4.0 ± 2.1	NR	NR	1	17	12	0
Kempny *et al.*[23]	22	Symptomatic, severe AS	71 ± 12	8	0.73 ± 0.24	7.2 ± 4.7	NR	NR	1	4	17	0
Quick *et al.*[16]	63	Symptomatic, severe AS	73.8 ± 8.1	22	NR	6.5 ± 3.7	2.2 ± 1.8	NR	40		23	
Okada *et al.*[18]	15	Severe AS	79.6 ± 5.9	9	NR	NR	NR	NR	NR	NR	NR	NR
Crouch *et al.*[19]	21	Severe AS	79.6 ± 4.0	8	NR	NR	5.9 ± 3.4	NR	2.7 ± 0.6			
Gronlykke *et al.*[12]	106	Isolated severe AS	78.4 ± 4.7	58	NR	8.7 ± 4.1	3.2 ± 1.7	NR	3	57	42	4
Keyl *et al.*[20]	20	AS	77 ± 4	9	NR	7.0 ± 3.3	10.7 ± 4.1	NR	NR	NR	NR	NR
Musa *et al.*[21]	56	Severe trileaflet degenerative AS	72.8 ± 7.2	38	0.82 ± 0.4	NR	NR	2.13 ± 0.73	NR	NR	NR	NR

Data presented as mean ± standard deviation, or number.
AS, aortic stenosis; NR, not reported; NYHA, New York Heart Association; pre-AVA, pre-operation aortic valve area; STS, Society of Thoracic Surgery

Table 3. Right ventricular function of pre- and post-transfemoral transcatheter aortic valve replacement.

Study	Measure method	*n*	TAPSE (mm)			RVEF (%)			FAC (%)		
			Pre-	Post-		Pre-	Post-		Pre-	Post-	
				<2 ws	3–6 ms		<2 ws	3–6 ms		<2 ws	3–6 ms
Quick *et al.*[16]	Echo	74	21.7 ± 5.0	22.1 ± 4.9 (<8 ds)	NR	NR	NR	NR	NR	NR	NR
Ayhan *et al.*[17]	Echo	50[a]	16.8 ± 0.3	17.9 ± 0.3 (24 h)	18.7 ± 0.2 (6 ms) (*n* = 47)	51.6 ± 10.1	53.7 ± 9.8 (24 h)	57.8 ± 10.2 (6 ms) (*n* = 47)	45.3 ± 7.6	50.1 ± 9.3 (24 h)	54.2 ± 8.7 (6 ms) (*n* = 47)
Okada *et al.*[18]	Echo	13	18 ± 5	19 ± 5 (1 w[#])	NR	NR	NR	NR	35 ± 10	42 ± 10 (1 w[#])	NR
Crouch *et al.*[19]	Echo/CMR	26	NR	NR	NR	61 ± 11	54 ± 13 (<2 ws)	NR	NR	NR	NR
Keyl *et al.*[20]	3D echo	20	24 ± 5	24 ± 7 (5–7 ds)	NR	54 ± 7	56 ± 8 (5–7 ds)	NR	NR	NR	NR
Musa *et al.*[21]	CMR	56[b]	19 ± 6	NR	19 ± 7 (6 ms)	52 ± 10	NR	52 ± 10 (6 ms)	NR	NR	NR
Gronlykke *et al.*[12]	Echo	114[c]	24 ± 5.1 (*n* = 107)	NR	24 ± 4.9 (3 ms) (*n* = 107)	NR	NR	NR	45 ± 9 (*n* = 97)	NR	45 ± 10 (3 ms) (*n* = 86)

Data presented as mean ± standard deviation.
[#]Median.
[a]Included two patients who underwent trans-subclavian artery transcatheter aortic valve replacement (TAVR).
[b]Included four patients who underwent trans-subclavian artery TAVR.
[c]Included three patients who underwent trans-subclavian artery TAVR, one patient who underwent trans-carotid artery TAVR and one patient who underwent direct trans-aortic TAVR.
ds, days; FAC, fractional area change; ms, months; NR, not reported; RVEF, right ventricular ejection fraction; CMR, cardiac magnetic resonance imaging; TAPSE, tricuspid annular plane systolic excursion; ws, weeks

Table 4. Right ventricular function of pre- and post-surgical aortic valve replacement.

Study	Measure method	*n*	TAPSE (mm)			RVEF (%)			FAC (%)		
			Pre-	Post-		Pre-	Post-		Pre-	Post-	
				<2 ws	3–6 ms		<2 ws	3–6 ms		<2 ws	3–6 ms
Harpole and Jones[24]	Radionuclide	11	NR	NR	NR	54 ± 13	64 ± 6 (18–24 h)	58 ± 8 (3.5 ms)	NR	NR	NR
Sandstede *et al.*[25]	MR	14	NR	NR	NR	66 ± 10	NR	62 ± 10 (3 ms)	NR	NR	NR
Zhao *et al.*[22]	Echo	30	21.6 ± 5.0	9.2 ± 3.2 (1 w)	NR	NR	NR	NR	NR	NR	NR
Kempny *et al.*[23]	Echo	22	24.1 ± 5.0	NR	15.9 ± 4.1 (100 ds)	NR	NR	NR	47.0 ± 7.0	NR	39.8 ± 10.7 (100 ds)
Quick *et al.*[16]	Echo	63	23.7 ± 4.0	15.6 ± 2.9 (<8 ds)	NR	NR	NR	NR	NR	NR	NR
Okada *et al.*[18]	Echo	15	18 ± 5	11 ± 7 (1 w#)	NR	NR	NR	NR	38 ± 12	−1 ± 5* (1 w#)	NR
Crouch *et al.*[19]	Echo/CMR	21	NR	NR	NR	59 ± 8	58 ± 8 (<2 ws)	NR	NR	NR	NR
Keyl *et al.*[20]	3D echo	20	26 ± 4	13 ± 2 (5–7 ds)	NR	55 ± 7	55 ± 6 (5–7 ds)	NR	NR	NR	NR
Musa *et al.*[21]	CMR	56	22 ± 5	NR	14 ± 3 (6 ms)	58 ± 8	NR	53 ± 9 (6 ms)	NR	NR	NR
Gronlykke *et al.*[12]	Echo	106	24 ± 5.2 (*n* = 99)	NR	16 ± 4.2 (3 ms) (*n* = 91)	NR	NR	NR	44 ± 11 (*n* = 91)	NR	39 ± 10 (3 ms) (*n* = 72)

Data presented as mean ± standard deviation.
*Mean change.
#Median.
CMR, cardiac magnetic resonance imaging; ds, days; FAC, fractional area change; ms, months; NR, not reported; RVEF, right ventricular ejection fraction; TAPSE, tricuspid annular plane systolic excursion; ws, weeks

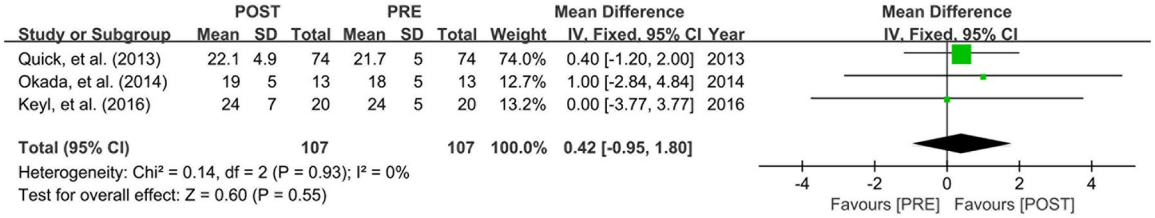

Figure 2. Fixed-effects meta-analysis of TF-TAVR post-procedure *versus* pre-procedure for the primary outcome of TAPSE at 1 week (including 5–7 days, 1 week and <8 days) follow-up.
CI, confidence interval; IV, inverse variance; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion; TF-TAVR, transfemoral transcatheter aortic valve replacement

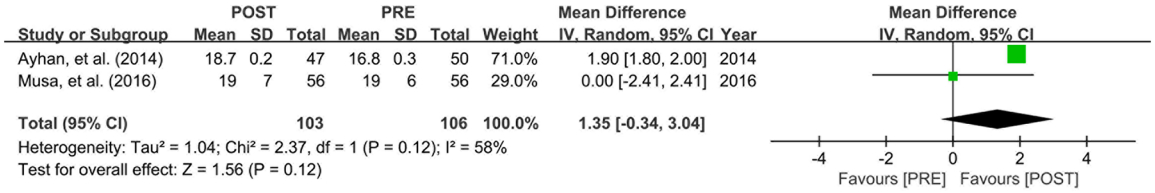

Figure 3. Random-effects meta-analysis of TF-TAVR post-procedure *versus* pre-procedure for the primary outcome of TAPSE at 6 month follow-up.
CI, confidence interval; IV, inverse variance; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion; TF-TAVR, transfemoral transcatheter aortic valve replacement

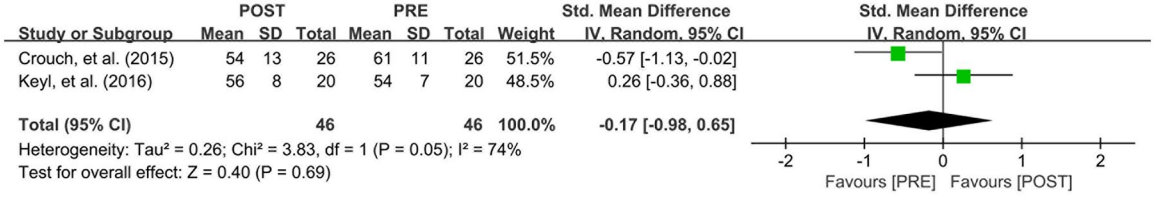

Figure 4. Random-effects meta-analysis of TF-TAVR post-procedure *versus* pre-procedure for the secondary outcome of RVEF at <2 week (including 5–7 days and <2 weeks) follow-up.
CI, confidence interval; IV, inverse variance; RVEF, right ventricular ejection fraction; SD, standard deviation; TF-TAVR, transfemoral transcatheter aortic valve replacement

The secondary outcome. The RVEF at <2 weeks (including 5–7 days and <2 weeks; Figure 4) and 6 months (Figure 5) post TF-TAVR were not significantly different from those at the baseline, respectively.

Meta-analysis of RVF in patients with AS after SAVR

The primary outcome. Compared with baseline, there was significant deterioration in TAPSE at 1 week (including <8 days, 5–7 days, and 1 week; Figure 6) and 3 months (including 100 days and 3 months; Figure 7) after SAVR.

The secondary outcome. The RVEF at <2 weeks (including 5–7 days and <2 weeks; Figure 8) and 3 months (including 3.5 months and 3 months; Figure 9) post SAVR did not significantly differ from the baseline levels, respectively; however, the FAC was significantly worse at 3 months (including 100 days and 3 months) post SAVR than that before SAVR (Figure 10).

Meta-analysis of RVF in patients with AS after TF-TAVR versus SAVR

TAPSE post-TF-TAVR was significantly better than TAPSE post-SAVR at 1 week and 3–6 month

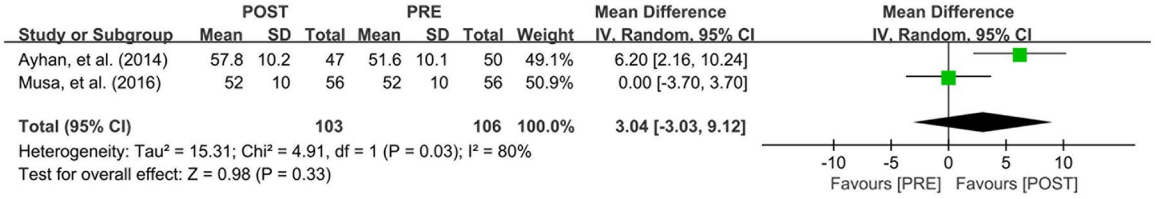

Figure 5. Random-effects meta-analysis of TF-TAVR post-procedure *versus* pre-procedure for the secondary outcome of RVEF at 6 month follow-up.
CI, confidence interval; IV, inverse variance; RVEF, right ventricular ejection fraction; SD, standard deviation; TF-TAVR, transfemoral transcatheter aortic valve replacement

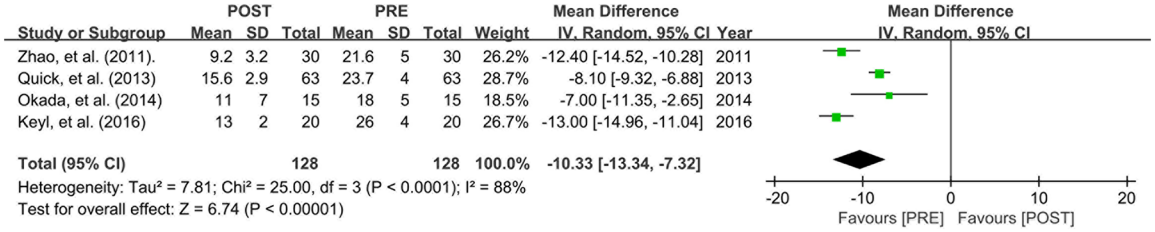

Figure 6. Random-effects meta-analysis of SAVR post-procedure *versus* pre-procedure for the primary outcome of TAPSE at 1 week (including 5–7 days, 1 week and <8 days) follow-up.
CI, confidence interval; IV, inverse variance; SAVR, surgical aortic valve replacement; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion

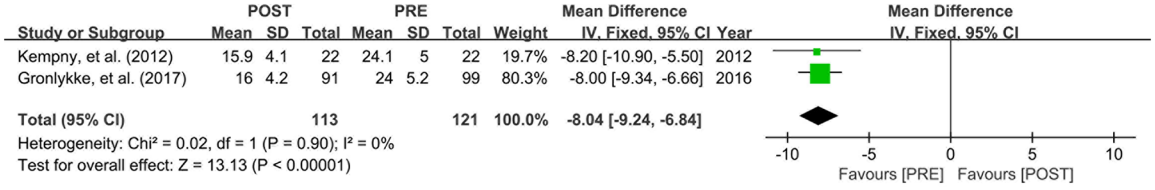

Figure 7. Fixed-effects meta-analysis of SAVR post-procedure *versus* pre-procedure for the primary outcome of TAPSE at 3 month (including 100 days and 3 months) follow-up.
CI, confidence interval; IV, inverse variance; SAVR, surgical aortic valve replacement; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion

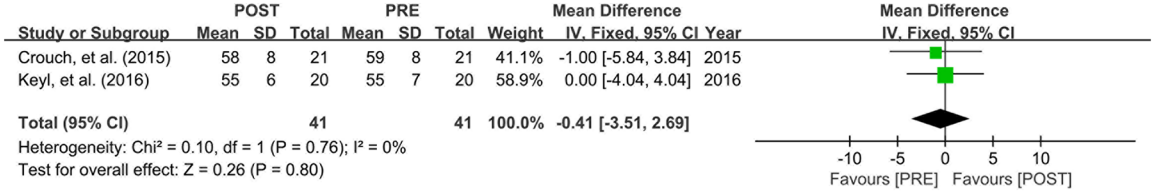

Figure 8. Fixed-effects meta-analysis of SAVR post-procedure *versus* pre-procedure for the secondary outcome of RVEF at <2 week (including 5–7 days and <2 weeks) follow-up.
CI, confidence interval; IV, inverse variance; RVEF, right ventricular ejection fraction; SAVR, surgical aortic valve replacement; SD, standard deviation

follow-ups (Supplemental Figures 2 and 3). Furthermore, ΔTAPSE, the difference of TAPSE between post- and pre-procedure, was significantly improved in TF-TAVR group in comparison with SAVR group at 1 week and 3–6 months following procedure (Figures 11 and 12).

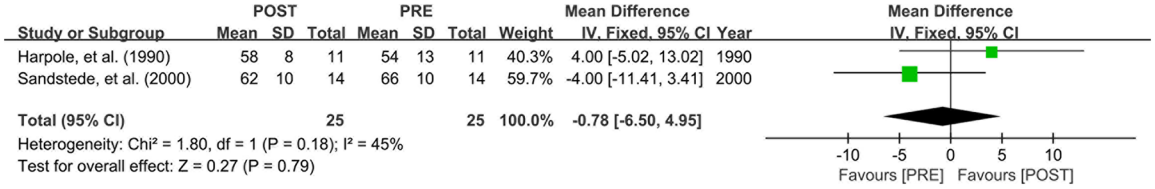

Figure 9. Fixed-effects meta-analysis of SAVR post-procedure *versus* pre-procedure for the secondary outcome of RVEF at 3 month (including 3.5 months and 3 months) follow-up.
CI, confidence interval; IV, inverse variance; RVEF, right ventricular ejection fraction; SAVR, surgical aortic valve replacement; SD, standard deviation

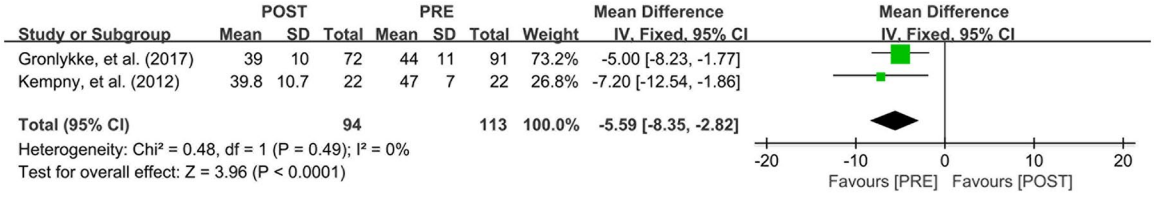

Figure 10. Fixed-effects meta-analysis of SAVR post-procedure *versus* pre-procedure for the secondary outcome of FAC at 3 month follow-up.
CI, confidence interval; FAC, fractional area change; IV, inverse variance; SAVR, surgical aortic valve replacement; SD, standard deviation

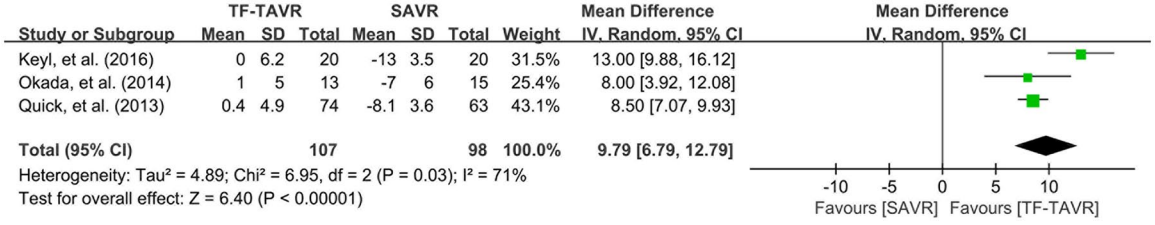

Figure 11. Random-effects meta-analysis of TF-TAVR *versus* SAVR for the primary outcome of ΔTAPSE at 1 week (including <8 days, 5–7 days and 1 week) follow-up.
Δ, post–pre; CI, confidence interval; IV, inverse variance; SAVR, surgical aortic valve replacement; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion; TF-TAVR, transfemoral-transcatheter aortic valve replacement

Discussion

This is the first meta-analysis evaluating the effect of TF-TAVR on RVF evaluated by a variety of parameters and comparing it with that of SAVR. Our main findings are: longitudinal RVF, indicated by TAPSE, is not adversely affected at 1 week and 6 months post TF-TAVR as compared with the baseline level. Moreover, RVEF (<2 weeks and 6 months) did not exhibit significant deterioration post TF-TAVR, either. On the other hand, TAPSE at 1 week and 3 months post SAVR and FAC at 3 months post SAVR were significantly aggravated, but RVEF did not show significant deterioration. Furthermore, both post-procedure TAPSE and ΔTAPSE were significantly improved in TF-TAVR group as compared with those in SAVR group.

RV dysfunction has been reported in one out of four patients with severe AS.[26,27] RV dysfunction at baseline has been associated with an elevated risk of cardiovascular mortality after SAVR.[28] Several explanations have been proposed for this association. Thoracotomy and pericardiotomy impact RV myocardial blood flow and may further result in RV failure.[29] Alternatively, the negative impact of cardiopulmonary bypass on inflammatory and coagulation cascades following SAVR may cause exacerbation in the RVF.[30,31] Other potential contributing factors may include loss of cardioprotection and atrioventricular synchrony, air embolism of right coronary, and increased pulmonary artery pressure as a result of impaired pulmonary perfusion.[8] On the other hand, the studies evaluating the effect of RV dysfunction at baseline

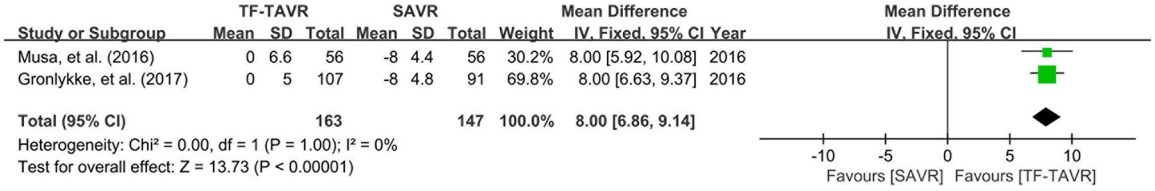

Figure 12. Fixed-effects meta-analysis of TF-TAVR *versus* SAVR for the primary outcome of ΔTAPSE at 3–6 month follow-up.
Δ, post-pre; CI, confidence interval; IV, inverse variance; SAVR, surgical aortic valve replacement; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion; TF-TAVR, transfemoral-transcatheter aortic valve replacement

on the patients undergoing TAVR have yielded conflicting results. Studies including sub-analysis of the PARTNER trial showed no influence of baseline RV dysfunction on outcomes of TAVR; whereas others have observed up to 2-fold increase in post-TAVR mortality in patients with baseline RV dysfunction.[32–34] Therefore, the effect of baseline RV dysfunction on TF-TAVR outcomes remains controversial.

A recent meta-analysis has shown that TAPSE remains unchanged post TAVR while it decreases by 12 months after SAVR; however, the inclusion of cases that have undergone alternative access TAVR may influence the results and no comparison was made specifically between the TF-TAVR and SAVR in that study.[13] In the present study, despite more comorbidities were presented in the TF-TAVR group than in the SAVR group,[35] TF-TAVR was superior to SAVR in regard to maintaining TAPSE level. This is similar to the findings reported by Quick *et al*. in a small observational study,[16] in which marked deterioration of TAPSE after SAVR (23.7 +/−4 mm *versus* 15.6 +/−2.9 mm, $p < 0.001$) and TA-TAVR (21.1 +/−4.7 mm *versus* 19.1 +/−4.7 mm, $p = 0.02$) was observed. TAPSE remained unchanged in the TF-TAVR group (21.7 +/−5 mm *versus* 22.1 +/−4.9 mm, $p = 0.38$).[16] Likewise, in 27 pairs of TAVR (TA-TAVR and TF-TAVR) and SAVR patients matched by gender, age, and LV function, Forsberg and colleagues demonstrated that TF-TAVR was associated with better longitudinal RVF than TA-TAVR; whereas SAVR was associated with worse longitudinal RVF than TAVR.[36] In addition, a sub-analysis from the randomized CoreValve US high-risk Clinic Study showed that RV systolic function was significantly compromised in the patients subjected to SAVR ($p < 0.001$) and was inferior to that in the patients subjected to TAVR at discharge and 1 month post procedure. However, RVF was not significantly different between the treatment groups at 6-month ($p = 0.83$) or 1-year ($p = 0.14$) follow-up.[37] Studies have indicated that the reduction in the TAPSE following SAVR was presumably due to conformational rather than functional changes in the RV after cardiac surgery, and such a reduction in most cases occurred shortly after weaning from cardiopulmonary bypass.[38] However, the present study showed that both the TAPSE, representing longitudinal RVF, and the FAC, reflecting the whole RVF, were significantly exacerbated as long as 3 months following SAVR, implicating the possible functional impairments elicited by the surgical procedure. Admittedly, one should also note that RVEF did not show statistically significant aggravation following SAVR. This could be due to the compensated latitudinal RVF in the face of reduced longitudinal RVF, as reflected by the diminished TAPSE post SAVR. Therefore, further study might be needed to evaluate the RVEF using cardiac magnetic resonance imaging or 3D echocardiography. Taken together, these results indicate that TF-TAVR might avoid the acute insults to the RV likely caused by conformational changes, cardioplegia, and cardiopulmonary bypass that are entailed in SAVR.[16,38,39]

Limitations

The heterogeneity among trials was significant, which was related to the type of study. Some studies were not randomized control trials and the sample size was small.[16,20,22] We chose random effects based solely on I^2 more than 50, which may increase the risk of Type 2 error due to lack of power. Secondly, there are discrepancies in follow-up time periods and outcomes among the selected studies.

Conclusion

TAPSE and RVEF were maintained post TF-TAVR; whereas TAPSE and FAC were significantly deteriorated post SAVR, while RVEF did not exhibit significant deterioration. In addition, post-TAPSE and ΔTAPSE are significantly improved in TF-TAVR group as compared with those in SAVR group. These results implicate that RVF is maintained post TF-TAVR and at least longitudinal RVF is compromised post SAVR. Therefore, baseline RV dysfunction should be considered when selecting TF-TAVR or SAVR, and TF-TAVR could be a preferred option in patients with RV dysfunction.

Conflict of interest statement

The authors declare that there is no conflict of interest.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the National Natural Science Foundation of China (81770300, 81860059, 81460072); CAS "Light of West China" Program; International Joint Research Program of Gansu Province (18YF1WA046); Innovation and Entrepreneurship Program of Lanzhou City (2018-RC-78); the Science Foundation of Gansu Provincial Hospital (18GSSY5-4)

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Supplemental material

Supplemental material for this article is available online.

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Appendix 1

Electronic database search hedges

Four databases were used to identify the study. The search strategies of PubMed are as follows:

PubMed (694 records) 2/14/2020

((((((((((SAVR[Title/Abstract]) OR surgical aortic valve replacement[Title/Abstract]) OR (((Aortic Valve Stenosis[Title/Abstract]) AND Heart Valve Prosthesis Implantation[Title/Abstract]) AND Surgical Procedures, Operative[Title/Abstract]))) OR aortic valve replacement[Title/Abstract])) AND (((((((Supravalvar aortic stenosis, eisenberg type[Title/Abstract]) OR (Subvalvular aortic stenosis, Eisenberg type)) OR Bicuspid Aortic Valve[Title/Abstract]) OR Aortic Stenosis, Subvalvular[Title/Abstract]) OR Aortic Stenosis, Supravalvular[Title/Abstract]) OR "Aortic Valve Stenosis"[Mesh]) OR Aortic Valve Stenosis[Title/Abstract]))) OR (((((((((TAVR[Title/Abstract]) OR transcatheter aortic valve implantation [Title/Abstract]) OR TAVR[Title/Abstract]) OR Transcatheter Aortic Valve Replacement[Title/Abstract]) OR "Transcatheter Aortic Valve Replacement"[Mesh])) OR aortic valve replacement [Title/Abstract])) AND (((((((Supravalvar aortic stenosis, eisenberg type[Title/Abstract]) OR (Subvalvular aortic stenosis, Eisenberg type)) OR Bicuspid Aortic Valve[Title/Abstract]) OR Aortic Stenosis, Subvalvular[Title/Abstract]) OR Aortic Stenosis, Supravalvular[Title/Abstract]) OR "Aortic Valve Stenosis"[Mesh]) OR Aortic Valve Stenosis[Title/Abstract])))) AND (((((((((right ventricular[Title/Abstract]) OR right[Title/Abstract]) OR ventricular functions, right[Title/Abstract]) OR ventricular function, right[Title/Abstract]) OR functions, right ventricular[Title/Abstract]) OR function, right ventricular[Title/Abstract]) OR right ventricular functions[Title/Abstract]) OR right ventricular function[Title/Abstract]) OR "Ventricular Function, Right"[Mesh])

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