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Direct and adjusted indirect comparisons of perioperative mortality after sutureless or rapid-deployment aortic valve replacement versus transcatheter aortic valve implantation

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ABSTRACT

Objectives: To determine which procedure, aortic valve replacement (AVR) with a sutureless or rapid-deployment prosthesis (SL-AVR) or transcatheter aortic valve implantation (TAVI), achieves better perioperative survival for severe aortic stenosis (AS), we conducted direct-comparison meta-analyses (DC-MAs) and an adjusted indirect-comparison meta-analysis (IDC-MA).
Methods: We searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials through April 2016. Eligible studies were randomized controlled trials (RCTs) and propensity-score matched (PSM) studies. We performed a DC-MA-[A] of SL-AVR versus TAVI, a DC-MA-[B] of SL-AVR versus conventional AVR (C-AVR), and a DC-MA-[C] TAVI versus C-AVR. Then, we computed a IDC-MA-[A′] of TAVI versus SL-AVR from the results of the DC-MA-[B] and the DC-MA-[C].
Results: We identified 6 RCTs and 30 PSM studies enrolling a total of 15,887 patients. The 3 DC-MAs demonstrated significantly lower perioperative (30-day or in-hospital) all-cause mortality after SL-AVR than after TAVI (odds ratio [OR], 0.48; 95% confidence interval [CI], 0.28 to 0.80; $p = 0.005$) and no significant differences between SL-AVR and C-AVR (OR, 1.07; 95% CI, 0.60 to 1.94; $p = 0.81$) and between TAVI and C-AVR (1.07; 95% CI, 0.90 to 1.27; $p = 0.45$). The computed IDC-MA-[A′] indicated no significant difference in mortality between SL-AVR and TAVI (1.01; 95% CI, 0.54 to 1.86). Combining the results of the DC-MA-[A] and IDC-MA [A′] showed significantly lower mortality after SL-AVR than after TAVI (OR, 0.65; 95% CI, 0.44 to 0.97; $p = 0.03$).
Conclusions: For patients with severe AS, SL-AVR may achieve better perioperative survival than TAVI.

1. Introduction

Our preliminary meta-analysis [1] suggests that perioperative all-cause mortality is lower after aortic valve replacement (AVR) with a sutureless or rapid-deployment prosthesis (SL-AVR) than after transcatheter aortic valve implantation (TAVI) for severe aortic stenosis (AS). Statistical power of this meta-analysis [1], however, may be insufficient, because merely 7 observational comparative studies were included in it. Limited or no evidence is often obtained from direct-comparison (DC) studies, and thus an adjusted indirect comparison (IDC) may be required [2]. Additionally, to augment statistical power or precision, it would be possible to quantitatively combine results of the DC and those of the IDC [3]. To determine which procedure, SL-AVR or TAVI, achieves better perioperative overall survival for severe AS, a DC meta-analysis (DC-MA) and an IDC meta-analysis (IDC-MA) were performed, and then results of them were combined.

2. Methods

We identified all randomized controlled trials (RCTs) and propensity-score matched (PSM) studies of SL-AVR versus TAVI, those of SL-AVR versus conventional AVR (C-AVR), and those of TAVI versus C-AVR for severe AS by the use of a 2-level search strategy. First, we searched databases of MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials by means of Web-based search engines of PubMed and OVID through April 2016. Second, we identified relevant studies via manual searching secondary sources such as references in articles initially identified, reviews, and commentaries. The following search term were included: *sutureless*, *rapid-deployment*, *Enable*, *Intuity*, *Perceval*, or *Trilogy*; *percutaneous*, *transcatheter*, *transluminal*, *transarterial*, *transapical*, *transaortic*,

Abbreviations: ACC, aortic cross-clamp; AS, aortic stenosis; AVR, aortic valve replacement; C-AVR, conventional AVR; CI, confidence interval; CPB, cardiopulmonary bypass; DC, direct comparison; DC-MA, DC meta-analysis; E/e′, early mitral velocity/annulus velocity; EF, ejection fraction; EuroSCORE, European System for Cardiac Operative Risk Evaluation; HR, hazard ratio; IDC, adjusted indirect comparison; IDC-MA, IDC meta-analysis; OR, odds ratio; PAR, paravalvular aortic regurgitation; PARTNER, Placement of AoRTic TraNscathetER Valves; PMI, pacemaker implantation; PSM, propensity-score matched; RCT, randomized controlled trial; SL-AVR, AVR with a sutureless or rapid-deployment prosthesis; TAVI, transcatheter aortic valve implantation.

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transcarotid, *transaxillary*, *transsubclavian*, *transiliac*, *transfemoral*, or *transiliofemoral*; *aortic valve*; *replacement*; and *randomized*, *randomised*, *randomly*, *randomization*, or *propensity*. To consolidate, eliminate duplicates, and further analyze, we downloaded all references.

Studies deemed to be included when the following criteria were fulfilled: the design was a RCT or a PSM study; the study population was patients with severe AS; patients underwent SL-AVR versus TAVI, SL-AVR versus C-AVR, or TAVI versus C-AVR; and outcomes included perioperative (30-day or in-hospital) all-cause mortality. From each individual study, we abstracted data regarding detailed inclusion criteria, prosthesis type, predicted mortality, duration of follow-up, and perioperative mortality as available.

We generated odds ratios (ORs) and 95% confidence intervals (CIs) for each study by the use of data regarding mortality in both the experimental and control groups. We combined study-specific estimates by means of inverse variance-weighted averages of logarithmic ORs in both fixed-effect and random-effects models. We analyzed between-study heterogeneity by the use of standard χ^2 tests, with $p < 0.05$ considered to be statistically significant. When we identified no statistically significant heterogeneity, we preferentially used the fixed-effect estimate as the summary measure.

First, we performed the DC-MA-[A] of SL-AVR versus TAVI, the DC-MA-[B] of SL-AVR versus C-AVR, and the DC-MA-[C] of TAVI versus C-AVR (Fig. 1). Second, the IDC-MA [A′] of TAVI versus SL-AVR was computed from the summary estimate of the DC-MA-[B] (SL-AVR versus C-AVR) and that of the DC-MA-[C] (TAVI versus C-AVR) by means of the methods of Bucher and colleagues [4]. We deemed the estimate of DC-MA-[A] to be one "study" whereas considered that of the IDC-MA-[A′] to be a second "study." Finally, we combined these two "studies" in a normal meta-analysis. We conducted all analyses by the use of Review Manager version 5.3 (available from http://tech.cochrane.org/revman).

3. Results

We identified 6 eligible studies [5–10] of SL-AVR versus TAVI, 6 ones [9,11–15] of SL-AVR versus C-AV, and 24 ones [9,16–38] of TAVI versus C-AVR (Table 1). These included no RCT and 6 PSM studies [5–10] (enrolling a total of 1478 patients) of SL-AVR versus TAVI, one RCT [11] (including 94 patients) and 5 PSM studies [9,11–15] (enrolling a total of 1375 patients) of SL-AVR versus C-AVR, and 5 RCTs [16,25,27,32,35] (including a total of 3828 patients) and 19 PSM studies [9,17–24,26,28–31,33,34,36–38] (enrolling a total of 9112 patients) of TAVI versus C-AVR. Mean age in studies of SL-AVR (77.5 years) versus C-AVR (77.9 years) was the lowest, and that in those of TAVI (80.8 years) versus C-AVR (81.1 years) was the highest (Table 1). Mean European System for Cardiac Operative Risk Evaluation (EuroSCORE) I in studies of SL-AVR (12.4) versus C-AVR (12.2) was the lowest, and that in those of TAVI (18.5) versus C-AVR (18.2) was the highest (Table 2).

Significantly lower perioperative all-cause mortality after SL-AVR than after TAVI (fixed-effect OR, 0.48; p for effect = 0.005) was demonstrated in the direct-comparison meta-analysis of 6 studies enrolling a total of 1478 patients (Figs. 2 and 3, DC-MA-[A]). There was no statistically significant difference in mortality between SL-AVR and C-AVR in the direct-comparison meta-analysis of 6 studies including a total of 1469 patients (Fig. 2, DC-MA-[B]). No statistically significant difference in mortality between TAVI and C-AVR was indicated in the direct-comparison meta-analysis of 24 studies enrolling a total of 12,940 patients (Fig. 2, DC-MA-[C]). Then, we computed the indirect-comparison meta-analysis of SL-AVR versus TAVI (IDC-MA [A′]) from the summary estimate of the direct-comparison meta-analysis of SL-AVR versus C-AVR (DC-MA-[B]) and that of the direct-comparison meta-analysis of TAVI versus C-AVR (DC-MA-[C]) (Fig. 1), which showed no statistically significant difference in mortality between TAVI and SL-AVR (30 studies including a total of 14,409 patients; Fig. 3). Finally, combining the estimate of the direct-comparison meta-analysis of SL-AVR versus TAVI (DC-MA-[A]) and that of the indirect-comparison meta-analysis of SL-AVR versus TAVI (IDC-MA-[A′]) (Fig. 1) generated an attenuated but still significantly lower mortality after SL-AVR than after TAVI (36 studies enrolling a total of 15,887 patients; fixed-effect OR, 0.65; p for effect = 0.03; Fig. 3). Moderate (statistically non-significant but trend toward significant) heterogeneity between the estimate of the DC-MA-[A] and that of the IDC-MA-[A′], however, was identified (p for heterogeneity = 0.07; Fig. 3). Pooling the estimate of the DC-MA-[A] and that of the IDC-MA-[A′] by means of the random-effects model produced no statistically significant difference in mortality between SL-AVR and TAVI (random-effects OR, 0.68; 95% CI, 0.33 to 1.41; p for effect = 0.30). All statistics in the fixed-effect model were summarized in Fig. 4.

4. Discussion

In the present analysis of RCTs and PSM studies, the DC demonstrated significantly lower perioperative all-cause mortality after SL-AVR than after TAVI, whereas the IDC indicated no statistically significant difference in mortality between SL-AVR and TAVI. Even adding the result of the IDC to that of the DC (combining the result of the DC and that of the IDC), however, showed still significantly lower mortality after SL-AVR than after TAVI. The final analysis included 36 studies enrolling a total of approximately 16,000 patients with severe AS. For patients with severe AS, SL-AVR may achieve better perioperative overall survival than TAVI. So as to exalt minimal invasiveness in the approach or handle the aortic annulus calcified exceedingly, SL-AVR advancing management of AVR endeavors to reduce cardiopulmonary bypass (CPB) and aortic cross-clamp (ACC) times [39]. The differences between SL-AVR and TAVI are the following: the degenerated leaflets of the native valve are removed and CPB is necessary in the former; whereas the leaflets are left as they are and CPB is generally unnecessary in the latter. These differences between the procedures may impact early or follow-up outcomes [39]. A specific learning curve, however, is necessary for all sutureless valves, regardless of the prosthesis model and the minimally invasive approach, and thus the experts recommend proper education and proctoring by experienced surgeons for the introduction of both programs to avoid complications [40].

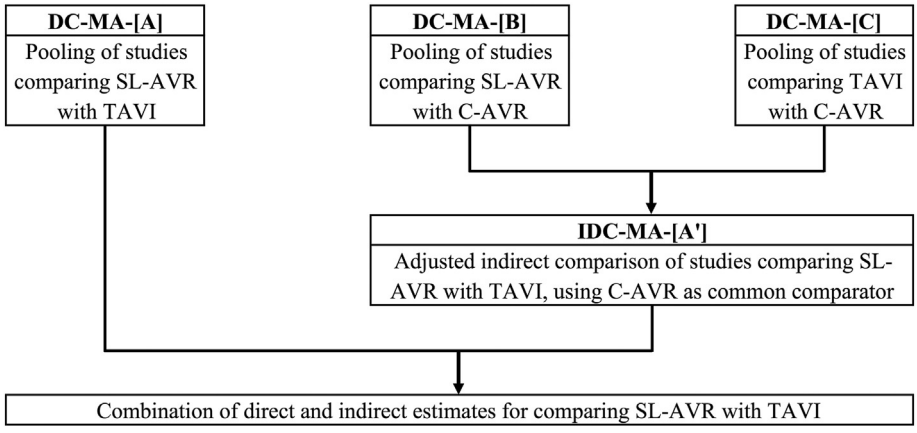

Fig. 1. Analysis design. AVR = aortic valve replacement; C-AVR = conventional AVR; DC-MA = direct-comparison meta-analysis; IDC-MA = adjusted indirect-comparison meta-analysis; SL-AVR = AVR with a sutureless or rapid-deployment prosthesis; TAVI = transcatheter aortic valve implantation.