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A meta-analysis of effects of transcatheter versus surgical aortic valve replacement on left ventricular ejection fraction and mass

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ABSTRACT

Objectives: To determine which procedure, transcatheter aortic valve implantation (TAVI) or surgical aortic valve replacement (SAVR), for severe aortic stenosis (AS) improves follow-up left ventricular (LV) function or hypertrophy more effectively, we performed the first meta-analysis of comparative studies reporting LV ejection fraction (LVEF) or mass (LVM) after TAVI versus SAVR.

Methods: Studies considered for inclusion met the following criteria: the article was written in English; the design was a comparative study; the study population was patients with severe AS; patients were assigned to TAVI versus SAVR; and outcomes included follow-up (6–12-month) LVEF or LVM. For each study, data regarding fractional changes in LVEF or LVM in both the TAVI and SAVR groups were used to generate mean differences (MDs) and 95% confidence intervals (CIs).

Results: Our search identified 8 eligible studies. Two studies with baseline LVEF < 40% demonstrated significantly greater fractional changes in LVEF after TAVI than after SAVR. A pooled analysis of 6 studies demonstrated no statistically significant difference in fractional changes in LVEF between TAVI and SAVR (MD, 3.25%; 95% CI, −1.30% to 7.80%; $p = 0.16$). Another pooled analysis of 5 studies demonstrated significantly greater fractional changes (i.e. less fractional "reductions") in LVM after TAVI than after SAVR (MD, 4.75%; 95% CI, 2.18% to 7.32%; $p = 0.0003$).

Conclusions: For patients with severe AS, SAVR may be associated with greater improvement in LVM, probably not in LVEF, at 6–12 months. For limited patients with reduced LVEF, TAVI might be associated with greater improvement in LVEF.

1. Introduction

Aortic stenosis (AS) is frequently accompanied by left ventricular (LV) hypertrophy (LVH) and remodeling [1]. Lower LV mass (LVM) is associated with lower rates of clinical end points such as cardiovascular death, fatal or nonfatal myocardial infarction, and fatal or nonfatal stroke [2]. A significant reduction in LVH occurs during the first 18 months after surgical aortic valve replacement (SAVR) for severe AS [3]. Insufficient regression of LVH is related to indices of irreversible myocardial disease, which also prevents functional LV improvement despite successful SAVR and a hemodynamically well-functioning valve [3]. It is still controversial whether incomplete regression of LVH is associated with poorer long-term survival [1]. Gaudino et al. [4] demonstrated that the extent of LVM regression after SAVR did not correlate with 28 ± 9-month survival. Whereas, Zybach-Benz et al. [5] indicated that LVH at 5.8 ± 5.4 years after SAVR was an independent predictor of cardiac-related morbidity. The introduction of transcatheter aortic valve implantation (TAVI) in clinical practice has widened options for symptomatic patients at high surgical risk [1]. However, it is not known whether TAVI has equivalent or prolonged benefits in terms of LV functional improvement and reverse remodeling [1]. No quantitative meta-analysis regarding this topic has been conducted to date. To determine which procedure, TAVI or SAVR for severe AS, improves follow-up LV function or LVH more effectively, we performed the first meta-analysis of studies comparing LV ejection fraction (LVEF) or LVM after TAVI with that after SAVR.

Abbreviations: AR, aortic regurgitation; AS, aortic stenosis; CABG, coronary artery bypass grafting; CI, confidence interval; CHOICE, Randomized Comparison of Transcatheter Heart Valves in High Risk Patients With Severe Aortic Stenosis: Medtronic CoreValve Versus Edwards SAPIEN XT; EF, ejection fraction; LV, left ventricle; LVH, LV hypertrophy; LVM, LV mass; LVMI, LVM index; MD, mean difference; PARTNER, Placement of AoRTic TraNscathetER Valves; PPM, prosthesis-patient mismatch; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

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2. Methods

2.1. Search strategy

All studies comparing follow-up LVEF or LVM after TAVI with that after SAVR for severe AS were identified using a 2-level search strategy. First, databases including MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials were searched through February 2016 using Web-based search engines (PubMed and OVID). Second, relevant studies were identified through a manual search of secondary sources including references of initially identified articles and a search of reviews and commentaries. All references were downloaded for consolidation, elimination of duplicates, and further analysis. Search terms included *ejection fraction* or *ventricular mass/remodeling/remodelling/geometry*; *aortic valve*; *percutaneous*, *transcatheter*, *transluminal*, *transarterial*, *transapical*, *transaortic*, *transcarotid*, *transaxillary*, *transsubclavian*, *transiliac*, *transfemoral*, or *transiliofemoral*; and *replacement*.

2.2. Study selection and data extraction

Studies considered for inclusion met the following criteria: the article was written in English; the design was a comparative study; the study population was patients with severe AS; patients were assigned to TAVI versus SAVR; and outcomes included follow-up (6–12-month) LVEF or LVM. From each individual study, we extracted fractional changes (from baseline to follow-up) in LVEF (%) and LVM (g) (or LVM index = LVMI [g/m^2]). When baseline and follow-up values were available without changes, we calculated absolute and fractional changes [6,7]. Data were extracted in duplicate by two investigators (H.T., T.A.) and independently verified by a third investigator (T.U.). Disagreements were resolved by consensus.

2.3. Statistical analysis

For each study, we generated mean differences (MDs) and 95% confidence intervals (CIs) using data regarding fractional changes of LVEF or LVM in both the TAVI and SAVR groups [8]. Study-specific estimates were combined using inverse variance-weighted averages [8] of MDs in the random-effects model [9]. Sensitivity analyses were performed by excluding individual studies one at a time and recalculating the pooled MD estimates for the remaining studies. Publication bias was assessed graphically using a funnel plot [10] and mathematically using an adjusted rank-correlation test [11] and a linear-regression test [12]. All analyses were conducted using Review Manager version 5.3 (available from http://tech.cochrane.org/revman) and Comprehensive Meta-Analysis version 3 (Biostat, Englewood, NJ).

3. Results

3.1. Search results

Of 278 potentially relevant articles screened initially, our search identified 8 eligible studies [13–20] as outlined in Supplemental Fig. S1. Study characteristics (patient number; mean pressure gradient of aortic valve; approach and device of TAVI; and staged or concomitant coronary revascularization) were summarized in Table 1. LVEF and LVM (measurement modality; follow-up duration; baseline and follow-up LVEF and LVM, and absolute and percent [fractional] change in LVEF and LVM) were abstracted in Table 2. Baseline and follow-up aortic valve area (AVA) index (AVAI) were summarized in Supplemental Table S1. Follow-up prosthesis-patient mismatch (PPM) and aortic regurgitation (AR) were abstracted in Supplemental Table S2. Three studies [17,19,20] were sub-analyses of randomized controlled trials (RCTs) (Placement of AoRTic TraNscathetER Valves [PARTNER] [17,19] and CoreValve US High Risk Pivotal [20]). Whereas, the other 5 [13–16,18] were observational studies. Clavel et al. [13] exclusively enrolled patients with reduced LVEF (≤50%), and O'Sullivan et al. [18] selectively included those with low-flow (LVEF <50%) and low-gradient (mean gradient ≤40 mm Hg) severe AS. Baseline mean pressure gradients were <40 mm Hg in the former [13] and <30 mm Hg in the latter [18]. Whereas, they were >50 mm Hg in the other 6 studies [14–17,19,20] (Table 1). Mean baseline LVEF was <40% in these 2 studies [13,18], whereas it was >50% in the other 6 studies [14–17,19,20] (Table 2). CoreValve was exclusively used in 3 studies [14,16,20], and SAPIEN was selectively implanted in 3 studies [13,17,19]. From only one study by Gavina et al. [15], LVMI was extracted instead of unavailable LVM.

3.2. LVEF

Two studies by Clavel et al. [13] and O'Sullivan et al. [18] (both with baseline LVEF < 40%) demonstrated significantly greater fractional changes in LVEF after TAVI than after SAVR (MD, 7.00%; 95% CI, 2.00% to 12.00% [13]; MD, 13.80%; 95% CI, 2.75% to 24.85% [18]; Fig. 1), which indicated significantly greater improvement in LVEF after TAVI than after SAVR. A pooled analysis of 6 studies [13–15,17,18,20] (representing 1279 patients) demonstrated no statistically significant difference in fractional changes in LVEF between TAVI and SAVR (MD, 3.25%; 95% CI, −1.30% to 7.80%; $p = 0.16$; Fig. 1). There was statistically significant between-study heterogeneity (p for heterogeneity = 0.005; $I^2 = 71\%$). To assess the impact of qualitative heterogeneity in study design and patient selection on the pooled effect estimate, we performed several sensitivity analyses. Exclusion of 2 studies with low-flow and low-gradient AS [13,18] from the meta-analysis did not substantially change the pooled result (MD, −0.27%; 95% CI, −3.51% to 2.98%; p = 0.87) with minimal between-study heterogeneity (p for heterogeneity = 0.24; $I^2 = 28\%$). Eliminating a study by Zorn et al. [20] generated significantly greater fractional changes in LVEF after TAVI than after SAVR (MD, 4.78%; 95% CI, 0.86% to 8.70%; $p = 0.02$; Supplemental Fig. S2). Exclusion of any single study (except for the study by Zorn et al. [20]) from the analysis did not substantively alter the overall result of our analysis (Supplemental Fig. S2). To assess publication bias, we generated a funnel plot of the effect size versus the precision (reciprocal of standard error) for each study (Supplemental Fig. S3). There was no evidence of significant publication bias (2 tailed p with continuity correction =

Table 1
Study characteristics.

Study	Patient number		Aortic valve			TAVI			Coronary revascularization (%)	
			Mean pressure gradient (mm Hg)			Approach (%)		Device	Staged/concomitant PCI in TAVI	Concomitant CABG in SAVR
	TAVI	SAVR	TAVI	SAVR	p	TF	TA			
Clavel 2010 [13]	83	200	37 ± 14	35 ± 14	0.27	53.0	47.0	SAPIEN	50.6	58.5
Fairbairn 2013 [14]	25	25	57 ± 22	47 ± 13	0.05	TF/TS, 100	0	CoreValve	4.0	12.0
Gavina 2014 [15]	42	45	54.67 ± 15.77	57.89 ± 13.91	0.317	71.4	28.6	CoreValve/SAPIEN	0	0
Giannini 2011 [16]	58	58	59.3 ± 18.1	56.6 ± 22.8	N/S	TF/TS, 100	0	CoreValve	N/A	5
Hahn (PARTNER) 2013 [17]	326	310	43.1 ± 14.5 (N=307)	43.4 ± 14.3 (N=295)	0.7929	70.2	29.8	SAPIEN	Excluded	
O'Sullivan 2015 [18]	108	52	28.6 ± 10.3	29.3 ± 9.5	0.69	N/A		CoreValve/SAPIEN/Symetis	36.1	69.2
Pibarot (PARTNER) 2014 [19]	1941	270	44 ± 15*,†	43 ± 15*,†	0.30*	51.0	49.0	SAPIEN	Excluded	
Zorn (CoreValve US High Risk Pivotal Trial) 2015 [20]	367	334	48.15 ± 13.74*,† (N = 270)	47.82 ± 14.32*,† (N = 221)	0.80*	TF/TS/TAo, 100	0	CoreValve	N/A	

CABG = coronary artery bypass grafting; N/A = not available; N/S = not significant; PARTNER = Placement of AoRTic TraNscathetER Valves; PCI = percutaneous coronary intervention; SAVR = surgical aortic valve replacement; TA = transapical; TAo = transaortic; TAVI = transcatheter aortic valve implantation; TF = transfemoral; TS = transsubclavian.
* Calculated by us.
† Combining values of subgroups.

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