Does Quicker Mean Better? Comparison of Rapid Deployment Versus Conventional Aortic Valve Replacement
A Meta-Analysis

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Summary

The aim of this meta-analysis was to compare the clinical outcomes in patients who underwent rapid deployment aortic valve replacement (RDA VR) and conventional bio prosthetic aortic valve replacement (CA VR).

We performed a literature search by August 2018. The primary outcomes were hospital and 1-year mortality, and the secondary endpoints included the aortic cross-clamp (ACC), cardiopulmonary bypass (CPB) time, and postoperative and valve-related complications.

Two randomized controlled trials and 13 propensity score-matched studies were included. There was no difference between RDA VR and CA VR in hospital mortality (2.5% versus 2.1%; risk ratio (RR) 1.16 [95% confidence interval (CI) 0.80-1.68]) or 1-year mortality (2.9% versus 4.1%; RR 0.69 [95% CI 0.34-1.34]). RDA VR significantly reduced the ACC time ((mean difference (MD) −24.33 [95% CI −28.35 to −20.32]) and CPB time (MD −21.51 [95% CI −22.83 to −20.20]). The pooled analysis showed that RDA VR doubled the occurrence of permanent pacemaker implantation (8.6% versus 4.3%; RR 2.05 [95% CI 1.62-2.60]). Meanwhile, the blood transfusion amount (MD −1.54 [95% CI −2.22 to −0.86]) and postoperative atrial fibrillation (POAF) occurrence (RR 0.83 [95% CI 0.69-0.99]) was reduced. The difference of paravalvular leakage frequency between RDA VR and CA VR was marginal (RR 1.77 [95% CI 1.00-3.17]; P = 0.05). Furthermore, RDA VR was related to larger valves (MD 0.70 cm [95% CI 0.33-1.07]) and lower mean pressure gradients (MD −1.93 mmHg [95% CI −3.58 to −0.28]).

The hospital and 1-year survival rates between RDA VR and CA VR are comparable. RDA VR reduces POAF occurrence and blood transfusion but is associated with a higher occurrence of pacemaker implantation.

Key words: Aortic stenosis, Rapid deployment valves

Aortic stenosis (AS) is the most prevalent valvular disease in developed countries, especially in elderly populations.1 The prognosis for patients with symptomatic severe AS is poor, and the only effective treatment is aortic valve replacement (AVR). Surgical AVR is considered the treatment of choice for patients with severe AS.2

Conventional AVR (CA VR) refers to surgical AVR with either biological or mechanical valve prosthesis through a median sternotomy. The recent emergence of rapid deployment AVR (RDA VR) brings another choice for patients with AS. These rapid deployment valves (RDVs) are made of biological tissue with an atypical stent frame. So far, three RDVs have been used in clinical practice, including the balloon expanding Edwards Intuity valve (Edwards Lifesciences LLC, Irvine, CA, USA), the Perceval Sutureless (Sorin Biomedica Cardio S.r.l., Saluggia VC, Italy) valve, and the self-expanding 3F Enable valve (ATS Medical Inc., Minneapolis, MN, USA).

Theoretically, the special anchoring mechanisms of RDVs contribute to a shorter aortic cross-clamp (ACC) and cardiopulmonary bypass (CPB) times and to the feasibility of minimal access.3 However, the recent meta-analysis by Sohn, et al.3 showed that the shorter ACC and CPB time in RDA VR did not translate into better postoperative outcomes compared with those in CA VR.
Moreover, Ensminger, et al. reported rather disappointing results for RDAVR, including that RDAVR had no better clinical outcomes and even exacerbated the occurrence of stroke in a large-population study.48 These results led us to conduct the updated meta-analysis to compare the clinical outcomes of RDAVR with those of CAVR.

Methods

Data source and search strategy: This meta-analysis was performed under the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses.55 We searched PubMed, EMBASE, CENTRAL, and the Cochrane databases and conducted hand searching to identify studies that we missed in our primary literature search. The detailed search strategy was provided in the Supplemental Text. The last search was performed on August 28, 2018, and we acquired a total of 2715 publications after removal of duplicates.

Study selection: Two independent reviewers (YL and JFW) performed study selection following the inclusion criteria: (1) patients who underwent AVR with or without coronary artery bypass grafting (CABG); (2) direct comparison of RDAVR versus CAVR; (3) randomized controlled trials (RCTs) designed or using propensity matched scores for statistical adjustment; and (4) intact information provided on the clinical outcomes. Exclusion criteria were defined as follows: (1) unpublished data or abstract only; (2) studies without relevant clinical outcomes. Study selection was first carried out by screening the title and abstract, which excluded most of the publications. We further performed full-text screening for the remaining publications.

Definitions of endpoints: The primary outcome of the present study was early mortality, including hospital and 1-year mortality. Hospital mortality referred to all-cause 30-day mortality or in-hospital mortality in this meta-analysis. The secondary endpoints were the ACC time and CPB time, ICU and hospital stay, perioperative complications, paravalvular leakage (PVL), valve size, and mean pressure gradients post-operation. The data regarding the perioperative complications and echocardiography were obtained within 30 days after the operation. Perioperative complications included cerebral thromboembolic events including transient ischemic attack and permanent stroke, postoperative atrial fibrillation (POAF), permanent pacemaker implantation (PPM), perioperative myocardial infarction (MI), acute kidney failure (including de novo dialysis), and units of blood transfused.

Data extraction: The data were collected independently by two authors (YL and JFW) who reviewed each publication. Information on the study characteristics, quality components, and outcomes of interest was collected on the included trials. Disagreements were resolved by consensus.

Quality assessment: We adapted methods recommended by a Cochrane Collaboration tool for assessing the risk of bias to evaluate the quality of the included studies. The risk of bias of the included two RCTs was evaluated with the Cochrane Risk of Bias 2 tool. We used ROBINS-I (Risk of Bias In Nonrandomized Studies of Interventions) to estimate the risk of bias for the remaining 13 non-randomized studies (NRS).56 No disagreements arose in the quality assessment.

Statistical analysis: For non-continuous outcomes, the results of all the relative studies were combined to estimate the risk ratios (RRs) and 95% confidence intervals (CIs). For continuous outcomes, the data were extracted directly if the study reported the data as the mean differences (MDs) and standard deviation (SD). In cases in which studies reported overall ranges or median and interquartile range, we used the method suggested by Luo, et al. to estimate the MD and SD.57 The I² statistic was used to evaluate the heterogeneity between the studies. An I² value ≥ 50% indicated significant heterogeneity. A random-effects and fixed-effect model was applied for I² ≥ 50% and I² < 50%, respectively. In cases where heterogeneity was present, we conducted a sensitivity analyses by omitting one study at a time to test the influence of a single study. We used the Mantel-Haenszel and inverse variance methods to calculate binary variables and continuous variables, respectively. Funnel plot analyses were used to test the possibility of publication bias. P < 0.05 was considered as statistically significant, and the data were presented as MD ± SD or RR or MD with 95% CI. All analyses were performed using Review Manager version 5.3 (Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).

Results

Identification of studies: A total of 2715 publications were obtained. Through careful screening of articles’ titles and abstracts, 2681 articles were excluded. We retrieved the full articles and assessed for the eligibility of the remaining 34 articles. After scrutinizing these articles, we excluded two meeting abstracts and two publications without relevant clinical outcomes. We also excluded two duplicated publications with overlapping study populations and included studies that reported updated data on follow-up (Figure 1).5,8,10,20

The remaining 15 articles include 2 RCTs8,12) and 13 propensity score-matched NRS, as presented in Supplemental Table I. A total of 2187 and 2453 subjects were included in the RDAVR and CAVR groups, respectively. Notably, nine studies2,4,8,11,14,17,20) reported the result of the lone AVR operation, whereas the other six studies included patients who underwent both AVR with and without CABG. A further subgroup analysis was conducted in subjects who underwent lone AVR and AVR + CABG. Moreover, five studies9,15,17,20) exclusively used the Intuity valve, eight studies10,14,16,19) used the Perceval S valve, one study18) used 3F Enable, and one study4) reported the result of all three types of valves. Given the different design of RDVs, we performed another subgroup analysis in subjects implanted with different types of RDVs. Because of the withdrawn and scarce data of the 3F Enable valve, we mainly focused on the Intuity valve and the Perceval S valve.

Quality assessment and baseline characteristics of included studies: Quality assessment of the two RCTs demonstrated low risk of bias. The overall risk of bias...
was graded as severe for 1 study\(^9\) and moderate for the other 12 NRS (Supplemental Tables II, III).

The baseline characteristics of the patients in the included trials are shown in Supplemental Table IV. Because the baseline was strictly matched by using propensity score matching strategies, we only further compared the baseline demographic of two RCTs. There was no difference between RDAVR and CAVR in age, gender, minimally invasive technique, Logistic EuroScore II, Society of Thoracic Surgeons (STS) score, and heart function grade in both studies.\(^8\),\(^12\)

Notably, eight studies\(^2\),\(^4\),\(^11\)-\(^14\),\(^16\),\(^18\) compared the result of Logistic EuroScore II between RDAVR and CAVR. The average Logistic Score II score was 8.56 ± 6.02 and 8.43 ± 6.39, respectively. Another seven studies\(^2\),\(^4\),\(^8\),\(^9\),\(^13\),\(^17\) used the STS score to evaluate the risk for cardiac surgery. The STS scores were also comparable between RDAVR and CAVR (3.19 ± 2.61 versus 3.31 ± 2.93).

Hospital and 1-year mortality: All but one study\(^9\) reported the result of hospital death. There was no difference between RDAVR and CAVR with respect to hospital mortality (2.5% versus 2.1%; RR 1.16 [95% CI 0.80-1.68]; \(\hat{F} = 0\); \(P = 0.44\)). No difference was noted in hospital mortality in the subgroup analysis of lone AVR and AVR + CABG (RR 1.31 [95% CI 0.86-2.01]; \(\hat{F} = 0\); \(P = 0.21\) and RR 0.76 [95% CI 0.35-1.67]; \(\hat{F} = 0\); \(P = 0.49\), respectively) (Figure 2A). The hospital mortality of both the Intuity valve and Perceval S valve was not different from that of CAVR (RR 1.40 [95% CI 0.46-4.27]; \(\hat{F} = 0\); \(P = 0.55\) and RR 1.07 [95% CI 0.63-1.81]; \(\hat{F} = 0\); \(P = 0.80\), respectively) (Figure 2B).

Five studies\(^2\),\(^4\),\(^11\)-\(^14\),\(^20\) reported the data of 1-year mortality, which only included patients with a lone AVR. The 1-year mortality of the RDAVR group was lower than that of the CAVR group (2.9% versus 4.1%), although the difference was not statistically significant (RR 0.68 [95% CI 0.34-1.34]; \(\hat{F} = 0\); \(P = 0.26\)) (Figure 2C). Subgroup analysis showed that the 1-year mortality of the Intuity valve and Perceval S valve was similar to that of CAVR (RR 0.76 [95% CI 0.27-2.12]; \(\hat{F} = 0\); \(P = 0.60\) and RR 0.62 [95% CI 0.25-1.55]; \(\hat{F} = 0\); \(P = 0.31\), respectively) (Figure 2D).

No publication bias was found in the funnel plot for either the hospital or 1-year mortality (Supplemental Figure 1).

ACC, CPB, and ICU or hospital length of stay (LOS): The mean ACC time was 46.0 ± 19.0 minutes and 67.9 ± 23.8 minutes for the RDAVR and CAVR groups, respectively (MD −24.33 [95% CI −28.35 to −20.32]; \(\hat{F} = 0\); \(P < 0.00001\)) (Figure 3A). Interestingly, the differences were −20.21 (95% CI −24.02 to −16.41; \(\hat{F} = 48\%\); \(P < 0.00001\)) and −27.27 minutes (95% CI −33.21 to −21.33; \(\hat{F} = 92\%\); \(P < 0.00001\)) in the Intuity subgroup and Perceval S subgroup, respectively (Supplemental Figure 3A).

The mean CPB time was 71.6 ± 27.0 minutes and 91.7 ± 33.9 minutes for RDAVR and CAVR (MD −21.51...
Figure 2. Forest plot of studies assessing the effect of rapid deployment aortic valve replacement (RDAVR) and conventional aortic valve replacement (CAVR) on hospital (A) and 1-year mortality (C) with subgroup analysis in subjects with lone AVR or AVR + CABG and hospital (B) and 1-year mortality (D) with subgroup analysis in subjects with different valves. AVR indicates aortic valve replacement; CABG, coronary artery bypass grafting; CI, confidence interval; df, degree of freedom; and M-H, Mantel-Haenszel.

[95% CI −22.83 to −20.20]; I² = 87%; P < 0.00001] (Figure 3B). Compared with CAVR, the Intuity and Perceval S subgroup was associated with a −16.1-minute [95% CI −20.41 to −11.80; I² = 0%; P < 0.00001] and −25.19-minute [95% CI −30.62 to −19.76; I² = 76%; P < 0.00001] reduction in CPB time (Supplemental Figure 2B), respectively.

Both ICU LOS (2.1 ± 2.7 versus 2.1 ± 2.9 days; MD −0.04 [95% CI −0.30-0.23]; I² = 79%; P = 0.79, Supplemental Figure 2A) and in-hospital time (10.1 ± 4.9 versus 10.0 ± 5.1 days; MD −0.53 [95% CI −1.41-0.34]; I² = 88%; P = 0.23, Supplemental Figure 2B) were comparable between the RDAVR and CAVR groups. No clinically significant difference was noted in the subgroup analysis.

Postoperative complications: The pooled results of the postoperative complications including the subgroup analysis in lone AVR and AVR + CABG are presented in the Table. RDAVR was related to a significantly higher occurrence of PPM implantation and less RBC transfusion regardless of the valve type (Supplemental Table V). However, the difference in PPM was not significant among the AVR + CABG subgroup (Table and Figure 4A).

Interestingly, the occurrence of POAF was lower in the RDAVR patients (RR 0.83 [95% CI 0.69-0.99]; F = 48%; P = 0.04). The subgroup analysis indicated that the difference mainly existed in the AVR + CABG subgroup but disappeared in the lone AVR subgroup (Table and Figure 4C). Compared with using the Intuity and Perceval S valves, CAVR did not differ in POAF occurrence (Supplemental Table V).

No difference was noted in the occurrence of cerebral thromboembolic events, acute kidney failure and MI between RDAVR and CAVR (Table and Supplemental Table V). Interestingly, the subgroup analysis among the AVR + CABG subjects demonstrated that RDAVR was associated with a higher occurrence of acute kidney failure compared with CAVR (Table).

Valve-related complications: The frequency of PVL in the RDAVR and CAVR groups was 1.6% and 1.0%, respectively, but the difference was only marginal (RR 1.77 [95% CI 1.00-3.17]; F = 0; P = 0.05) (Table and Figure 5A). However, when we omitted the study conducted by Ensminger, et al.4 (which included the data of the 3F Enable valve), there was no difference between RDAVR and CAVR (RR 1.60 [95% CI 0.80-3.21]; I² = 0; P = 0.18), regardless of the valve type (Supplemental Table V and Supplemental Figure 4A).

Only three studies conducted in patients who underwent lone AVR2,14,17 compared the implanted valve size between the two groups. The RDAVR group used significantly larger valves with a mean size of 23.5 ± 2.0 mm, whereas the mean valve size in the CAVR group was 22.8 ± 1.9 mm (MD 0.70 [95% CI 0.33-1.07]; F = 66%; P = 0.0002) (Figure 5B and Supplemental Figure 4B)
mean pressure gradient of the RDA VR group was significantly lower than that of the CA VR group (10.5 ± 5.7 mmHg versus 12.9 ± 5.7 mmHg; MD −1.93 [95% CI −3.58 to −0.28]; I² = 88%; P = 0.02) (Figure 5C and Supplemental Figure 4C).

**Discussion**

The major findings were as follows: (1) The hospital and 1-year survival were comparable between RDAVR and CAVR; (2) RDAVR significantly reduced both ACC time and CPB time, but did not change the ICU and in-hospital LOS compared with CA VR; (3) the occurrence of POAF and blood transfusion amount were decreased in the RDA VR group, especially among the A VR + CABG subgroup, but we witnessed an increase in PPM in the RDA VR group; (4) RDAVR was associated with a larger valve size and lower mean transvalvular gradient; and (5)

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**Figure 3.** Forest plot of studies assessing the effect of rapid deployment aortic valve replacement (RDAVR) and conventional aortic valve replacement (CAVR) on aortic cross-clamp time (A) and cardiopulmonary bypass time (B). CI indicates confidence interval; df, degree of freedom; SD, standard deviation; and IV, inverse variance.
PVL occurrence was similar between RDAVR and CAVR, especially for current commercialized valves.

It is well established that a prolonged ACC time was an independent predictor of hospital mortality and morbidity.\(^2\) Our meta-analysis reaffirms the advantage of RDAVR in shortening the ACC time by 21.9 minutes. This might be explained by the enrollment of low to moderate risk patients RDA VR group. Compared with CA VR, compression of red blood cells, Unit 824 1.6 ± 1.9 3.0 ± 3.8 −1.54 (−2.22, −0.86) 69 < 0.001

Lone AVR 1 342 1.4 ± 1.7 2.4 ± 2.7 −1.00 (−1.48, −0.52) \(p < 0.001\)

AVR + CABG 3 482 3.8 ± 2.3 7.0 ± 8.5 −1.83 (−2.44, −1.19) 32 < 0.001

POAF, % 8 3065 9.9 15.6 0.83 (0.69, 0.99) 48 0.04

Lone AVR 3 2368 6.9 7.2 0.95 (0.72, 1.26) 29 0.74

AVR + CABG 5 697 23.7 38.0 0.73 (0.58, 0.92) 57 0.01

Stroke/TIA, % 12 4286 2.9 2.4 1.16 (0.80, 1.69) 0 0.43

Lone AVR 7 3621 2.8 1.9 1.39 (0.91, 2.13) 5 0.13

AVR + CABG 5 665 2.9 4.5 0.58 (0.24, 1.37) 0 0.21

AF, % 8 3549 4.5 6.1 1.15 (0.65-2.05) 65 0.63

Lone AVR 5 3098 3.0 3.9 0.96 (0.39, 2.32) 65 0.92

AVR + CABG 3 451 23.9 16.7 1.57 (1.07, 2.29) 0 0.02

MI, % 6 2976 0.4 0.5 0.92 (0.36-2.39) 0 0.87

Lone AVR 4 2524 0.4 0.5 1.02 (0.35, 2.97) 0 0.97

AVR + CABG 3 482 3.8 ± 2.3 7.0 ± 8.5 −1.83 (−2.44, −1.19) 32 < 0.001

AVR + CABG 1 236 13.0 ± 5.0 13.0 ± 6.0 0.00 (−1.55, 1.55) \(p < 0.001\)

Lone AVR 3 2368 6.9 7.2 0.95 (0.72, 1.26) 29 0.74

AVR + CABG 5 697 23.7 38.0 0.73 (0.58, 0.92) 57 0.01

PVL, % 10 3773 1.6 1.0 1.77 (1.00, 3.17) 0 0.05

Lone AVR 6 3158 1.5 0.7 2.01 (1.01, 3.99) 0 0.05

AVR + CABG 4 615 2.3 2.2 1.27 (0.43, 3.75) 0 0.66

Valve size, mm 3 1000 23.5 ± 2.0 22.8 ± 1.9 0.70 (0.33, 1.07) 66 < 0.001

Lone AVR 3 1000 23.5 ± 2.0 22.8 ± 1.9 0.70 (0.33, 1.07) 66 < 0.001

Pressure gradient, mmHg 6 1267 10.5 ± 5.7 13.4 ± 5.5 −1.93 (−3.58, −0.28) 88 0.02

Lone AVR 5 1031 10.2 ± 5.7 13.7 ± 5.2 −2.31 (−4.10, −0.53) 88 0.01

AVR + CABG 1 236 13.0 ± 5.0 13.0 ± 6.0 0.00 (−1.55, 1.55) \(p < 0.001\)

AKF indicates acute kidney failure; CAVR, conventional aortic valve replacement; MD, mean difference; MI, myocardial infarction; POAF, post-operative atrial fibrillation; PPM, permanent pacemaker implantation; PVL, paravalvular leakage; RBCs, red blood cells; RDAVR, rapid deployment aortic valve replacement; RR, risk ratio; and TIA, transient ischemic attack.

Another concern of RDA VR is PVL. PVL occurring in RDAVR is partially due to inadequate sizing and positioning.\(^8\) Additionally, the way of placing the prosthesis, i.e., by suturing the sewing ring into the native annulus or relying on the intra-annular radial force, may also play a role in PVL incidence.
Figure 4. Forest plot of studies assessing the effect of rapid deployment aortic valve replacement (RDAVR) and conventional aortic valve replacement (CAVR) on permanent pacemaker implantation (A), units of RBC transfusion (B), and postoperative atrial fibrillation (C). CI indicates confidence interval; df, degree of freedom; SD, standard deviation; IV, inverse variance; and M–H, Mantel-Haenszel.
Figure 5. Forest plot of studies assessing the effect of rapid deployment aortic valve replacement (RDAVR) and conventional aortic valve replacement (CAVR) on paravalvular leakage (A), valve size (B), and mean pressure gradient (C). CI indicates confidence interval; df, degree of freedom; SD, standard deviation; IV, inverse variance; and M-H, Mantel-Haenszel.

### A

**Study or Subgroup** | **RDAVR** | **CAVR** | **Weight** | **Risk Ratio** | **Risk Ratio**
--- | --- | --- | --- | --- | ---
|  | Events | Total | Events | Total | M-H, Fixed, 95% CI | M-H, Fixed, 95% CI |
| Ione AVR | 1 | 46 | 1 | 48 | 2.9% | 5.6% | 1.04 [0.67, 1.62] |
| Bruno et al., 2016 | 1 | 30 | 0 | 30 | 2.9% | 3.00 [0.13, 70.83] |
| Daen et al., 2016 | 4 | 171 | 4 | 171 | 22.9% | 1.00 [0.25, 3.93] |
| Ensinniger et al., 2018 | 11 | 1021 | 5 | 1021 | 28.6% | 3.20 [0.77, 12.51] |
| Munneretto et al., 2015 | 4 | 204 | 1 | 204 | 5.7% | 0.90 [0.45, 1.83] |
| Waylens et al., 2018 | 2 | 106 | 0 | 106 | 2.9% | 5.00 [0.24, 102.92] |
| **Subtotal (95% CI)** | 1578 | 1580 | 68.5% | 2.01 [0.10, 2.99] |
| **Total events** | 23 | 11 |
| Heterogeneity: Chi² = 2.04; df = 5 (P = 0.84); I² = 0%
Test for overall effect: Z = 1.98 (P = 0.05) |

**AVR+CABG**

| Study or Subgroup | **RDAVR** | **CAVR** | **Weight** | **Risk Ratio** | **Risk Ratio** |
| --- | --- | --- | --- | --- | --- |
| Forcillo et al., 2016 | 0 | 65 | 0 | 130 | Not estimable |
| Nguyen et al., 2018 | 3 | 59 | 8 | 177 | 22.9% | 1.13 [0.31, 4.10] |
| Pollari et al., 2014 | 1 | 82 | 1 | 82 | 5.7% | 1.00 [0.06, 15.72] |
| Thiruvilvan et al., 2018 | 1 | 10 | 0 | 10 | 2.9% | 3.00 [0.14, 65.90] |
| **Subtotal (95% CI)** | 216 | 399 | 31.5% | 1.27 [0.43, 3.75] |
| **Total events** | 5 | 9 |
| Heterogeneity: Chi² = 0.36; df = 2 (P = 0.84); I² = 0%
Test for overall effect: Z = 0.44 (P = 0.66) |

**Total (95% CI)** | 1794 | 1979 | 100.0% | 1.77 [1.00, 3.17] |
| **Total events** | 28 | 20 |
| Heterogeneity: Chi² = 2.82; df = 8 (P = 0.95); I² = 0%
Test for overall effect: Z = 1.94 (P = 0.05) |
| Test for subgroup differences: Chi² = 0.48; df = 1 (P = 0.49); I² = 0% |

### B

**Study or Subgroup** | **RDAVR** | **CAVR** | **Weight** | **Mean Difference** |
--- | --- | --- | --- | --- |
|  | Mean | SD | Total | Mean | SD | Total | Mean, Random, 95% CI | Mean, Random, 95% CI |
| Ione AVR |  |  |  |  |  |  |  |  |
| Gilmanov et al., 2014 | 24.2 | 1.5 | 133 | 23.3 | 1.9 | 133 | 0.90 [0.49, 1.31] |
| Munneretto et al., 2015 | 23.3 | 2.7 | 204 | 22.4 | 2 | 204 | 28.4% | 0.90 [0.44, 1.86] |
| Rahman et al., 2018 | 23.2 | 0.8 | 163 | 22.8 | 1.5 | 163 | 40.5% | 0.00 [0.14, 0.66] |
| **Subtotal (95% CI)** | 500 | 0 | 500 | 100.0% | 0.70 [0.38, 1.07] |
| **Heterogeneity:** Tau² = 0.07; Chi² = 5.92, df = 2 (P = 0.05); I² = 66%
Test for overall effect: Z = 3.70 (P = 0.0003) |
| **Total (95% CI)** | 500 | 0 | 500 | 100.0% | 0.70 [0.33, 1.07] |
| **Heterogeneity:** Tau² = 0.07; Chi² = 5.92, df = 2 (P = 0.05); I² = 66%
Test for overall effect: Z = 3.70 (P = 0.0003) |
| Test for subgroup differences: Not applicable |

### C

**Study or Subgroup** | **RDAVR** | **CAVR** | **Weight** | **Mean Difference** |
--- | --- | --- | --- | --- |
|  | Mean | SD | Total | Mean | SD | Total | Mean, Random, 95% CI | Mean, Random, 95% CI |
| Ione AVR |  |  |  |  |  |  |  |  |
| Berger et al., 2016 | 10.3 | 5.4 | 46 | 10.4 | 3.4 | 48 | 15.5% | -0.50 [-2.22, 1.22] |
| Bruno et al., 2016 | 10.9 | 3.5 | 30 | 12.1 | 2.6 | 30 | 16.6% | -1.49 [-2.90, 0.10] |
| U'Onofrio et al., 2014 | 11.4 | 4.4 | 41 | 16.5 | 5.8 | 112 | 16.8% | -5.40 [-10.21, 0.41] |
| Munneretto et al., 2015 | 10.8 | 6.8 | 204 | 11.4 | 6 | 204 | 17.3% | -0.60 [-1.84, 0.64] |
| Rahman et al., 2018 | 9.2 | 4.9 | 163 | 12.8 | 4.8 | 165 | 17.8% | -3.60 [-5.84, -2.35] |
| **Subtotal (95% CI)** | 474 | 0 | 557 | 83.6% | -2.31 [-4.13, -0.50] |
| **Heterogeneity:** Tau² = 3.58; Chi² = 32.21, df = 4 (P < 0.00001); I² = 88%
Test for overall effect: Z = 2.55 (P = 0.01) |
| **AVR+CABG** |  |  |  |  |  |  |  |  |
| Nguyen et al., 2018 | 13 | 5 | 59 | 13 | 6 | 177 | 16.4% | 0.00 [-1.55, 1.55] |
| **Subtotal (95% CI)** | 59 | 0 | 177 | 16.4% | 0.00 [-1.55, 1.55] |
| Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00) |
| **Total (95% CI)** | 533 | 0 | 734 | 100.0% | -1.93 [-3.58, -0.28] |
| **Heterogeneity:** Tau² = 3.69; Chi² = 40.34, df = 5 (P < 0.00001); I² = 88%
Test for overall effect: Z = 2.50 (P = 0.02) |
| Test for subgroup differences: Chi² = 1.69, df = 1 (P = 0.5), I² = 72.9%
Test for overall effect: Z = 2.50 (P = 0.02) |
role in the difference of PVL occurrence in RDAVR and CAVR.\(^2\) Also, inadequate decalcification of the aortic annulus during RDV implantation may cause an uneven surface and resulted in PVL.\(^3\) In the current meta-analysis, the frequency of PVL in the RDAVR and CAVR groups was 1.6% and 1.0%, respectively, which was only marginal. Further subgroup analysis indicated that increased PVL occurrence in the RDAVR group might be attributed to the 3F Enable valves. Additionally, as Martinez-Comendador, et al. concluded, the occurrence of PVL has been decreasing over the years after a short learning curve.\(^2\)

Importantly, our meta-analysis determined that the 1-year mortality tends to be lower in the RDAVR group, although the difference is not statistically significant. Further interpretation of this 1-year mortality result was hampered by the limited data and compliance during follow-up. The shortcomings of RDAVR including increased PPM implantation may dilute the merits of less POAF and hemodynamic advantages. The ongoing European Aortic Valve Registry trial,\(^3\) a prospective and multicenter study designed with a minimum of 5 years of follow-up, might give us the answer to the long-term safety of RDAVR.

CAVR is still the golden standard for treating severe AS. Yet it still faces many challenges in clinical practice. For patients with severe calcification involving the annulus, aortic wall, and even the myocardium, RDAVR needs few sutures or even no suture, which may reduce the risk of aortic root bleeding. In addition, for patients with small aortic annulus, prosthesis mismatch is prone to occur after CAVR. RDAVR had improved hemodynamic performance, which would avoid additional procedures such as aortic root enlargement. One of the concerns in minimally invasive surgery has been the longer ACC time and CPB time, particularly when using a right anterior mini thoracotomy approach. Therefore, RDAVR may be an alternative for patients with the aforementioned situations. However, there is no best technology for all patients, but only most suitable for certain individuals. Comprehensive assessment of the patient’s age, valve calcification, annulus size, cardiac function, surgical tolerance, combined underlying diseases, prosthesis selection willingness, insurance costs, etc., is needed to maximize patient’s benefits.

The limitations of our study include the following: (1) our study included 13 propensity score-matched NRS with different matching strategies. (2) The potential publication bias favoring the new technique RDAVR may also have negatively impacted the results of our review. (3) Some included articles reported data as median and interquartile range, and the transformation of the median in mean can generate bias. Fixed-effect model was used for I\(^2\) < 50%, which may still overestimate the difference. And the inclusion of limited number of studies in subgroup analyses may lead to inaccurate results. (4) It was a pity that we could not wipe out the effect of surgical approach, especially on POAF and RBC transfusion, because most of the include papers did not stratify subjects according to surgical approach. (5) We found that RDAVR was associated with a larger valve size. However, Perceval S is an intermediate size, which may compromise this result.

In summary, the perioperative mortality of RDAVR is comparable with that of CAVR, but its 1-year mortality tends to be better than that of CAVR but did not reach the statistical significance. Despite the increased PPM rate, RDAVR is associated with a lower occurrence of POAF and blood transfusion and improved hemodynamic results. Currently commercialized valves do not increase the occurrence of PVL. These facts make it a good option for high-risk subset patients or minimally invasive surgeries. Future RCTs with long-term follow-up are warranted to prove the durability of the valve and emphasize its potential benefit in reducing late mortality.

**Disclosure**

**Conflicts of interest:** None.

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**Supplemental Files**

Supplemental Text
Supplemental Figures 1-4
Supplemental Tables 1-V
Please see supplemental files; https://doi.org/10.1536/ihj.19-717