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# Sutureless vs. rapid-deployment valve: a systemic review and meta-analysis for a direct comparison of intraoperative performance and clinical outcomes

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**Background:** Sutureless and rapid-deployment valves are bioprostheses anchoring within the aortic annulus with few sutures, and they act as a hybrid of conventional surgical and transcatheter valves under aortic valve replacement. Considering that the 3F Enable valve is now off-market, the only two sutureless and rapid-deployment valves available on the world marketplace are the Perceval and Intuity valves. However, a direct comparison of the function of these two valves eludes researchers.

**Purpose:** Against this background, we performed this systematic review and metaanalysis comparing the intraoperative performance and early clinical outcomes between the Perceval valve and the Intuity valve under sutureless and rapiddeployment aortic valve replacement.

**Methods:** We systematically searched electronic databases through PubMed/ MEDLINE, OvidWeb, Web of Science, and Cochrane Central Register of Controlled Trials (from the establishment of the database to November 17, 2022, without language restriction) for studies comparing the sutureless valve (the Perceval) and the rapid-deployment valve (the Intuity) under aortic valve replacement. Our primary outcomes were early mortality and postoperative transvalvular pressure gradients. The secondary outcomes were defined to include aortic cross-clamp and cardiopulmonary bypass time, paravalvular leak (any paravalvular leak, moderate-to-severe paravalvular leak) after aortic valve replacement, need for pacemaker implantation, postoperative neurological events (stroke), and intensive care unit stay.

**Results:** This meta-analysis included ten non-randomized trials with 3,526 patients enrolled (sutureless group = 1,772 and rapid-deployment group = 1,754). Quality assessments were performed, with the mean scores of the studies reading 6.90 (SD = 0.99) out of 9 according to the Newcastle–Ottawa Scale. Compared with rapid-deployment aortic valve replacement, sutureless aortic valve replacement was associated with higher mean and peak transvalvular pressure gradients postoperatively. In contrast, aortic valve replacement vs. rapid-deployment aortic valve replacement. There was no evidence of significant publication bias observed by the funnel plot and Egger's test.

**Conclusions:** For postoperative hemodynamics, sutureless aortic valve replacement was associated with increased mean and peak transvalvular pressure gradients compared with rapid-deployment aortic valve replacement. In sharp contrast, sutureless aortic valve replacement significantly reduced the amount of time needed for fixing the aortic cross-clamp and the cardiopulmonary bypass procedure.

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KEYWORDS

Perceval, Intuity elite, aortic valve replacement, pressure gradient, CPB (cardiopulmonary bypass), aortic cross clamp

## Introduction

Aortic stenosis (AS) will become one of the most common valvular heart diseases as the population ages and life expectancy increases (1). Surgical aortic valve replacement (SAVR) is always considered the golden standard for treating AS (2). However, considering the high surgical risks involved, more than 30% of patients with severely symptomatic AS do not undergo surgery in clinical practice. Transcatheter aortic valve implantation (TAVI) has become an effective alternative established for the purpose of providing less-invasive treatment. Nevertheless, a crucial limitation of TAVI is that it is almost impossible to remove all native valve cusps or a degenerated prosthesis (3–6).

Recently, sutureless and rapid-deployment valves have emerged as prospective substitutes for typical valves (2). These valves are biological prostheses anchoring within the aortic annulus with at most three sutures (7, 8). With sufficient radial force to allow annular implantation without sutures in a sutureless valve and the rapid-deployment valve system providing an innovative extended balloon structure requiring only three sutures for fast deployment, these valves facilitate minimally invasive surgery and complex intervention in annulus decalcification and degenerated valve removal. Evidence from the Sutureless and Rapid-Deployment Aortic Valve Replacement International Registry (SURD-IR) enrolling more than 4,500 patients suggests that SURD-AVR is a secure and efficacious substitute for the conventional aortic valve replacement procedure (7, 9, 10).

Three sutureless and rapid-deployment prosthesis valves have received CONFORMITE EUROPEENNE (CE) market approval: the Perceval S, the Intuity, and the 3f Enable. , The 3f Enable valve was recalled in 2014 most probably because of elevated migration risks (8). Sutureless valve Perceval and rapiddeployment valve Intuity are the only two representatives of valves in SURD-AVR, both of which function well in sutureless and rapiddeployment aortic implantation by reducing aortic cross-clamp and cardiopulmonary bypass time and delivering excellent hemodynamic results (10, 11). At the same time, a previous study demonstrated that SURD-AVR was associated with an increased rate of pacemaker implantation postoperatively compared with SAVR (12). However, there are limited published data directly comparing both promising devices, and most of these data are only observational and retrospective studies rather than randomized controlled trials or only small sample studies riddled with deficiencies. In this study, we performed a systematic review and metaanalysis to evaluate the intraoperative performance and early clinical outcomes between the sutureless and the rapiddeployment aortic valve replacement methods.

## Methods

#### Data source and search strategy

We searched Pubmed/Medline, Ovidweb, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) for relevant articles, from the date of establishment of the database to November 17, 2022, in all languages, using a combination of main terms and MeSH terms such as "aortic valve[MeSH terms]" or "heart valve prosthesis[MeSH terms]" or "aortic valve replacement" or "aortic valve implantation" and "sutureless" or "Perceval" and "rapid deployment" or "Intuity". Next, we performed a search for additional sources of information for the literature supplement, including Google Scholar and abstracts/ presentations from major international cardiovascular-relevant conferences. Finally, the reference lists of relevant works of literature were also checked for the supplement. The complete retrieval strategy is presented in **Supplementary Table S1**.

#### Study selection and data extraction

Two investigators (CW and YX) independently performed the study selection on the basis of predetermined selection criteria. Any discrepancy among the investigators was resolved by a third investigator (JH). After removing duplicates, we performed selection through two levels: the title and abstract of each searched study were screened for relevance as part of the first level, and a full-text analysis of the remaining studies was done for inclusion as the second level. Studies were considered eligible for inclusion in our systematic review and meta-analysis if they fulfilled the following criteria: (1) enrolled patients undergoing aortic valve replacement and who used both sutureless and rapid-deployment valves; (2) those who reported at least one primary outcome, defined as early mortality (30-day all-cause mortality and in-hospital mortality) and postoperative transvalvular pressure gradients (mean/peak); (3) the sample size of each group should be more than 10; (4) there should be no duplicated population figures across studies. Without any restrictions as full texts, abstract reports from important conferences that met the inclusion criteria were also considered in our study.

Using standardized data collection sheets that recorded essential items, we extracted the following data from each included study: study characteristics [publication characteristics (authors, publication year), study era, study country, study design, statistical analysis adjustment, study population], patient characteristics [age, sex, body surface area, body mass index, EuroScoreII, surgical approach (proportion of the minimally invasive approach), proportion of isolated AVR], and outcomes (primary outcomes: early mortality, transvalvular pressure gradients; secondary outcomes: aortic cross-clamp time, cardiopulmonary bypass time, paravalvular leak, pacemaker implantation, stroke, ICU stay). Data extraction was performed by two investigators (CW and YX), and discrepancies were resolved by a third investigator (JH).

#### Quality assessment

We assessed the overall study quality using NEWCASTLE-OTTAWA SCALE (NOS) for observational studies (13), based on the three domains: selection of participators, comparability between study groups, and outcomes. Each study in this rating system (with a maximum of 9 stars) can receive up to 1 star for each numbered entry in the Selection and Outcome categories and up to 2 stars for the majority of entries in the Comparability category. A score of 9 stars received in the study indicates a low risk of bias, and a study that receives 8 or 7 stars is assessed as having a moderate risk of bias. In contrast, an assigned score of 6 or less indicates a high risk of bias.

### Outcomes

The primary outcomes of interest in the study were early mortality and transvalvular pressure gradients of the aortic valve after AVR. Early mortality was defined as 30-day all-cause mortality and in-hospital mortality. Transvalvular pressure gradients included mean transvalvular pressure gradients and peak transvalvular pressure gradients. The secondary outcomes of interest included ACC and CPB time, paravalvular leak (any paravalvular leak, moderate-to-severe paravalvular leak) after AVR, the need for pacemaker implantation, postoperative neurological events (stroke), and ICU stay.

### Statistical analysis

For continuous outcomes (transvalvular pressure gradients, aortic cross-clamp time, cardiopulmonary bypass time, and ICU stay), results were presented as the mean difference (MD) with a 95% confidence interval (CI) using an Inverse Variance fixed

effect model, followed by real events, significance for effect estimate (*p*-value),  $I^2$  statistic, and Q statistic. We estimated the mean values and standard deviations using the formula if studies reported only the median and interquartile/overall range (14). The results of dichotomous outcomes (early mortality, paravalvular leak, pacemaker implantation, and stroke) were presented as the odds ratio (OR) with a 95% confidence interval (CI) using the Mantel-Haenszel fixed effect model. Total events, significance for effect estimate (*p*-value),  $I^2$  statistic, and Q statistic were also presented in pooling. When a moderate-tohigh heterogeneity was discovered in the trial, the random effects model with the Inverse Variance or Mantel-Haenszel method was used in continuous or dichotomous outcomes, respectively. Operative time, including the aortic cross-clamp time and cardiopulmonary time, were pooled and presented in minutes, whereas ICU stay was presented in days. The magnitude of the statistical heterogeneity between studies was assessed using the Higgins  $I^2$  test, with rates of 25%, 50%, and 75% being indicative of low, moderate, and high heterogeneity, respectively (15). Furthermore, Cochran's Q statistic was used to assess the heterogeneity between the studies. We performed the leave-oneout sensitivity analysis to explore potential sources of heterogeneity by removing individual studies each time. Subgroup analysis was also performed to further stratify outcomes. We visually assessed potential publication bias by considering the asymmetry in the funnel plots of the effect size of each estimate against the standard error. A formal calculation of the possibility of publication bias was done by using Egger's test, which defines publication bias as significant if p < 0.1 (16). All study analyses were performed using Stata 16.0 (StataCorp LLC) and Review Manager Version 5.4.1 (The Cochrane Collaboration).

## **Results**

## Study search

Our initial systematic electronic literature yielded 1,015 articles. After removing 374 duplicates, 771 articles were screened at the title/abstract level. Among these articles, 743 publications were excluded, which did not fulfill the selection criteria based on the title and abstract. With 28 articles remaining and assessed for eligibility, 10 publications were deemed eligible and included in the meta-analysis (**Figure 1**) (11, 17–25).

# Study characteristics and patient populations

The included 10 studies, nine full-text studies and one abstract with integral statistical reports, were all non-randomized studies (NRSs). Because there were three studies from the same registry, another two were used only to report supplementary data (19, 21). All studies covered 3,526 patients (sutureless group = 1,772 and rapid-deployment group = 1,754). Among these studies, propensity score matching was used in five studies (11, 17, 20,



24, 25), whereas in one study, the multivariable analysis method was used for determining early mortality in risk factor analysis (Table 1) (21). A larger proportion of male patients were

enrolled in the rapid-deployment group. The mean age of patients in all studies ranged from 70 to 83 years, with most of them in their 70s (Table 2). Six studies reported about the body

#### TABLE 1 Study characteristics.

Study (author, year)	Study	Country	Study	Statistical analysis		Study popula	ation
	era		design	adjustment	Total	SU (Perceval)	RD (Intuity)
Paolo Berretta et al., 2022 (isolated SURD-AVR) <sup>a</sup>	2007-2019	Multinational <sup>b</sup>	NRS	PSM	1,646	823	823
Paolo Berretta et al., 2022 (combined SURD-AVR) <sup>a</sup>	2007-2019	Multinational <sup>b</sup>	NRS	PSM	934	467	467
Liakopoulos et al., 2021	2012-2019	Germany	NRS	PSM	214	107	107
Martin Hartrumpf et al., 2020	2012-2017	Germany	NRS	None	119	80	39
Max Gotzmann et al., 2020	2016-2017	Germany	NRS	None	54	21	33
Augusto D'Onofrio et al., 2020	2011-2017	Italy	NRS	PSM	234	117	117
Paolo Berretta et al., 2019 <sup>c</sup>	2007-2018	Multinational <sup>b</sup>	NRS	MVA <sup>d</sup>	1,418	1,011	407
Di Eusanio et al., 2018 <sup>c</sup>	2007-2017	Multinational <sup>b</sup>	NRS	None	3,218	2,461	757
Stephan Ensminger et al., 2018	2011-2015	Germany	NRS	PSM	204	102	102
Federica Jiritano et al., 2016	2013-2015	Italy	NRS	None	43	16	27
Nguyen et al., 2015	2011-2015	Canada	NRS	PSM	78	39	39

SURD-AVR, sutureless and rapid-deployment aortic valve replacement; SU, sutureless; RD, rapid-deployment; NRS, non-randomized study; PSM, propensity score matching; MVA, multivariable analysis.

<sup>a</sup>According to the studies, two sets of data were reported.

<sup>b</sup>From Sutureless and Rapid Deployment Aortic Valve Replacement International Registry (SURD-IR): Australia, Austria, Belgium, Canada, France, Germany, Italy, and Switzerland.

<sup>c</sup>Because this study was from the same registry as the study by Berretta et al. in 2021, it was only used to report data pertaining to pressure gradients, cardiopulmonary bypass time, and aortic cross-clamp time of patients overall, which were not reported in the study by Berretta et al. in 2021.

<sup>d</sup>The MVA was performed in risk factor analysis for determining early mortality.

surface area in each group, with the rapid-deployment group having a statistically significant higher index (11, 18, 21, 22, 24, 25). One study reported data by dividing isolated AVR patients and combined AVR patients into two separate cohorts, which led us to perform a statistical analysis of these cohorts (25). All studies provided data on early mortality or transvalvular pressure gradients as primary outcomes, whereas specific secondary outcomes were unavailable in every study.

## Quality assessment

The methodological quality of each study varied, and the mean scores of the studies were 6.90 (SD = 0.99) out of 9 according to the Newcastle–Ottawa Scale (NOS), representing the included studies as moderate-to-high quality. A detailed quality assessment is presented in **Supplementary Table S2**.

#### Early mortality

All included studies reported early mortality, defined as 30-day all-cause mortality in five studies (11, 17, 18, 22, 24) and inhospital mortality in another three studies (20, 23, 25), respectively. Effect sizes were expressed by ORs, whereas ORs were not calculated in one study because the early mortality in both groups was 0 (18). The calculated overall early mortality rate was 2.3%, being 2.5% in patients receiving Perceval valve implantation and 2.1% in those who underwent Intuity valve implantation (p = 0.31). The SU group showed no statistically significant difference in early mortality rates compared with the RD group (8 studies and 3,526 patients, OR: 1.26; 95% CI: 0.81– 1.96; p = 0.31;  $I^2 = 0\%$ , Figure 2). No significant publication bias was observed, which was assessed by considering the asymmetry in the funnel plot visually and formally by using Egger's regression test (p = 0.5190, Supplementary Figure S5A). Finally, a sensitivity analysis was used to examine the influence of each study on the OR by excluding one individual study at one time. The exclusion of each study did not significantly change the pooled OR, and the estimates for each case were within the overall 95% confidence interval.

## Transvalvular pressure gradients

#### Mean transvalvular pressure gradients

Overall, the patients' mean transvalvular pressure gradients were presented in seven studies (11, 17, 20, 22-25), and five studies reported the mean transvalvular pressure gradients in each size of both valve types (11, 19, 22-24). The pooled analysis from seven studies covering 3,483 patients demonstrated that the SU group was associated with statistically significant higher mean transvalvular pressure gradients in patients overall, compared with the RD group (MD: 2.93; 95% CI: 2.19–3.67; *p* < 0.00001;  $I^2 = 65\%$ , Figure 3A). Next, we performed subgroup analyses by matching the sizes of the Perceval and Intuity valves to further explore the relationship between valve size and transvalvular pressure gradients and make a hierarchical contrast between the two types of valves. Subgroup 1 compared SU with RD valve sizes under radical matching by small with 21 mm, medium with 23 mm, large with 25 mm, and extralarge with 27 mm, whereas subgroup 2 compared SU with RD valve sizes under conservative matching by small with 19 mm, medium with 21 mm, large with 23 mm, and extralarge with 25 mm. Subgroup analyses

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TABLE 2 Patient characteristics.

Study (author, year)	Age (year)	year)	Male (%)	(%)	BSA (m <sup>2</sup> )	m <sup>2</sup> )	BMI (kg/m <sup>2</sup> )	g/m²)	EuroScore II (%)	e II (%)	Minimally invasive approach (%)	invasive h (%)	Isolated AVR (%)	VR (%)
	SU	RD	SU SU	RD . :	SU SU	RD	SU SU	RD : ;	sU SU	RD	SU SU	RD	sU SU	RD
	(Perceval)	(Intuity)	(Perceval)	(Intuity)	(Perceval)	(Intuity)	(Perceval)	(Intuity)	(Perceval)	(Intuity)	(Perceval)	(Intuity)	(Perceval)	(Intuity)
Paolo Berretta et al., 2022 (isolated SURD-AVR)	75.4 ± 7.3	$74.8 \pm 7.3$	42.5	45.3	$1.81\pm0.17$	$1.84\pm0.19$	$27.6 \pm 4.7$	$27.9 \pm 4.9$	$7.8 \pm 4.6^{a}$	$7.1 \pm 5.3^{a}$	74.6	80.1	63.8	63.8
Paolo Berretta et al., 2022 (combined SURD-AVR)	75.8 ± 7.2	$75.4 \pm 6.2$	52.9	54	$1.82 \pm 0.18$	$1.85 \pm 0.19$	$27.5 \pm 4.4$	$27.4 \pm 4.8$	$9.9\pm6.7^{a}$	$9.3 \pm 7.1^{a}$	6.9	5.3	63.8	63.8
Oliver J. Liakopoulose et al., 2021	$74.0 \pm 8.0$	$76.0 \pm 5.0$	38	47	$1.9 \pm 0.2$	$1.9 \pm 0.2$	$28 \pm 5$	28±5	4 ± 5	$4 \pm 3$	28	5.6	42	40
Martin Hartrumpf et al, 2020	72.3 ± 6.5	$72.8 \pm 5.5$	53.8	56.4	I	I	$28.85 \pm 4.80$	28.99 ± 5.30	$6.44 \pm 3.89^{a}$	$11.78 \pm 11.32^{a}$	I	I	75	48.7
Max Gotzmann et al., 2020	$75.5 \pm 6.6$	$71.7 \pm 7.9$	61.9	81.8	$1.90\pm0.15$	$1.94\pm0.21$	$28.14\pm4.55$	$27.85\pm4.62$	$4.52\pm4.44$	$5.21\pm5.56$	I	I	47.6	0
Augusto D'Onofrio et al., 2020	78.33 ± 6.70	77.97 ± 5.37	38.5	39.3	$1.75 \pm 0.19^{b}$	$1.78 \pm 0.18^{\mathrm{b}}$	$27.5 \pm 4.9^{b}$	$26.5 \pm 4.2^{b}$	$3.98 \pm 3.06$	$3.95 \pm 2.98$	27.4	20.5	51.3	46.2
Paolo Berretta et al., 2019	$76.7 \pm 6.5$	73.8 ± 7.8	32.6	46.9	$1.83\pm0.2$	$1.86\pm0.2$	$27.5 \pm 5$	$27.4 \pm 5.2$	$9.4\pm6.5^{a}$	$6.8 \pm 4.9^{a}$	46.6	80.8	100	100
Di Eusanio et al., 2018	$76.8 \pm 6.7$	41.1	I	I	$27.4 \pm 4.8$	$11.3 \pm 9.7$	45.8	70.7						
Stephan Ensminger et al., 2018	74. 649 ± 5.2	41.1	I	I	$27.4 \pm 5.3$	$27.7 \pm 4.5$	$2.2 \pm 1.3^{a}$	33.3	30.4	68.6	71.6			
Federica Jiritano et al., 2016	75.94 ± 7.07	73.37 ± 6.79	62.5	66.7	$1.77 \pm 0.19$	$1.88 \pm 0.24$	I	I	$9.26 \pm 4.49$	$11.63 \pm 4.15$	I	I	100	100
Nguyen et al., 2015	$83 \pm 2$	70 ± 7.6	I	I	I	I	I	1	$4.7 \pm 4.2$	$2.5 \pm 1.8$	I	I	I	I
AVR, aortic valve replacement; SU, sutureless; RD, rapid-deployment; BSA, body surface area; BMI, body mass index	nt; SU, sutureles	s; RD, rapid-de	eployment; BSA	, body surface	area; BMI, bod	y mass index.								

AVR, aortic valve replacement; SU, sutureless; RD, rapid-dep Values are presented as mean <u>±</u> standard deviation. <sup>a</sup>Logistic EuroScore. <sup>b</sup>Data before propensity-score matching (PSM).

Study or Subaroup	Events	Total	Events	Total	Weight	M-H. Fixed, 95% CI Y	(ear	M-H, Fixed, 95% CI	
Paolo Berretta et al, 2022 (combined SURD-AVR)	21	467	16	467	43.1%	1.33 [0.68, 2.58] 2			
Paolo Berretta et al, 2022 (isolated SURD-AVR)	13	823	.0	823	22.2%	1.64 [0.67, 3.97] 2		_ <b>_</b>	
Oliver J. Liakopoulos et al, 2021	4	107	3	107	8.1%	1.35 [0.29, 6.16] 2		<b>-</b>	
Augusto D'Onofrio et al, 2020	2	117	4	117	11.1%	0.49 [0.09, 2.74] 2			
Martin Hartrumpf et al, 2020	1	80	1	39	3.7%	0.48 [0.03, 7.90] 2			
Max Gotzmann et al, 2020	1	21	3	33	6.3%	0.50 [0.05, 5.15] 2			
Stephan Ensminger et al, 2018	0	102	1	102	4.2%	0.33 [0.01, 8.20] 2			
Federica Jiritano et al, 2016	0	16	0	27		Not estimable 2	016		
A Nguyen et al, 2015	3	39	0	39	1.3%	7.58 [0.38, 151.72] 2	015		
Total (95% CI)		1772		1754	100.0%	1.26 [0.81, 1.96]		•	
Total events	45		36						
Heterogeneity: Chi <sup>2</sup> = 4.62, df = 7 (P = 0.71); l <sup>2</sup> = 0%							+		
Test for overall effect: Z = 1.03 (P = 0.31)							0.005	0.1 1 10 Favours [SU] Favours [R	200 D]
2									

demonstrated that under radical matching of valve size, the SU group was still associated with statistically significant higher mean transvalvular pressure gradients in each size-matching compared with the RD group (MD: 3.57; 95% CI: 3.20–3.94; p < 0.00001;  $I^2 = 26\%$ , Figure 3B). However, under conservative matching of valve size, it presented a lower mean transvalvular pressure gradient in the S SU valve than the 19 mm RD valve, but it was still significantly higher in the M, L, and XL SU valves than in the 21, 23, and 25 mm RD valves, respectively (MD: 1.68; 95% CI: 0.77–2.58; p = 0.0003;  $I^2 = 74\%$ , Figure 3C). No significant publication bias was observed in patients overall, which was assessed by considering the asymmetry in the funnel plot visually and formally by using Egger's regression test (p = 0.5879, Supplementary Figure S5B).

= 0.31; I<sup>2</sup> = 0%). M-H, Mantel-Haenszel; CI, confidence interval

#### Peak transvalvular pressure gradients

For peak transvalvular pressure gradients, statistical analyses demonstrated the same tendency as the mean transvalvular pressure gradients. Five studies and 3,201 patients were covered in an overall pooled analysis (11, 22-25), which demonstrated that the SU group was associated with statistically significant higher peak transvalvular pressure gradients in patients overall, compared with the RD group (MD: 5.11; 95% CI: 4.45-5.78; p < 0.00001;  $I^2 = 47\%$ , Figure 4A). Subgroup analyses were also performed by small with 21 mm, medium with 23 mm, large with 25 mm, and extralarge with 27 mm as radical matching and small with 19 mm, medium with 21 mm, large with 23 mm, and extralarge with 25 mm as conservative matching. For radical matching, the SU group was associated with statistically significant higher peak transvalvular pressure gradients in each size-matching compared with the RD group (MD: 6.00; 95% CI: 5.34–6.65; p < 0.00001;  $I^2 = 0\%$ , Figure 4B). For conservative matching, the peak pressure gradients in the SU group were still significantly higher in the M, L, and XL SU valves than in the 21, 23, and 25 mm RD valves (MD: 2.86; 95% CI: 1.18-4.55; p = 0.0008;  $I^2 = 82\%$ , Figure 4C). No significant publication bias was observed in patients overall, which was assessed by taking into account the asymmetry in the funnel plot visually and formally by using Egger's regression test (p = 0.8425, **Supplementary** Figure S5C).

#### Secondary outcomes

For secondary outcome studies, extracted estimates were reported in the supplementary material. Overall pooled analyses from isolated AVR patients, combined AVR patients, and AVR patients demonstrated that, compared with the RD group, the SU group was associated with a significantly less aortic cross-clamp time (MD: -10.12; 95% CI: -13.90 to -6.33; p < 0.00001;  $I^2 =$ 94%, Figure 5A), and similarly, with a significantly less cardiopulmonary bypass time (MD: -11.63; 95% CI: -17.14 to -6.13; p < 0.0001;  $I^2 = 94\%$ , Figure 5B). There were no statistically significant differences between the SU group and the RD group for any paravalvular leak (OR: 1.95; 95% CI: 1.01-3.77; p = 0.05;  $I^2 = 75\%$ , Supplementary Figure S1A), paravalvular leak (moderate to severe) (OR: 1.07; 95% CI: 0.61-1.87; p = 0.82;  $I^2 = 0\%$ , Supplementary Figure S1B), pacemaker implantation (OR: 1.16; 95% CI: 0.92–1.47; p = 0.20;  $I^2 = 0\%$ , Supplementary Figure S2), stroke (OR: 1.07; 95% CI: 0.70-1.64; p = 0.75;  $I^2 = 0\%$ , Supplementary Figure S3), and intensive care unit (ICU) stay (MD: -0.03; 95%CI: -0.37 to 0.31; p = 0.87;  $I^2 =$ 75%, Supplementary Figure S4). A visual assessment of the symmetry of the funnel plots suggested that there was no significant publication bias, and a formal assessment by using Egger's test confirmed this point (Supplementary Figure S5).

## Discussion

In this study, we conducted a meta-analysis covering 10 nonrandomized trials and 3,526 patients, highlighting two key findings. First, compared with the RD group, the SU group was associated with statistically significant higher mean and peak transvalvular pressure gradients of the aortic valve. Second, the SU group was associated with an overall decrease of ACC and

				SU		RD			Mean Differ				lean Difference	
Study or Subgroup			Mean	SD To				Weight	IV, Random			IV.	Random, 95% Cl	
Paolo Berretta et al, 2022 (combined SL			14.1 14.5		67 10 23 11			20.4%	3.60 [2.9				- I	
Paolo Berretta et al, 2022 (isolated SUR Oliver J. Liakopoulos et al, 2021	D-AVR)		14.5			.6 5.5 10 5		21.3% 14.7%	2.90 [2.3 2.00 [0.7					
Augusto D'Onofrio et al, 2020			11.84		17 10.4			14.7%	1.37 [0.2					
Martin Hartrumpf et al, 2020			14.8		80 12			5.2%	2.50 [-0.3				<u> </u>	
Max Gotzmann et al, 2020						.0 1.0 79 4.78		3.6%	4.69 [1.0					_
Stephan Ensminger et al, 2018			14.6			.8 4.7		11.1%	4.80 [3.1					
A Nguyen et al, 2015			15.5		39 12			8.0%	3.00 [0.8					
Total (95% CI)				17	56		1727	100.0%	2.93 [2.1	9, 3.67]			•	
Heterogeneity: Tau <sup>2</sup> = 0.59; Chi <sup>2</sup> = 20.03		(P = (	0.005); I								-1	<del>   </del> 10 -5	0 5	10
Test for overall effect: $Z = 7.76$ (P < 0.00	JUU1)											Favou	rs [SU] Favours [RD]	
3														
-		SU			RD				Difference				n Difference	
Study or Subgroup 1.2.1 Small-21	Mean	SD	Total	Mean	SD	Total	Weight	<u>IV, F</u>	ixed, 95% C	I Year		IV, F	ixed, 95% Cl	
Oliver J. Liakopoulos et al, 2021	15	5	12	12	8	29	0.8%	3.00	[-1.06, 7.06]	2021			+	
Martin Hartrumpf et al, 2020		7.8	4	12.1	3.8	9	0.2%		5.86, 21.94]				· · · · · ·	
Max Gotzmann et al, 2020	10	0.7	1	20	4.8	4	0.270		ot estimable					
Augusto D'Onofrio et al, 2020	13	5	15	10.3	4.0 3.2	44	1.8%		[-0.00, 5.40]				<u> </u>	
-	15.1												-	
Di Eusanio 2018 Subtotal (95% CI)	15.1	5.9	317 <b>349</b>	11.8	4	210 <b>296</b>	18.8% <b>21.7%</b>		[2.45, 4.15]	2018				
( )	<b>D</b> - 0 0	01.12				290	21.770	3.34	[2.55, 4.13]				•	
Heterogeneity: $Chi^2 = 6.88$ , df = 3 ( Test for overall effect: Z = 8.31 (P <			= 56%											
1.2.2 Medium-23														
	40		20	10		20	4.00/	2.00	14 00 4 701	0004				
Oliver J. Liakopoulos et al, 2021	13	4	39	10	4	39	4.3%		[1.22, 4.78]					
Max Gotzmann et al, 2020	21.3		3	10.5	4.8	14	0.2%		[1.95, 19.65]					
Augusto D'Onofrio et al, 2020	10.9		40	9.3	3.9	37	3.1%		[-0.49, 3.69]					
Martin Hartrumpf et al, 2020	15.1		15	14.5	10.6	15	0.3%		[-5.91, 7.11]					
Di Eusanio 2018 Subtotal (95% CI)	15	6.1	876 973	11	4.9	242 347	24.7% 32.5%		[3.26, 4.74] [3.00, 4.29]	2018			•	
Heterogeneity: Chi <sup>2</sup> = 8.41, df = 4 (			= 52%											
Test for overall effect: Z = 11.11 (P	< 0.00	001)												
1.2.3 Large-25														
Oliver J. Liakopoulos et al, 2021	12	4	34	8	4	30	3.5%	4.00	[2.04, 5.96]	2021				
Augusto D'Onofrio et al, 2020	11.5	2.8	42	8	3.4	11	2.8%	3.50	[1.32, 5.68]	2020				
Martin Hartrumpf et al, 2020	13.4	6.9	29	10.6	3.8	11	1.2%	2.80	[-0.57, 6.17]	2020			<b>—</b>	
Max Gotzmann et al, 2020	19.2	7.5	9	9.2	4.8	12	0.4%	10.00	4.40, 15.60]	2020				-
Di Eusanio 2018	13.4		906	9.8	4.4	163	23.2%		[2.84, 4.36]					
Subtotal (95% CI)			1020			227	31.1%		[3.04, 4.35]				♦	
Heterogeneity: $Chi^2 = 5.32$ , df = 4 (	P = 0.2	6)· I²							. , .					
Test for overall effect: Z = 11.01 (P			2070											
1.2.4 Xlarge-27														
Oliver J. Liakopoulos et al, 2021	9	3	22	7	4	9	1.6%	2.00	[-0.90, 4.90]	2021			+	
Max Gotzmann et al, 2020		7.5	8	7.5	4.8	2	0.2%		6.14, 10.74]					
Augusto D'Onofrio et al, 2020		3.7	20	8.4	3.8	6	1.1%	-	[-2.05, 4.85]				<b></b>	
Martin Hartrumpf et al, 2020	14.3		32	9.8	6.5	4	0.3%		2.29, 11.29]					
•						4 59			-					
Di Eusanio 2018	12.2	J.J	257	8.3	3.4		11.5%		[2.82, 4.98]	2018			•	
Subtotal (95% CI)	D - 0 -	01.10	339			80	14.7%	5.49	[2.53, 4.45]				▼	
Heterogeneity: $Chi^2 = 3.14$ , $df = 4$ ( Test for overall effect: $Z = 7.15$ (P <			= 0%											
Total (95% CI)		,	2681			050	100 00/	2 57	13 20 2 041				•	
( )	0 /			0/		930	100.0%	3.57	[3.20, 3.94]		_			
Heterogeneity: $Chi^2 = 24.30$ , df = 18			ı² = 26	%							-20	-10	0 10	20
Test for overall effect: $Z = 19.09$ (P			- 11-										SU] Favours [RD]	
Test for subaroup differences: Chi <sup>2</sup>	= 0.54	df =	3 (P =	0.91). l <sup>a</sup>	² = 0%									

Mean difference (MD) of mean transvalvular pressure gradients (mmHg) in sutureless (SU) versus rapid-deployment (RD) aortic valve replacement. Overall pooled analyses from patients (A), subgroup 1 (B) and subgroup 2 (C) are shown. Subgroup 1 matches SU with RD valve sizes as small with 21 mm, medium with 23 mm, large with 25 mm, and extralarge with 27 mm, and subgroup 2 matches SU with RD valve sizes as small with 19 mm, medium with 21 mm, large with 23 mm, and extralarge with 25 mm. Compared with the RD group, the SU group is associated with a significantly higher mean transvalvular pressure gradient in patients overall (MD: 2.93; 95% CI: 2.19–3.67; p < 0.00001;  $I^2 = 65\%$ ), subgroup 1 (MD: 3.57; 95% CI: 3.20–3.94; p < 0.00001;  $I^2 = 26\%$ ) and subgroup 2 (MD: 1.68; 95% CI: 0.77–2.58; p = 0.0003;  $I^2 = 74\%$ ). SD, standard deviation; IV, inverse-variance; CI, confidence interval. (continued)

CPB times for 10.12 min and 11.63 min, respectively, compared with the RD group. In terms of early mortality, paravalvular leak, moderate-to-severe paravalvular leak, pacemaker implantation, stroke, or ICU stay, data analysis revealed commonalities between the two groups.

Our honest opinion is that selecting the appropriate valve for a defined patient based on the information revealed in our study

remains a challenging proposition. Although our study revealed that the two valves displayed varied hemodynamic and intraoperative performances, this did not translate into different clinical outcomes for patients. However, there is still a lack of medium- to long-term follow-up and comprehensive data to determine critical outcomes in terms of survival and major adverse cardiac and cerebral events. Therefore, it is important to

		SU			RD			Mean Difference			Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year		IV, Random, 95% Cl	
1.3.1 Small-19												
Augusto D'Onofrio et al, 2020	13	5	15	13.2	3.8	19	4.9%	-0.20 [-3.25, 2.85]	2020		-+-	
Max Gotzmann et al, 2020	10	0	1	10	0	1		Not estimable	2020			
Di Eusanio 2018	15.1	5.9	317	17.2	5.2	74	8.9%	-2.10 [-3.45, -0.75]	2018		-	
Subtotal (95% CI)			333			94	13.7%	-1.66 [-3.23, -0.10]			•	
Heterogeneity: $Tau^2 = 0.35$ ; Chi <sup>2</sup> = Test for overall effect: Z = 2.08 (P		f = 1 (	(P = 0.2	26); I² =	20%							
1.3.2 Medium-21												
Oliver J. Liakopoulos et al, 2021	13	4	39	12	8	29	4.7%	1.00 [-2.17, 4.17]	2021		- <del>-</del>	
Augusto D'Onofrio et al, 2020	10.9	5.4	40	10.3	3.2	44	7.4%	0.60 [-1.32, 2.52]			+	
Martin Hartrumpf et al, 2020	15.1	7.3	15	12.1	3.8	9	3.0%	3.00 [-1.45, 7.45]	2020		+	
Max Gotzmann et al, 2020	21.3	7.5	3	20	4.8	4	0.8%	1.30 [-8.40, 11.00]	2020		<u> </u>	
Di Eusanio 2018	15	6.1	876	11.8	4	210	10.4%	3.20 [2.52, 3.88]				
Subtotal (95% CI)			973			296	26.2%	2.07 [0.53, 3.61]			◆	
Heterogeneity: Tau <sup>2</sup> = 1.27; Chi <sup>2</sup> = Test for overall effect: Z = 2.63 (P			(P = 0.1	0); I <sup>2</sup> =	48%							
1.3.3 Large-23												
Oliver J. Liakopoulos et al, 2021	12	4	34	10	4	39	7.6%	2.00 [0.16, 3.84]	2021			
Max Gotzmann et al, 2020	19.2	7.5	9	10.5	4.8	14	2.2%	8.70 [3.19, 14.21]				
Augusto D'Onofrio et al, 2020	11.5		42	9.3	3.9	37	8.4%	2.20 [0.68, 3.72]				
Martin Hartrumpf et al. 2020	13.4	6.9	29	14.5	10.6	15	1.9%	-1.10 [-7.02, 4.82]				
Di Eusanio 2018	13.4		906	11	4.9	242	10.3%	2.40 [1.69, 3.11]				
Subtotal (95% CI)			1020			347	30.4%	2.38 [1.30, 3.46]			•	
Heterogeneity: $Tau^2 = 0.54$ ; $Chi^2 = Test$ for overall effect: $Z = 4.32$ (P			(P = 0.1	6); I² =	39%							
1.3.4 Xlarge-25												
Oliver J. Liakopoulos et al, 2021	9	3	22	8	4	30	7.4%	1.00 [-0.90, 2.90]	2021		+	
Martin Hartrumpf et al, 2020	14.3	-	32	10.6	3.8	11	4.5%	3.70 [0.45, 6.95]				
Max Gotzmann et al, 2020		7.5	8	9.2	4.8	12	1.9%	0.60 [-5.26, 6.46]			<del></del>	
Augusto D'Onofrio et al, 2020		3.7	20	8	3.4	11	5.8%	1.80 [-0.78, 4.38]			+	
Di Eusanio 2018	12.2		257	9.8	4.4	163	9.9%	2.40 [1.46, 3.34]				
Subtotal (95% CI)	_		339	-		227	29.6%	2.16 [1.39, 2.93]			◆	
Heterogeneity: $Tau^2 = 0.00$ ; $Chi^2 =$ Test for overall effect: Z = 5.50 (P			(P = 0.5	68); I² =	0%							
Total (95% CI)			2665			964	100.0%	1.68 [0.77, 2.58]			◆	
Heterogeneity: Tau <sup>2</sup> = 1.92; Chi <sup>2</sup> =	= 62.72, (	df = 1	6 (P <	0.00001	);  ² =	74%			_	-20	-10 0 10	20
Test for overall effect: Z = 3.64 (P Test for subgroup differences: Ch		'	= 3 (P =	0 0001	)  2 =	85.6%					Favours [SU] Favours [RD]	20
	20.1	u. ur •	511 -	0.0001		55.070						
E 3												
inued.												

have risk predictors that impact the long-term prognosis for the two valves when analyzing the advantages and disadvantages of each valve, with implications to guide clinicians in their selection.

It has been proved that SURD-AVR possesses a better hemodynamic function compared with SAVR (25). The following interpretations, according to several investigations, could account for this satisfactory observation: (1) the non-pledged sutures may contribute to a huger laminar flow; (2) as the thin stent allows the leaflets to move freely without being firmly bound to bulky stents, the Perceval valve result in the pressure gradients drops; (3) seated below the annulus, the skirt frame of the stent of the Intuity valve has a flared configuration in the left ventricular outflow, which may play a role in active constriction limitation in the left ventricular outflow tract (LVOT) (25–29).

Our meta-analysis performed using both radical and conservative matching revealed that when compared with the Intuity valve, the Perceval valve had statistically significant higher mean transvalvular pressure gradients across all patients and subgroup analyses.

Theoretically, in terms of valve structure, as the Intuity valve has the valve annulus stent covered by a polyester sealing cloth (8, 30), the Perceval valve could offer a larger effective outflow orifice area, leading to its better hemodynamic performance. Nevertheless, this hypothesis is in stark contrast to our metaanalysis observation, which should be highlighted purposely. A previous study reported this theory-contradicted finding (31). If the stent in the Perceval valve undergoes compression or deformation after the prosthesis implantation procedure, it could indicate oversizing relative to the annulus or procedural misoperation by the surgeon, potentially resulting in a high gradient. This grossly oversized prosthesis mismatched with the patient tends to spring back, causing incomplete valve opening and contact loss from the annulus, which possibly results in high paravalvular leakage, besides an increase in the pressure gradients. Several published studies reported that Perceval valve rebounds were observed in clinical implantation and laboratories (32, 33). This feasible explanation for cracking the paradox of valvepressure gradients is consistent with the trend of paravalvular leak in our meta-analysis results (SU group: 184 in 1,530; RD group: 96 in 1,542. OR: 1.95; 95% CI: 1.01–3.77; p = 0.05;  $I^2 = 75\%$ ). Strikingly, another theoretical possibility was proposed by Campbell D. Flynn et al. to the effect that the Intuity valve that has better pressure gradients focuses on the valve skirt (34). The subannular balloonexpanded valve skirt in the Intuity valve is proposedly attributed to

A Study or Subgroup			Mean	SU	Total	Mean	RD SD 1	Total	Weight	Mean Differ IV. Fixed.		Year		Difference ed. 95% Cl	
Paolo Berretta et al, 2022 (combined S	SURD-AV		25.9	11.7	467	19.6	8.1	467	26.5%	6.30 [5.01					
Paolo Berretta et al, 2022 (isolated SU			26.5	10.2	823	21.5	9.7	823	47.8%	5.00 [4.04		2022		-	
Oliver J. Liakopoulos et al, 2021			22	8	107	17	7	107	10.9%	5.00 [2.99	9, 7.01]	2021			
Augusto D'Onofrio et al, 2020			22.45	8.11		19.56		117	12.2%	2.89 [0.99		2020			
Martin Hartrumpf et al, 2020			26	13.2	80	21.6		39	1.4%	4.40 [-1.18					
Max Gotzmann et al, 2020			27.6	11.79	21	19.76	9.56	33	1.2%	7.84 [1.83,	13.85]	2020			
Total (95% CI)					1615			1586	100.0%	5.11 [4.45	, 5.78]			•	
Heterogeneity: $Chi^2 = 9.41$ , df = 5 (P = Test for overall effect: Z = 15.08 (P < C		= 47%										_	-10 -5 Favours ISU	0 5 [] Favours [RD]	10 10
3		SU			RD				Mean Dif	fference			Mean Diff		
Study or Subgroup	Mean		Total	Mean		Tota	Weic			ed, 95% C	l Year		IV. Fixed.		
1.5.1 Small-21															
Oliver J. Liakopoulos et al, 2021	27	10	12	17	· 7	29	1.1	1%	10.00 [3	.79, 16.21]	2021				
Augusto D'Onofrio et al, 2020	23.9	9.6	15		2 6.2			5%		0.49, 9.89]			H		
Martin Hartrumpf et al, 2020	42.4		4		5.6				-	.27, 42.53]					
Di Eusanio 2018	28.4		317							4.22, 7.18]				÷.	
Subtotal (95% CI)			348			292				4.54, 7.30]				•	
Heterogeneity: $Chi^2 = 4.53$ , df = 3	(P = 0.2	1); l² =	34%						-	-					
Test for overall effect: Z = 8.40 (P	< 0.0000	01)													
1.5.2 Medium-23															
Oliver J. Liakopoulos et al, 2021	24	8	39	18	8 8	39	3.4	4%	6.00 [	2.45, 9.55]	2021				
Augusto D'Onofrio et al, 2020	21.7	9.2	40	18.1	7.9	37	2.9	9%	3.60 [-	0.22, 7.42]	2020		F	-	
Martin Hartrumpf et al, 2020	24.6	10.7	15	21.2	2 7.3	15	i 1.0	0%	3.40 [-:	3.15, 9.95]	2020		+		
Di Eusanio 2018	27.6	10.9	876	20.9	7.4	242	30.5	5%	6.70 [	5.52, 7.88]	2018				
Subtotal (95% CI)			970			333	37.8	8%	6.31 [	5.25, 7.37]				•	
Heterogeneity: Chi <sup>2</sup> = 3.14, df = 3 (	(P = 0.3	7); l² =	4%												
Test for overall effect: Z = 11.68 (F	o < 0.000	001)													
1.5.3 Large-25															
Oliver J. Liakopoulos et al, 2021	22	6	34	17	6	30	9 4.9	9%	5.00 [	2.05, 7.95]	2021				
Augusto D'Onofrio et al, 2020	22.1	6	42	14.8	3 9	11	1.3	3%	7.30 [1	.68, 12.92]	2020		·		
Martin Hartrumpf et al, 2020	21.9	8.8	29	18.3	3.9	11	2.7	7%	3.60 [-	0.35, 7.55]	2020		t t	-	
Di Eusanio 2018	25.5	10.2	906	19.6	8.7	163				4.41, 7.39]	2018			<b>.</b>	
Subtotal (95% CI)			1011			215	28.0	0%	5.59 [4	4.36, 6.82]				•	
Heterogeneity: $Chi^2 = 1.65$ , $df = 3$ Test for overall effect: $Z = 8.90$ (P	•	<i>'</i>	0%												
1.5.4 Xlarge-27															
Oliver J. Liakopoulos et al, 2021	18	6	22	12	2 8	9	1.3	3%	6.00 [0	.20, 11.80]	2021		F		
Augusto D'Onofrio et al, 2020	19.9	7.5	20	17	6.8	6	<b>1</b> .1	1%	2.90 [-	3.46, 9.26]	2020		+		
Martin Hartrumpf et al, 2020	22.3	7.8	32	18.8	8 18	4	0.1	1% :	3.50 [-14	.35, 21.35]	2020				
Di Eusanio 2018	23.5	10.2	257	17	6.7	59			6.50 [	4.38, 8.62]	2018			-	
Subtotal (95% CI)			331			78	11.9	9%	6.10 [4	4.21, 7.98]				◆	
Heterogeneity: Chi <sup>2</sup> = 1.19, df = 3			0%												
Test for overall effect: Z = 6.33 (P	< 0.0000	)1)													
Total (95% CI)			2660			918	100.0	0%	6.00 [	5.34, 6.65]				•	
Heterogeneity: Chi <sup>2</sup> = 11.31, df = 1	5 (P = 0	.73): I	² = 0%												
Test for overall effect: Z = 18.04 (F	•												-20 -10 0	10 20	
Test for subaroup differences: Chi			(P = (	).85). I²	= 0%								Favours [SU]	ravours [RD]	
4															

Mean difference (MD) of peak transvalvular pressure gradients (mmHg) in sutureless (SU) versus rapid-deployment (RD) aortic valve replacement. Overall pooled analyses from patients (A), subgroup 1 (B), and subgroup 2 (C) are shown. Subgroup 1 matches SU with RD valve sizes as small with 21 mm, medium with 23 mm, large with 25 mm, and extralarge with 27 mm. Subgroup 2 matches SU with RD valve sizes as small with 19 mm, medium with 21 mm, large with 23 mm, and extralarge with 25 mm. Compared with the RD group, the SU group is associated with significantly higher peak transvalvular pressure gradients in patients overall (MD: 5.11; 95% CI: 4.45-5.78; p < 0.00001;  $l^2 = 47\%$ ), subgroup 1 (MD: 6.00; 95% CI: 5.34-6.65; p < 0.00001;  $l^2 = 0\%$ ) and subgroup 2 (MD: 2.86; 95% CI: 1.18-4.55; p = 0.0008;  $l^2 = 82\%$ ). SD, standard deviation; IV, inverse-variance; CI, confidence interval.

the recognized excellent transvalvular pressure gradients in the RD group, in which the LVOT is enlarged, promoting an increase in blood flow through the valve annulus (35, 36). Although the expandable frame skirt in the Intuity valve may enlarge the LVOT, it is certain that the stent located at the leaflet attachment margin narrows the orifice area. To sum up, our study was more inclined to conclude that the incomplete valve opening in the Perceval valve caused a higher gradient and showed a higher tendency toward paravalvular leak, for which further studies should confirm the potential mechanism.

Furthermore, it is necessary to highlight that the difference in valve gradient between these two groups (MD = 2.93 mmHg in mean aortic pressure gradients; MD = 5.11 mmHg in peak aortic pressure gradients) did not translate into differences in early clinical outcomes. In the meantime, the hemodynamic performance of the two valves needs to be further followed up and explored. Only then will it be possible to show the impact of the difference in transvalvular pressure gradients on the long-term prognosis of patients who received SU and RD-AVR. Notably, patients with smaller aortic annuli who undergo aortic

		SU			RD			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year	IV, Random, 95% CI
1.6.1 Small-19										
Augusto D'Onofrio et al, 2020	23.9	9.6	15	24.2	4.8	19	5.1%	-0.30 [-5.62, 5.02]	2020	
Di Eusanio 2018	28.4	10.3	317	34.3	10.1	74	8.3%	-5.90 [-8.47, -3.33]	2018	
Subtotal (95% CI)			332			93	13.4%	-3.60 [-9.00, 1.79]		
Heterogeneity: Tau <sup>2</sup> = 11.15; Chi <sup>2</sup> Test for overall effect: $Z = 1.31$ (P		df = 1	(P = 0.0	06); I² =	71%					
1.6.2 Medium-21										
Oliver J. Liakopoulos et al, 2021	24	8	39	17	7	29	7.0%	7.00 [3.42, 10.58]	2021	
Augusto D'Onofrio et al, 2020	21.7	9.2	40	19.2	6.2	44	7.3%	2.50 [-0.89, 5.89]	2020	+
Martin Hartrumpf et al, 2020	24.6	10.7	15	20	5.6	9	4.0%	4.60 [-1.93, 11.13]	2020	
Di Eusanio 2018	27.6	10.9	876	22.7	7	210	9.8%	4.90 [3.71, 6.09]	2018	
Subtotal (95% CI)			970			292	28.2%	4.82 [3.57, 6.08]		•
Heterogeneity: $Tau^2 = 0.20$ ; $Chi^2 =$ Test for overall effect: Z = 7.54 (P			P = 0.36	5); I² = 8	%					
1.6.3 Large-23										
Oliver J. Liakopoulos et al, 2021	22	6	34	18	8	39	7.5%	4.00 [0.78, 7.22]	2021	
Augusto D'Onofrio et al, 2020	22.1	6	42	18.1	7.9	37	7.6%	4.00 [0.87, 7.13]	2020	
Martin Hartrumpf et al, 2020	21.9	8.8	29	21.2	7.3	15	5.5%	0.70 [-4.19, 5.59]	2020	
Di Eusanio 2018	25.5	10.2	906	20.9	7.4	242	9.9%	4.60 [3.46, 5.74]	2018	
Subtotal (95% CI)			1011			333	30.5%	4.32 [3.32, 5.32]		•
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = Test for overall effect: Z = 8.48 (P	,	``	P = 0.49	9); I <sup>2</sup> = 0	%					
1.6.4 Xlarge-25										
Oliver J. Liakopoulos et al, 2021	18	6	22	17	6	30	7.4%	1.00 [-2.30, 4.30]	2021	
Martin Hartrumpf et al, 2020	22.3	7.8	32	18.3	3.9	11	7.1%	4.00 [0.45, 7.55]	2020	
Augusto D'Onofrio et al, 2020	19.9	7.5	20	14.8	9	11	4.3%	5.10 [-1.15, 11.35]		
Di Eusanio 2018	23.5	10.2	257	19.6	8.7	163	9.2%	3.90 [2.07, 5.73]	2018	
Subtotal (95% CI)			331			215	27.9%	3.44 [2.02, 4.86]		
Heterogeneity: $Tau^2 = 0.00$ ; $Chi^2 =$ Test for overall effect: Z = 4.75 (P		•	P = 0.44	l); l² = 0	%					
Total (95% CI)			2644			933	100.0%	2.86 [1.18, 4.55]		◆
Heterogeneity: Tau <sup>2</sup> = 7.12; Chi <sup>2</sup> =	= 70.41, 0	df = 13	8 (P < 0	.00001)	; l² = 8	2%				-10 -5 0 5 10
Test for overall effect: Z = 3.34 (P	= 0.0008	3)								Favours [SU] Favours [RD]
Test for subaroup differences: Ch	i <sup>2</sup> = 10.10	). df =	3 (P = )	0.02). I²	= 70.3	3%				
E 4										
nued.										

valve replacement often exhibit higher transvalvular pressure gradients, and the presence of a small aortic annulus may augment the risk of patient–prosthesis mismatch (37, 38). Hence, it is plausible that the Intuity valve may offer superior postoperative benefits to patients with a small aortic annulus.

In our study, overall pooled analyses from isolated AVR patients, combined AVR patients, and AVR patients demonstrated that, compared with the RD group, the SU group was associated with significantly less aortic cross-clamp time (MD: -10.12; 95% CI: -13.90 to -6.33; p < 0.00001;  $I^2 = 94\%$ ). We suspected that this discrepancy arose because of these two valves possessing distinct suture structures. The Perceval valve is a bovine pericardium prosthesis attached to the automated anchor used for stabilization and a fastened implantation site. When the valve is placed down to the annulus, three intercommissural sutures are used for guiding, which will be removed after valve deployment is completed (8, 39). In addition, the Perceval valve with a collapsed design may maximize visualization and simplify implantation (25). In contrast, three braided, non-pledged sutures are placed at the bottom of every valve sinus using a figure-of-eight or horizontal mattress technique without removal if the Intuity valve is selected for use in the AVR. Once annular seating is verified, the balloon will be inserted through the holder, and the stent will be deployed by inflating it to the appropriate level of pressure with saline for 10 s (40). Therefore, the Perceval valve is the only one that precisely matches the definition of "sutureless" during operation. Because of these structural and procedural differences with the Perceval valve, some opponents have argued that the Intuity valve cannot strictly be labeled as a "rapid-deployment" valve (30). However, it was noted that the magnitude assessment showed high heterogeneity, with subgroup analysis and leave-one-out sensitivity analysis being inefficient for elimination.

Postoperative mortality and morbidity are strongly associated with the duration of both ACC and CPB. A previously published study has indicated that ACC time is a critical and independent risk predictor of severe cardiovascular morbidities, with the risk increasing by 1.4% for each additional minute of ACC time (41). Kenji Lino et al. also revealed that ACC time serves as an independent risk predictor of postoperative morbidity for aortic valve replacement, with a prolonged ACC duration significantly increasing the rates of renal failure, gastrointestinal complications, pneumonia, and multiorgan failure (42). In addition, a study conducted in China has reported that CPB time is independently linked to an increased risk of acute kidney injury following surgery for acute DeBakey Type I aortic dissection (43). Therefore, for high-risk patients undergoing AVR, reducing the ACC and CPB times may confer substantial advantages in using the Perceval valve, particularly for patients with pre-existing organ damage and infections or for those undergoing redo surgery (44, 45).

4	5	SU		R	RD			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD T	otal I			otal	Neight	IV, Random, 95% CI Ye	ear	IV, Random, 95% Cl
I.1.1 Isolated AVR patients										
Paolo Berretta et al, 2022	40.6	17.8	823	56.5 2	21.5	823	7.0% -	15.90 [-17.81, -13.99] 20	)22	-
Dliver J. Liakopoulos et al, 2021	42	13	45	44	29	43	5.0%	-2.00 [-11.46, 7.46] 20		
Augusto D'Onofrio et al, 2020	52	14	60	62	24	54		-10.00 [-17.32, -2.68] 20		
Martin Hartrumpf et al, 2020	50.9		60	64.9 1		19		-14.00 [-22.93, -5.07] 20		
Stephan Ensminger et al, 2018			693	52.7 1		314	7.0%	-8.70 [-10.98, -6.42] 20		· 1
Federica Jiritano et al, 2016 Subtotal (95% CI)	40.6	3.2	16 <b>697</b>	40.8	2.4	27 <b>280</b>	7.1% <b>36.8%</b>	-0.20 [-2.01, 1.61] 20 -8.48 [-15.28, -1.69]	010	
Heterogeneity: Tau <sup>2</sup> = 63.11; Chi <sup>2</sup>	= 141 15			00001)			50.070	-0.40 [-10.20, -1.00]		-
Test for overall effect: Z = 2.45 (P		, ur o	(1 - 0.	00001),	, 1 0	570				
I.1.2 Combined AVR patients										
Paolo Berretta et al, 2022	66.5	31.2	467	80.8 3	30.5	467	6.6% -	14.30 [-18.26, -10.34] 20	)22	
Dliver J. Liakopoulos et al, 2021	62	25	62	66	17	64	5.6%	-4.00 [-11.49, 3.49] 20	)21	
Augusto D'Onofrio et al, 2020	69	23	57	101	36	63		32.00 [-42.71, -21.29] 20		
Stephan Ensminger et al, 2018	64.4		207	80.6		152		16.20 [-22.08, -10.32] 20	)18	
Subtotal (95% CI)			793			746	22.9%	-15.82 [-23.76, -7.87]		
Heterogeneity: Tau <sup>2</sup> = 52.64; Chi <sup>2</sup> Fest for overall effect: Z = 3.90 (P			J = 0.0	004); I²	= 83%	•				
4.1.3 Overall AVR patients										
Oliver J. Liakopoulos et al, 2021	53	23	107	57	25	107	5.9%	-4.00 [-10.44, 2.44] 20	)21	+
Max Gotzmann et al, 2020	73.4	30.1	21	77.9 2	22.6	33	3.4%	-4.50 [-19.51, 10.51] 20		
Augusto D'Onofrio et al, 2020	60		117	83		117		23.00 [-30.71, -15.29] 20		
Martin Hartrumpf et al, 2020	56.5		80	73.4	21	39		-16.90 [-25.30, -8.50] 20		
Paolo Berretta et al, 2019	51.2		983	59 2		392	6.9%	-7.80 [-10.38, -5.22] 20		
Stephan Ensminger et al, 2018	49			53.3 2		102 27	6.1% 7.1%	-4.30 [-10.09, 1.49] 20		· · · · ·
Federica Jiritano et al, 2016 Subtotal (95% CI)	40.62		426	10.77 2		817	40.3%	-0.15 [-1.96, 1.66] 20 -8.28 [-13.70, -2.86]	010	
Heterogeneity: Tau <sup>2</sup> = 41.19; Chi <sup>2</sup>	= 58 16			0001)			40.070	-0.20 [-13.70, -2.00]		•
Test for overall effect: Z = 2.99 (P		ui – 0 (i	- 0.0	0001), 1	- 30	/0				
otal (95% CI)		3	916		2	843	100.0%	-10.12 [-13.90, -6.33]		•
Heterogeneity: Tau <sup>2</sup> = 52.03; Chi <sup>2</sup>	= 267 41	df = 16	S (P < (	00001	): $ ^2 = 9$	94%				-20 -10 0 10 20
					<i>,</i> ,					
Test for overall effect: Z = 5.24 (P	< 0.0000	1)								Favours [experimental] Favours [control]
Test for overall effect: Z = 5.24 (P Test for subaroup differences: Chi	< 0.0000	1)								
Test for overall effect: Z = 5.24 (P Test for subaroup differences: Chi	< 0.0000	1) df = 2 (F			24.1%			Mean Difference		Favours [experimental] Favours [control]
Fest for overall effect: Z = 5.24 (P Fest for subaroup differences: Chi	< 0.0000 i <sup>2</sup> = 2.64. (	1) df = 2 (F SU	P = 0.2	7). I² = :	24.1% RD		l Weigh	Mean Difference	) Year	Favours [experimental] Favours [control] Mean Difference
Test for overall effect: Z = 5.24 (P Test for subaroup differences: Chi Study or Subgroup	< 0.0000	1) df = 2 (F SU	P = 0.2		24.1% RD		l Weigh		CI Year	Favours [experimental] Favours [control]
Test for overall effect: Z = 5.24 (P Test for subaroup differences: Chi S Study or Subgroup 4.2.1 Isolated AVR patients	< 0.0000 i² = 2.64. o Mean	1) df = 2 (F SU SD	P = 0.2	7).  ² = : <u>Mean</u>	24.1% RD SD	Tota	-	t IV. Random, 95% C		Favours [experimental] Favours [control] Mean Difference
Fest for overall effect: Z = 5.24 (P Fest for subaroup differences: Chi Study or Subgroup 4.2.1 Isolated AVR patients Paolo Berretta et al, 2022	< 0.0000 i <sup>2</sup> = 2.64. o <u>Mean</u> 64.8	1) df = 2 (F SU SD 27.5	P = 0.2 Total 823	7).  ² = : <u>Mean</u> 86.4	24.1% RD SD 29.7	<u>Tota</u> 823	7.0%	t IV. Random. 95% C	2022	Favours [experimental] Favours [control] Mean Difference
Fest for overall effect: Z = 5.24 (P Fest for subgroup differences: Chi Study or Subgroup 4.2.1 Isolated AVR patients Paolo Berretta et al, 2022 Diiver J. Liakopoulos et al, 2021	< 0.0000 i <sup>2</sup> = 2.64. o <u>Mean</u> 64.8 74	1) df = 2 (F SU SD 27.5 27	P = 0.2 Total 823 45	7). I <sup>2</sup> = : <u>Mean</u> 86.4 78	24.1% RD SD 29.7 46	<u>Tota</u> 823 43	5 7.0% 5 4.5%	t IV. Random, 95% C -21.60 [-24.37, -18.83] -4.00 [-19.85, 11.85]	2022 2021	Favours [experimental] Favours [control] Mean Difference
Fest for overall effect: Z = 5.24 (P Fest for subgroup differences: Chi Study or Subgroup 4.2.1 Isolated AVR patients Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020	< 0.0000 i <sup>2</sup> = 2.64. o <u>Mean</u> 64.8 74	1) df = 2 (F SU SD 27.5	P = 0.2 Total 823	7). I <sup>2</sup> = : <u>Mean</u> 86.4 78	24.1% RD SD 29.7 46	<u>Tota</u> 823	7.0% 4.5% 4.9%	t IV. Random. 95% C -21.60 [-24.37, -18.83] -4.00 [-19.85, 11.85] -17.00 [-31.09, -2.91]	2022 2021 2020	Favours [experimental] Favours [control] Mean Difference
Fest for overall effect: Z = 5.24 (P Fest for subgroup differences: Chi Study or Subgroup 4.2.1 Isolated AVR patients Paolo Berretta et al, 2022 Diiver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020 Augusto D'Onofrio et al, 2020	< 0.0000 j <sup>2</sup> = 2.64. o <u>Mean</u> 64.8 74 83.3	1) df = 2 (F SU 27.5 27 35.8 18	P = 0.2 Total 823 45 60	7).  ² = : <u>Mean</u> 86.4 78 100.3 89	24.1% RD SD 29.7 46 24	<b>Tota</b> 823 43 19	7.0% 4.5% 4.9% 5.6%	IV. Random, 95% C           -21.60 [-24.37, -18.83]           -4.00 [-19.85, 11.85]           -17.00 [-31.09, -2.91]           -14.00 [-24.87, -3.13]	2022 2021 2020 2020	Favours [experimental] Favours [control] Mean Difference
Fest for overall effect: Z = 5.24 (P Fest for subgroup differences: Chi Study or Subgroup 4.2.1 Isolated AVR patients Paolo Berretta et al, 2022 Diiver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020 Stephan Ensminger et al, 2018	< 0.0000 i <sup>2</sup> = 2.64. o Mean 64.8 74 83.3 75	1) df = 2 (F SU 27.5 27 35.8 18	P = 0.2 Total 823 45 60 60	7).  ² = : <u>Mean</u> 86.4 78 100.3 89	24.1% RD 29.7 46 24 37 23.1	Tota 823 43 19 54	7.0% 4.5% 4.9% 5.6% 7.0%	t IV. Random, 95% C -21.60 [-24.37, -18.83] -4.00 [-19.85, 11.85] -17.00 [-31.09, -2.91] -14.00 [-24.87, -3.13] -11.40 [-14.39, -8.41]	2022 2021 2020 2020 2020 2018	Favours [experimental] Favours [control] Mean Difference
rest for overall effect: Z = 5.24 (P rest for subgroup b.2.1 Isolated AVR patients aolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020 Ostephan Ensminger et al, 2018 Federica Jiritano et al, 2016	< 0.0000 j <sup>2</sup> = 2.64. ( Mean 64.8 74 83.3 75 66.3	1) df = 2 (F SU 27.5 27 35.8 18 20.8	P = 0.2 Total 823 45 60 60 693	7). I <sup>2</sup> = : <u>Mean</u> 86.4 78 100.3 89 77.7	24.1% RD 29.7 46 24 37 23.1	Tota 823 43 19 54 314	7.0% 4.5% 4.9% 5.6% 7.0%	IV. Random, 95% C           -21.60 [-24.37, -18.83]           -4.00 [-19.85, 11.85]           -17.00 [-31.09, -2.91]           -14.00 [-24.87, -3.13]           -11.40 [-14.39, -8.41]           4.00 [0.83, 7.17]	2022 2021 2020 2020 2018 2018	Favours [experimental] Favours [control] Mean Difference
rest for overall effect: Z = 5.24 (P rest for subaroup differences: Chi Study or Subgroup L.2.1 Isolated AVR patients Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020 Stephan Ensminger et al, 2018 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 145.31; Cl	< 0.0000 i <sup>2</sup> = 2.64. d Mean 64.8 74 83.3 75 66.3 61.8 hi <sup>2</sup> = 144.	1) df = 2 (F SU 27.5 27 35.8 18 20.8 5.6	<b>Total</b> 823 45 60 693 16 <b>1697</b>	7). I <sup>2</sup> = ; <u>Mean</u> 86.4 78 100.3 89 77.7 57.8	24.1% <b>RD</b> 29.7 46 24 37 23.1 4.2	Tota 823 43 54 314 27 1280	7.0% 4.5% 4.9% 5.6% 7.0%	IV. Random, 95% C           -21.60 [-24.37, -18.83]           -4.00 [-19.85, 11.85]           -17.00 [-31.09, -2.91]           -14.00 [-24.87, -3.13]           -11.40 [-14.39, -8.41]           4.00 [0.83, 7.17]	2022 2021 2020 2020 2018 2018	Favours [experimental] Favours [control] Mean Difference
Test for overall effect: Z = 5.24 (P Test for subgroup differences: Chi Study or Subgroup L.2.1 Isolated AVR patients Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2020 Diver J. Liakopoulos et al, 2020 Stephan Ensminger et al, 2018 Stephan Ensminger et al, 2018 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 145.31; Cl Fest for overall effect: Z = 2.02 (f	< 0.0000 i <sup>2</sup> = 2.64. d Mean 64.8 74 83.3 75 66.3 61.8 hi <sup>2</sup> = 144.	1) df = 2 (F SU 27.5 27 35.8 18 20.8 5.6	<b>Total</b> 823 45 60 693 16 <b>1697</b>	7). I <sup>2</sup> = ; <u>Mean</u> 86.4 78 100.3 89 77.7 57.8	24.1% <b>RD</b> 29.7 46 24 37 23.1 4.2	Tota 823 43 54 314 27 1280	7.0% 4.5% 4.9% 5.6% 7.0%	IV. Random, 95% C           -21.60 [-24.37, -18.83]           -4.00 [-19.85, 11.85]           -17.00 [-31.09, -2.91]           -14.00 [-24.87, -3.13]           -11.40 [-14.39, -8.41]           4.00 [0.83, 7.17]	2022 2021 2020 2020 2018 2018	Favours [experimental] Favours [control] Mean Difference
Fest for overall effect: Z = 5.24 (P Fest for subaroup differences: Chi Study or Subgroup I.2.1 Isolated AVR patients Paolo Berretta et al, 2022 Diver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020 Augusto D'Onofrio et al, 2020 Stephan Ensminger et al, 2018 Federica Jiritano et al, 2018 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 145.31; CI Fest for overall effect: Z = 2.02 (f I.2.2 Combined AVR patients	< 0.0000 i <sup>2</sup> = 2.64. o Mean 64.8 74 83.3 75 66.3 61.8 hi <sup>2</sup> = 144. P = 0.04)	1) df = 2 (F SU 27.5 27 35.8 20.8 5.6 33, df =	P = 0.2 Total 823 45 60 693 16 1697 5 (P -	7). I <sup>2</sup> = : <u>Mean</u> 86.4 78 100.3 89 77.7 57.8 < 0.000	24.1% RD 29.7 46 24 37 23.1 4.2 01); I <sup>2</sup>	Tota 823 43 54 314 27 1280 = 97%	3 7.0% 3 4.5% 9 4.9% 4 5.6% 4 7.0% 7.0% 36.0%	t IV. Random, 95% C -21.60 [-24.37, -18.83] -4.00 [-19.85, 11.85] -17.00 [-31.09, -2.91] -14.00 [-24.87, -3.13] -11.40 [-44.39, -8.41] 4.00 [0.83, 7.17] -10.65 [-21.01, -0.30]	2022 2021 2020 2020 2018 2018	Favours [experimental] Favours [control] Mean Difference
rest for overall effect: Z = 5.24 (P rest for subaroup differences: Chi <b>Study or Subgroup</b> <b>1.2.1 Isolated AVR patients</b> Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020 Augusto D'Onofrio et al, 2020 Stephan Ensminger et al, 2020 Stephan Ensminger et al, 2016 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 145.31; Cl rest for overall effect: Z = 2.02 (f <b>1.2.2 Combined AVR patients</b> Paolo Berretta et al, 2022	< 0.0000 i <sup>2</sup> = 2.64. d Mean 64.8 74 83.3 75 66.3 61.8 hi <sup>2</sup> = 144. P = 0.04) 96.5	1) df = 2 (F SU 27.5 27 35.8 18 20.8 5.6 33, df = 41.6	<b>Total</b> 823 45 60 693 16 <b>1697</b> 5 (P •	7). I <sup>2</sup> = : <u>Mean</u> 86.4 78 100.3 89 77.7 57.8 < 0.000 116.5	24.1% RD 29.7 46 24 37 23.1 4.2 01); I <sup>2</sup> 40.9	Tota           823           43           19           54           314           27           1280           = 97%           467	3 7.0% 3 4.5% 9 4.9% 4 5.6% 4 7.0% 7 7.0% 36.0%	t IV. Random, 95% C -21.60 [-24.37, -18.83] -4.00 [-19.85, 11.85] -17.00 [-31.09, -2.91] -14.00 [-24.87, -3.13] -11.40 [-14.39, -8.41] 4.00 [0.83, 7.17] -10.65 [-21.01, -0.30] -20.00 [-25.29, -14.71]	2022 2021 2020 2020 2018 2016	Favours [experimental] Favours [control] Mean Difference
Fest for overall effect: Z = 5.24 (P Fest for subgroup differences: Chi Study or Subgroup 4.2.1 Isolated AVR patients Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020 Augusto D'Onofrio et al, 2020 Stephan Ensminger et al, 2020 Stephan Ensminger et al, 2018 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 145.31; CI Fest for overall effect: Z = 2.02 (f 4.2.2 Combined AVR patients Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021	< 0.0000 i <sup>2</sup> = 2.64. ( <u>Mean</u> 64.8 74 83.3 75 66.3 61.8 hi <sup>2</sup> = 144. P = 0.04) 96.5 94	1) df = 2 (F SU 27.5 27 35.8 18 20.8 5.6 33, df = 41.6 36	P = 0.2 Total 823 45 60 693 16 1697 5 (P 467 62	7). I <sup>2</sup> = : <u>Mean</u> 86.4 78 100.3 89 77.7 57.8 < 0.000 116.5 100	24.1% RD 29.7 46 24 37 23.1 4.2 01); I <sup>2</sup> 40.9 26	<u>Tota</u> 823 43 19 54 314 277 1280 = 97% 467 64	5 7.0% 4.5% 4.9% 5.6% 7.0% 7.0% 36.0%	IV. Random, 95% C           -21.60 [-24.37, -18.83]           -4.00 [-19.85, 11.85]           -17.00 [-31.09, -2.91]           -14.00 [-24.87, -3.13]           -11.40 [-14.39, -8.41]           4.00 [0.83, 7.17]           -10.65 [-21.01, -0.30]           -20.00 [-25.29, -14.71]           -6.00 [-16.99, 4.99]	2022 2021 2020 2020 2018 2016 2016	Favours [experimental] Favours [control] Mean Difference
Fest for overall effect: Z = 5.24 (P Fest for subgroup L.2.1 Isolated AVR patients Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020 Stephan Ensminger et al, 2018 Federica Jiritano et al, 2018 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 145.31; CI Fest for overall effect: Z = 2.02 (f L.2.2 Combined AVR patients Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Distributal (95% CI) Heterogeneity: Tau <sup>2</sup> = 145.31; CI Fest for overall effect: Z = 2.02 (f L.2.2 Combined AVR patients Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021	< 0.0000 i <sup>2</sup> = 2.64. d Mean 64.8 74 83.3 75 66.3 61.8 hi <sup>2</sup> = 144. P = 0.04) 96.5	1) df = 2 (f SD 27.5 27 35.8 18 20.8 5.6 33, df = 41.6 36 36	<b>Total</b> 823 45 60 693 16 <b>1697</b> 5 (P •	7). I <sup>2</sup> = : <u>Mean</u> 86.4 78 100.3 89 77.7 57.8 < 0.000 116.5	24.1% RD SD 29.7 46 24 37 23.1 4.2 01); I <sup>2</sup> 40.9 26 49	Tota           823           43           19           54           314           27           1280           = 97%           467	3 7.0% 4.5% 4.9% 5.6% 7.0% 7.0% 36.0% 6.7% 5.6% 4.6%	t IV. Random, 95% C -21.60 [-24.37, -18.83] -4.00 [-19.85, 11.85] -17.00 [-31.09, -2.91] -14.00 [-24.87, -3.13] -11.40 [-14.39, -8.41] 4.00 [0.83, 7.17] -10.65 [-21.01, -0.30] -20.00 [-25.29, -14.71]	2022 2021 2020 2020 2018 2016 2016	Favours [experimental] Favours [control] Mean Difference
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rest for overall effect: Z = 5.24 (P rest for subaroup differences: Chi <b>Study or Subgroup</b> <b>1.2.1 Isolated AVR patients</b> Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020 Augusto D'Onofrio et al, 2020 Stephan Ensminger et al, 2016 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 145.31; CI rest for overall effect: Z = 2.02 (f <b>1.2.2 Combined AVR patients</b> Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Augusto D'Onofrio et al, 2020 Stephan Ensminger et al, 2018 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 24.20; Chi rest for overall effect: Z = 5.23 (f <b>1.2.3 Overall AVR patients</b> Dilver J. Liakopoulos et al, 2021	< 0.0000 i <sup>2</sup> = 2.64. ( Mean 64.8 74 83.3 75 66.3 61.8 hi <sup>2</sup> = 144. P = 0.04) 96.5 94 105 96.4 105 96.4 i <sup>2</sup> = 6.53, P < 0.000 85	1) df = 2 (f SU 27.5 27 35.8 18 20.8 5.6 33, df = 41.6 36 33.6 df = 3 ( 01) 34	P = 0.2           Total           823           450           60           693           16           1697           5 (P -           467           62           57           207           793           P = 0.0           107	7).  ² = : Mean 86.4 78 100.3 89 77.7 57.8 < 0.000 116.5 100 132 116 00 132 116 99);  ² = : 91	RD SD 29.7 46 24.37 23.1 4.2 01); I <sup>2</sup> 40.9 26 49 43 554%	Tota 823 43 54 314 27 1280 = 97% 467 63 52 746 746	7.0% 4.5% 4.5% 5.6% 7.0% 7.0% 36.0% 6.7% 4.6% 6.2% 23.1%	t         IV. Random, 95% C           6         -21.60 [-24.37, -18.83]           6         -4.00 [-19.85, 11.85]           6         -17.00 [-31.09, -2.91]           6         -17.00 [-31.09, -2.91]           6         -17.00 [-31.09, -2.91]           6         -14.00 [-24.87, -3.13]           6         -11.40 [-14.39, -8.41]           7         -0.06 [-27.83, -1.37]           6         -20.00 [-25.29, -14.71]           6         -20.00 [-25.29, -14.71]           6         -20.00 [-25.29, -14.71]           6         -20.00 [-27.83, -11.37]           6         -17.91 [-24.61, -11.20]	2022 2021 2020 2020 2018 2018 2016 2022 2021 2021 2020 2018	Favours [experimental] Favours [control] Mean Difference
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Fest for overall effect: Z = 5.24 (P Fest for subgroup 4.2.1 Isolated AVR patients Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020 Stephan Ensminger et al, 2018 Federica Jiritano et al, 2020 Stephan Ensminger et al, 2018 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 145.31; CI Fest for overall effect: Z = 2.02 (f 4.2.2 Combined AVR patients Paolo Berretta et al, 2020 Stephan Ensminger et al, 2021 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 24.20; Chi Fest for overall effect: Z = 5.23 (f 4.2.3 Overall AVR patients Dilver J. Liakopoulos et al, 2020 Max Gotzmann et al, 2020	< 0.0000 i <sup>2</sup> = 2.64. ( Mean. 64.8 74 83.3 75 66.3 61.8 hi <sup>2</sup> = 144. P = 0.04) 96.5 94. 96.5 96.4 105 90.4 105 90.4 105 90.3 103 103 103 105 90.3 103 103 103 105 90.3 103 103 105 90.3 103 103 103 105 105 105 105 105 105 105 105	1) df = 2 (f SU 27.5 27 35.8 18 20.8 5.6 33. df = 41.6 36 33.6 df = 3 ( 01) 34 32 36 38 28.9 29.3	Total 823 45 60 693 16 793 793 P = 0.0 107 117 80 201 201 107	7).   <sup>2</sup> = : Mean 86.4 78 100.3 89 77.7 57.8 (< 0.000 132 116.5 100 132 116 (< 0.000) 132 116 91 112 113 98.8 89.4 80.4 8	RD SD 29.7 46 24 37 23.1 4.2 01); l <sup>2</sup> 40.9 26 49 43 554% 37 48 29.5 26.8 30.1 29.3		7.0% 4.5% 4.9% 5.6% 7.0% 7.0% 36.0% 5.6% 4.6% 23.1% 5.5% 5.3% 3.9% 7.0% 5.3% 3.9% 7.0% 6.2%	IV. Random, 95% C           -21.60 [-24.37, -18.83]           -4.00 [-19.85, 11.85]           -4.00 [-31.09, -2.91]           -14.00 [-24.87, -3.13]           -11.40 [-14.39, -8.41]           4.00 [0.83, 7.17]           -10.65 [-21.01, -0.30]           -27.00 [-42.29, -14.71]           -6.00 [-16.99, 4.99]           -27.00 [-42.29, -11.71]           -1.960 [-27.83, -11.37]           -20.00 [-32.45, -11.55]           -22.00 [-32.45, -11.55]           -22.01 [-34.86, -10.54]           -8.20 [-11.66, -4.74]           -8.40 [-14.44, 1.64]	2022   2021   2020   2020   2018   2016   2018   2022   2021   2020   2018   2021   2020   2020   2020   2019   2018	Favours [experimental] Favours [control] Mean Difference
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rest for overall effect: Z = 5.24 (P rest for subaroup differences: Chi <b>Study or Subgroup</b> <b>1.2.1 Isolated AVR patients</b> Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020 Augusto D'Onofrio et al, 2020 Stephan Ensminger et al, 2016 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 145.31; CI Fest for overall effect: Z = 2.02 (f <b>1.2.2 Combined AVR patients</b> Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Diver J. Liakopoulos et al, 2021 Diver J. Liakopoulos et al, 2021 Stephan Ensminger et al, 2022 Diver J. Liakopoulos et al, 2021 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 24.20; Chi Fest for overall effect: Z = 5.23 (f <b>1.2.3 Overall AVR patients</b> Dilver J. Liakopoulos et al, 2020 Martin Hartrumpf et al, 2020 Martin Hartrumpf et al, 2020 Paolo Berretta et al, 2019 Stephan Ensminger et al, 2018 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 76.51; Chi	< 0.0000 i <sup>2</sup> = 2.64. ( Mean 64.8 74 83.3 75 66.3 61.8 hi <sup>2</sup> = 144. P = 0.04) 96.5 96.4 i <sup>2</sup> = 6.53, P < 0.000 85 90 90.3 94.3 81.2 76.3 61.75 i <sup>2</sup> = 50.64	1) df = 2 (f SU 27.5 27 35.8 18 20.8 5.6 33. df = 41.6 36 36 33. df = 41.6 36 33. df = 41.6 36 33. df = 33. df = 32 35 32 35 35 35 35 35 35 35 35 35 35	P = 0.2           Total           823           45           60           603           16           1697           467           62           57           207           793           P = 0.0           107           107           102           102           104           105           102           16           1408	7).  ² = : Mean 86.4 78 100.3 89 77.7 57.8 (0.000 116.5 100 132 116 (0.09);  ² = 91 112 113 98.8 89.4 82.7 57.77	RD SD 29.7 46 24.1% 29.7 46 24 37 23.1 4.2 01); I <sup>2</sup> 40.9 26 49 43 30 4.2 54% 37 48 29.5 26.8 30.1 29.3 4.25	Tota 822 43 19 54 314 27 1280 = 97% 467 64 63 152 746 107 117 38 33 404 102 27 829	<ul> <li>7.0%</li> <li>4.5%</li> <li>4.9%</li> <li>5.6%</li> <li>7.0%</li> <li>7.0%</li> <li>36.0%</li> <li>7.0%</li> <li>5.6%</li> <li>4.6%</li> <li>6.2%</li> <li>23.1%</li> <li>5.5%</li> <li>5.7%</li> <li>5.3%</li> <li>3.9%</li> <li>7.0%</li> <li>6.2%</li> <li>7.0%</li> </ul>	IV. Random, 95% C           -21.60 [-24.37, -18.83]           -4.00 [-19.85, 11.85]           -17.00 [-31.09, -2.91]           -14.00 [-24.87, -3.13]           -11.40 [-14.39, -8.41]           -4.00 [0.23, 7.17]           -10.65 [-21.01, -0.30]           -20.00 [-25.29, -14.71]           -0.00 [-25.29, -14.71]           -0.00 [-25.29, -14.71]           -10.65 [-21.01, -0.30]           -20.00 [-25.29, -14.71]           -4.00 [-27.83, -11.71]           -20.00 [-25.29, -14.71]           -5.00 [-16.99, 4.99]           -27.00 [-42.29, -11.71]           -20.00 [-25.29, -14.71]           -20.00 [-25.29, -14.71]           -5.00 [-16.99, 4.99]           -27.00 [-42.29, -11.71]           -20.00 [-25.29, -14.71]           -3.00 [-25.20, -14.71]           -5.00 [-23.45, -11.20]           -4.50 [-23.45, -11.55]           -22.00 [-32.45, -11.55]           -22.00 [-32.45, -11.55]           -22.00 [-32.45, -11.55]           -22.00 [-32.45, -11.55]           -4.50 [-23.15, 14.15]           -4.50 [-23.15, 14.16]           -6.40 [-14.44, 1.64]           -3.98 [0.79, 717]	2022   2021   2020   2018   2016   2016   2022   2021   2020   2018   2020   2020   2020   2019   2016	Favours [experimental] Favours [control] Mean Difference
rest for overall effect: Z = 5.24 (P rest for subaroup differences: Chi <b>Study or Subgroup</b> <b>1.2.1 Isolated AVR patients</b> Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020 Augusto D'Onofrio et al, 2020 Stephan Ensminger et al, 2016 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 145.31; CI Fest for overall effect: Z = 2.02 (f <b>1.2.2 Combined AVR patients</b> Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Diver J. Liakopoulos et al, 2021 Diver J. Liakopoulos et al, 2021 Stephan Ensminger et al, 2022 Diver J. Liakopoulos et al, 2021 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 24.20; Chi Fest for overall effect: Z = 5.23 (f <b>1.2.3 Overall AVR patients</b> Dilver J. Liakopoulos et al, 2020 Martin Hartrumpf et al, 2020 Martin Hartrumpf et al, 2020 Paolo Berretta et al, 2019 Stephan Ensminger et al, 2018 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 76.51; Chi	< 0.0000 i <sup>2</sup> = 2.64. ( Mean 64.8 74 83.3 75 66.3 61.8 hi <sup>2</sup> = 144. P = 0.04) 96.5 96.4 i <sup>2</sup> = 6.53, P < 0.000 85 90 90.3 94.3 81.2 76.3 61.75 i <sup>2</sup> = 50.64	1) df = 2 (f SU 27.5 27 35.8 18 20.8 5.6 33. df = 41.6 36 36 33. df = 41.6 36 33. df = 41.6 36 33. df = 33. df = 32 35 32 35 35 35 35 35 35 35 35 35 35	P = 0.2           Total           823           45           60           603           16           1697           467           62           57           207           793           P = 0.0           107           107           102           102           104           105           102           16           1408	7).  ² = : Mean 86.4 78 100.3 89 77.7 57.8 (0.000 116.5 100 132 116 (0.09);  ² = 91 112 113 98.8 89.4 82.7 57.77	RD SD 29.7 46 24.1% 29.7 46 24 37 23.1 4.2 01); I <sup>2</sup> 40.9 26 49 43 30 4.2 54% 37 48 29.5 26.8 30.1 29.3 4.25	Tota 822 43 19 54 314 27 1280 = 97% 467 64 63 152 746 107 117 38 33 404 102 27 829	<ul> <li>7.0%</li> <li>4.5%</li> <li>4.9%</li> <li>5.6%</li> <li>7.0%</li> <li>7.0%</li> <li>36.0%</li> <li>7.0%</li> <li>5.6%</li> <li>4.6%</li> <li>6.2%</li> <li>23.1%</li> <li>5.5%</li> <li>5.7%</li> <li>5.3%</li> <li>3.9%</li> <li>7.0%</li> <li>6.2%</li> <li>7.0%</li> </ul>	IV. Random, 95% C           -21.60 [-24.37, -18.83]           -4.00 [-19.85, 11.85]           -17.00 [-31.09, -2.91]           -14.00 [-24.87, -3.13]           -11.40 [-14.39, -8.41]           -4.00 [0.23, 7.17]           -10.65 [-21.01, -0.30]           -20.00 [-25.29, -14.71]           -0.00 [-25.29, -14.71]           -0.00 [-25.29, -14.71]           -10.65 [-21.01, -0.30]           -20.00 [-25.29, -14.71]           -4.00 [-27.83, -11.71]           -20.00 [-25.29, -14.71]           -5.00 [-16.99, 4.99]           -27.00 [-42.29, -11.71]           -20.00 [-25.29, -14.71]           -20.00 [-25.29, -14.71]           -5.00 [-16.99, 4.99]           -27.00 [-42.29, -11.71]           -20.00 [-25.29, -14.71]           -3.00 [-25.20, -14.71]           -5.00 [-23.45, -11.20]           -4.50 [-23.45, -11.55]           -22.00 [-32.45, -11.55]           -22.00 [-32.45, -11.55]           -22.00 [-32.45, -11.55]           -22.00 [-32.45, -11.55]           -4.50 [-23.15, 14.15]           -4.50 [-23.15, 14.16]           -6.40 [-14.44, 1.64]           -3.98 [0.79, 717]	2022   2021   2020   2018   2016   2016   2022   2021   2020   2018   2020   2020   2020   2019   2016	Favours [experimental] Favours [control] Mean Difference
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est for overall effect: Z = 5.24 (P est for subarouo differences: Chi <b>Study or Subgroup</b> <b>1.2.1</b> Isolated AVR patients Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Martin Hartrumpf et al, 2020 Stephan Ensminger et al, 2018 Gederica Jiritano et al, 2016 Subtotal (95% CI) eterogeneity: Tau <sup>2</sup> = 145.31; Cl est for overall effect: Z = 2.02 (f <b>1.2.2 Combined AVR patients</b> Paolo Berretta et al, 2022 Dilver J. Liakopoulos et al, 2021 Mugusto D'Onofrio et al, 2020 Stephan Ensminger et al, 2021 Diver J. Liakopoulos et al, 2021 Subtotal (95% CI) eterogeneity: Tau <sup>2</sup> = 24.20; Chi est for overall effect: Z = 5.23 (f <b>4.2.3 Overall AVR patients</b> Dilver J. Liakopoulos et al, 2020 Aartin Hartrumpf et al, 2020 Martin Hartrumpf et al, 2020 Martin Hartrumpf et al, 2020 Martin Hartrumpf et al, 2020 Aas Gotzmann et al, 2020 Paolo Berretta et al, 2019 Stephan Ensminger et al, 2018 Subtotal (95% CI) eterogeneity: Tau <sup>2</sup> = 76.51; Chi est for overall effect: Z = 2.32 (f Fotal (95% CI)	< 0.0000 i <sup>2</sup> = 2.64. ( Mean 64.8 74 83.3 75 66.3 61.8 P = 0.04) 96.5 94 105 96.4 105 96.4 12 = 6.53, P < 0.000 855 900 90.3 94.3 81.2 76.3 61.75 92 12 = 50.64 P = 0.02)	1) df = 2 (f SU 27.5 27 35.8 18 20.8 5.6 33. df = 41.6 36 36 33. df = 3 ( 001) 34 32 36 38 28.9 29.3 5.62 , df = 6	P = 0.2           Total           823           45           60           603           16           1697           4677           62           57           207           793           P = 0.0           107           117           80           21           965           102           16           1408           (P < 0	7).  ² = : Mean 86.4 78 100.3 89 77.7 57.8 (0000) 116.5 100 132 116 009);  ² = 91 112 113 98.8 89.4 82.7 57.77 .00001	RD SD 29.7 46 24.1% 40.9 26 40.9 26 40.9 26 49 43 37 48 29.5 26.8 30.1 29.3 4.25 26.8 30.1 29.3 4.25	Tota 822 43 19 54 31 27 1280 = 97% 467 64 463 152 746 107 117 35 33 404 102 27 829 38%	<ul> <li>7.0%</li> <li>4.5%</li> <li>4.5%</li> <li>5.6%</li> <li>7.0%</li> <li>36.0%</li> <li>7.0%</li> <li>36.0%</li> <li>7.0%</li> <li>4.6%</li> <li>23.1%</li> <li>5.3%</li> <li>5.3%</li> <li>5.3%</li> <li>5.3%</li> <li>7.0%</li> <li>41.0%</li> <li>100.0%</li> </ul>	IV. Random, 95% C           -21.60 [-24.37, -18.83]           -4.00 [-19.85, 11.85]           -17.00 [-31.09, -2.91]           -14.00 [-24.87, -3.13]           -11.40 [-14.39, -8.41]           -4.00 [0.23, 7.17]           -10.65 [-21.01, -0.30]           -20.00 [-25.29, -14.71]           -0.00 [-25.29, -14.71]           -0.00 [-25.29, -14.71]           -10.65 [-21.01, -0.30]           -20.00 [-25.29, -14.71]           -4.00 [-27.83, -11.71]           -20.00 [-25.29, -14.71]           -5.00 [-16.99, 4.99]           -27.00 [-42.29, -11.71]           -20.00 [-25.29, -14.71]           -20.00 [-25.29, -14.71]           -5.00 [-16.99, 4.99]           -27.00 [-42.29, -11.71]           -20.00 [-25.29, -14.71]           -3.00 [-25.20, -14.71]           -5.00 [-23.45, -11.20]           -4.50 [-23.45, -11.55]           -22.00 [-32.45, -11.55]           -22.00 [-32.45, -11.55]           -22.00 [-32.45, -11.55]           -22.00 [-32.45, -11.55]           -4.50 [-23.15, 14.15]           -4.50 [-23.15, 14.16]           -6.40 [-14.44, 1.64]           -3.98 [0.79, 717]	2022   2021   2020   2018   2016   2018   2016   2022   2021   2020   2020   2020   2020   2020   2019   2016	Favours [experimental] Favours [control] Mean Difference
Test for overall effect: Z = 5.24 (P Test for subaroup differences: Chi Study or Subgroup	< 0.0000 i <sup>2</sup> = 2.64. ( Mean 64.8 74 83.3 75 66.3 61.8 P = 0.04) 96.5 94 105 96.4 i <sup>2</sup> = 6.53, P < 0.000 85 90 90.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 81.2 76.3 85.3 90.9 90.3 81.2 76.3 81.2 77.3 81.2 81.	1) df = 2 (f SU SD 27.5 27 35.8 18 20.8 5.6 33. df 41.6 36 33.6 df = 3 ( 01) 34 32 36 38 28.9 29.3 5.62 , df = 6 67, df = 6 67, df = 6	P = 0.2           Total           823           45           60           603           16           1697           4677           62           57           207           793           P = 0.0           107           117           80           21           965           102           16           1408           (P < 0	7).  ² = : Mean 86.4 78 100.3 89 77.7 57.8 (0000) 116.5 100 132 116 009);  ² = 91 112 113 98.8 89.4 82.7 57.77 .00001	RD SD 29.7 46 24.1% 40.9 26 40.9 26 40.9 26 49 43 37 48 29.5 26.8 30.1 29.3 4.25 26.8 30.1 29.3 4.25	Tota 822 43 19 54 31 27 1280 = 97% 467 64 463 152 746 107 117 35 33 404 102 27 829 38%	<ul> <li>7.0%</li> <li>4.5%</li> <li>4.5%</li> <li>5.6%</li> <li>7.0%</li> <li>36.0%</li> <li>7.0%</li> <li>36.0%</li> <li>7.0%</li> <li>4.6%</li> <li>23.1%</li> <li>5.3%</li> <li>5.3%</li> <li>5.3%</li> <li>5.3%</li> <li>7.0%</li> <li>41.0%</li> <li>100.0%</li> </ul>	<ul> <li>IV. Random, 95% C</li> <li>-21.60 [-24.37, -18.83]</li> <li>-4.00 [-19.85, 11.85]</li> <li>-17.00 [-31.09, -2.91]</li> <li>-14.00 [-24.87, -3.13]</li> <li>-11.40 [-14.39, -8.41]</li> <li>4.00 [0.83, 7.17]</li> <li>-10.65 [-21.01, -0.30]</li> <li>-27.00 [-42.29, -14.71]</li> <li>-6.00 [-16.99, 4.99]</li> <li>-27.00 [-42.29, -11.71]</li> <li>-19.60 [-27.83, -11.37]</li> <li>-17.91 [-24.61, -11.20]</li> <li>-20.00 [-32.45, -11.55]</li> <li>-22.00 [-32.45, -11.55]</li> <li>-22.00 [-34.86, -10.54]</li> <li>-4.50 [-23.15, 14.15]</li> <li>-8.20 [-14.64, 1.64]</li> <li>3.98 [0.79, 7.17]</li> <li>-8.77 [-16.18, -1.37]</li> </ul>	2022   2021   2020   2018   2016   2018   2016   2022   2021   2020   2020   2020   2020   2020   2019   2016	Favours [experimental] Favours [control] Mean Difference

FIGURE 5

Mean difference (MD) of aortic cross-clamp (ACC) (A) and cardiopulmonary bypass (CPB) (B) times in sutureless (SU) versus rapid-deployment (RD) aortic valve replacement (AVR). Overall pooled analyses from isolated AVR patients, combined AVR patients, and AVR patients are shown. Compared with the RD group, the SU group is associated with a significantly less aortic cross-clamp time (MD: -10.12; 95% CI: -13.90 to -6.33; p < 0.00001;  $I^2 = 94\%$ ), and similarly, with a significantly less cardiopulmonary bypass time (MD: -11.63; 95% CI: -17.14 to -6.13; p < 0.0001;  $I^2 = 94\%$ ). SD, standard deviation; IV, inverse-variance; CI, confidence interval.

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Two meta-analyses (30, 34) anchored on the comparison of the sutureless and rapid-deployment aortic valves in SURD-AVR had been published before our study was done. Nevertheless, two aspects (paravalvular leak and pacemaker implantation) of our analysis presented negative results, showing slight differences with the conclusions of the two previous studies. Published studies may be responsible for causing discrepancies at different times, discrepancies in inclusion criteria, and differences in the exact definition of study outcomes. However, it is noteworthy and distinctive that compared with other studies to date, our study covers the largest period, the largest number of patients, the most significant number of included studies, all types of early clinical results, and the use of two valve size gradient matching methods, to enable a comprehensive and objective comparative analysis.

There are several limitations in our analysis that merit a scrupulous consideration. First, we included only 10 studies overall; also, we did not include any RCT. Although propensity score matching was performed in more than half of the included studies to equalize confounders in non-randomized studies similar to randomization, there is no denying the potential selection bias of our investigators. Second, SURD-IR and Germany are the majority contributors to the patient data source that we collected in the study, which means a more homogeneous region and race limit the generalizability of analysis results. Third, because follow-up was patchy across studies, there is a need for comparing the efficacy and durability of the two valves in the medium and long term. Fourth, the results of ACC and CPB times showed high heterogeneity. Even though we performed leave-one-out sensitivity analysis and subgroup analysis, we still could not well locate and reduce the source of heterogeneity. Fifth, although we performed subgroup analysis by valve size to ensure precise matching, no clear distinction could be perceived between Perceval S (Livanova PLC, London, UK) and Perceval S (Sorin Group, Saluggia, Italy) in the results of pooled estimates reported in our study. Last, potential publication bias cannot be definitively ruled out, even though both Egger's test and the funnel plots suggest no potential publication bias.

# Conclusion

Although further trials and reviews are required for making a more detailed and deterministic comparison between the valves in SURD-AVR, particularly clinical outcomes in the medium and long term in practice, our findings lend support to the notion that sutureless aortic valve replacement is associated with significantly higher postoperative mean and peak transvalvular pressure gradients of the aortic valve compared with rapiddeployment aortic valve replacement in overall and subgroup analyses. Sutureless aortic valve replacement provided visible benefits to patients in terms of intraoperative performance as there was a significant reduction in ACC and CPB times compared with rapid-deployment aortic valve replacement. We also discussed the role of different risk predictors to guide valve selection. In conclusion, clinical decision-making should necessitate thoughtful valve selection for all patients prior to SURD-AVR, and in this context, it can be said that both Perceval and Intuity valves are rising stars in the bioprosthesis firmament, complementing each other very well.

## Data availability statement

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author.

## Author contributions

Conceptualization and design were done by YX, CW, HZ, CL, HW, and YZ; data collection and assembly were carried out by CW, ZX, and YL; analyses and interpretation of data were done by YX, CW, and PY; manuscript writing was done by YX and CW; reading and revising the manuscript were done by JH. All authors contributed to the article and approved the submitted version.

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# Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2023. 1123487/full#supplementary-material.

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