## Transcatheter aortic valve implantation (TAVI) versus sutureless aortic valve replacement (SUAVR) for aortic stenosis: a systematic review and meta-analysis of matched studies

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**Background:** With improving technologies and an increasingly elderly populations, there have been an increasing number of therapeutic options available for patients requiring aortic valve replacement. Recent evidence suggests that transcatheter aortic valve implantation (TAVI) is one suitable option for high risk inoperable patients, as well as high risk operable patients. Sutureless valve technology has also been developed concurrently, with facilitates surgical aortic valve replacement (SUAVR) by allow resection and replacement of the native aortic valve with minimal sutures and prosthesis anchoring required. For patients amenable for both TAVI and SUAVR, the evidence is unclear with regards to the benefits and risks of either approach. The objectives are to compare the perioperative outcomes and intermediate-term survival rates of TAVI and SUAVR in matched or propensity score matched studies.

**Methods:** A systematic literature search was performed to include all matched or propensity score matched studies comparing SUAVR versus TAVI for severe aortic stenosis. A meta-analysis with odds ratios (OR) and mean differences were performed to compare key outcomes including paravalvular regurgitation and short and intermediate term mortality.

**Results:** Six studies met our inclusion criteria giving a total of 741 patients in both the SUAVR and TAVI arm of the study. Compared to TAVI, SUAVR had a lower incidence of paravalvular leak (OR =0.06; 95% CI: 0.03–0.12, P<0.01). There was no difference in perioperative mortality, however SUAVR patients had significantly better survival rates at 1 (OR =2.40; 95% CI: 1.40–4.11, P<0.01) and 2 years (OR =4.62; 95% CI: 2.62–8.12, P<0.01).

**Conclusions:** The present study supports the use of minimally invasive SUAVR as an alternative to TAVI in high risk patients requiring aortic replacement. The presented results require further validation in prospective, randomized controlled studies.

**Keywords:** Transcatheter aortic valve replacement; sutureless aortic valve replacement; aortic stenosis; metaanalysis

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## Introduction

Aortic stenosis (AS) is the most common valvular heart disease and its incidence is increasing with an ageing population (1). Untreated AS carries a high mortality of up to 50% within 2 years of symptom appearance (2-4). Surgical aortic valve replacement remains the gold-standard treatment with proven benefits in survival (5,6). However, approximately a third of patients are unsuitable for operative management secondary to a number of factors including poor left ventricular ejection fraction, advanced age or pre-existing comorbidities (7-9). With advances in technology and technique refinement there is much interest in new treatment alternatives, namely: transcatheter aortic valve implantation (TAVI) and sutureless aortic valve replacement (SUAVR).

There has been an increasing emphasis in the realm of aortic stenosis management on the notion of minimally invasive techniques and interventions. Following the publication of the Cohort A results of the PARTNER (Placement of AoRTic TraNscathetER Valve) trial (10), there has been great debate regarding TAVI for high-risk patients with symptomatic severe aortic valve stenosis. In the PARTNER trial, paravalvular regurgitation was more frequent after TAVI, attributed to the nature of the procedure, which does not involve removal of the native calcified and diseased valve. Paravalvular leak in the PARTNER Cohort A trial was associated with increased late mortality, with significant differences in 2-year mortality reported between patients with mild-severe paravalvular leak versus trace paravalvular leak.

SUAVR was developed as an alternative option for this group of patients, and to help overcome drawbacks of traditional minimally invasive aortic valve replacement including prolonged cardiopulmonary bypass durations, cross-clamp times and operative time (11-15). The use of sutureless bioprosthesis has the potential to facilitate minimally invasive aortic valve replacement by reducing the need for sutures the time required for prosthesis anchoring, thus theoretically curtailing risks associated with prolonged operative durations (13,16). It also allows for minimal paravalvular leak since the native diseased valve is resected. A number of observational studies have reported satisfactory clinical and haemodynamic outcomes with reduced operative time (16-21). In comparison to conventional surgical aortic valve replacement, SUAVR delivers comparable mortality with shorter cross-clamp and cardiopulmonary bypass duration (22). Comparisons between SUAVR and TAVI were pooled in a meta-analysis

by Takagi & Umemoto (23), who identified significantly superior short term survival and paravalvular regurgitation rates with SUAVR compared to TAVI. However, small sample size and differences in patient characteristics at baseline may have largely contributed to the findings.

Therefore, the current meta-analysis aims to perform an updated meta-analysis to compare the outcomes of patients undergoing SUAVR and TAVI. To minimise selection bias and underlying differences in baseline characteristics between the two cohorts, we included propensity score matched studies only.

## Methods

### Literature search strategy

A systematic review of studies comparing SUAVR versus TAVI for the treatment of aortic stenosis was performed according to recommended guidelines (24,25). Five electronic databases including MEDLINE, PubMed, Embase, Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews were searched from their date of inception to September 2016. Appropriate free text and MeSH terms were used to identify all studies: "aortic stenosis", "AS", "aortic valve", "aortic valve replacement", "AVR", "sutureless aortic valve replacement", "transcatheter aortic valve implantation", "transcatheter aortic valve replacement", "TAVI", and "TAVR". Reference lists of all articles found were searched to further identify potentially relevant studies.

#### **Outcome measures**

Baseline parameters collected included age, gender, euroSCORE, diabetes mellitus, hypertension, left ventricular ejection fraction, renal insufficiency, recent myocardial infarction, chronic obstructive pulmonary disease, peripheral vascular disease and pulmonary hypertension. Outcome variables collected included short term mortality, intermediate term mortality (1 and 2 years), length of hospital stay, pacemaker implantation, major bleeding, stroke/transient ischemic attack, acute kidney injury and paravalvular regurgitation.

## Eligibility criteria

Studies eligible for this systematic review directly compared SUAVR versus TAVI for patients with aortic stenosis. Only

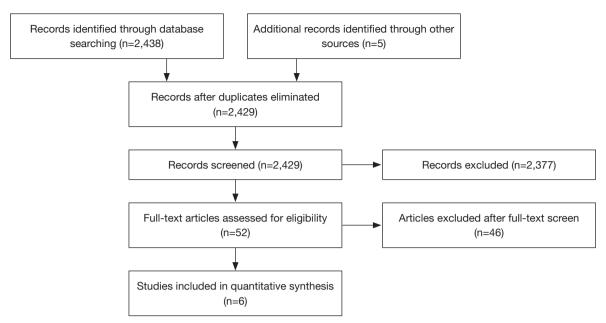


Figure 1 PRISMA flowchart diagram for systematic review from literature search to final analysis.

propensity-score matched studies were included in the present systematic review and meta-analysis. Case reports, series with less than ten patients, abstracts, editorials and expert opinions were excluded. If more than one article had been published from the same center with the same dataset, only the article with the most complete dataset published was used. All studies selected were human trials and in English.

## Data extraction and critical appraisal

Two reviewers (NW, KP) independently appraised studies from date of inception up to September 2016, using a standard form and extracted data on methodology, quality criteria and outcome measures. All extracted and tabulated data were checked by an additional reviewer (SP). The quality of studies was assessed using assessment criteria recommended by the Centre for Evidence Based Medicine (University of Oxford). Discrepancies between reviewers were resolved by discussion and consensus was reached.

#### Statistical analysis

The odds ratio (OR) was used as a summary statistic. In the present study, both fixed- and random-effect models were tested. A random-effects model was used as it was assumed that there were variations between studies.  $\chi^2$  tests were used

to study heterogeneity between trials. I<sup>2</sup> statistic was used to estimate the percentage of total variation across studies, owing to heterogeneity rather than chance, with values greater than 50% considered as substantial heterogeneity. I<sup>2</sup> can be calculated as: I<sup>2</sup> =100% × (Q – df)/Q, with Q defined as Cochrane's heterogeneity statistics and df defined as degree of freedom. If there was substantial heterogeneity, the possible clinical and methodological reasons for this were explored qualitatively. In the present meta-analysis, the results using the random-effects model were presented to take into account the possible clinical diversity and methodological variation between studies. Specific analyses considering confounding factors were not possible because raw data were not available. All P values were 2-sided.

#### Results

A total of 6 studies (26-31) were identified which compared SUAVR and TAVI via propensity score matching, giving a total of 741 patients in each arm (*Figure 1*; *Table 1*). Five of the 6 studies enrolled predominantly high risk patients for TAVI (26-29,31) whilst 1 study compared SUAVR and TAVI in intermediate-high risk patients (30). One study (32) which did not perform propensity score matching, was excluded. 5 of the 6 studies reported follow-up duration of at least 1 year (27-31), whilst one study confined the analysis to hospital outcomes (26). The quality assessment of each

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Table 1 Study characteristics

First author	Year	Country	Study period	Design	n (SUAVR)	n (TAVI)	Type of SUAV	Type of TAV	Predominant incision	Notes
Biancari	2016	Italy	2007–2014	PSM	144	144	Perceval	Sapien, CoreValve, Portico, Lotus	Mini sternotomy	High risk patients received TAVI
D'Onofrio	2016	Italy	2007–2014	PSM	214	214	Perceval	Sapien or Sapien XT	NR	High risk patients received TAVI; Aortic annulus size between 19 and 27 mm sinotubular: aortic annulus ratio <1.3
Kamperidis	2015	Netherlands	2007–2013	PSM	40	40	3F Enable	Sapien XT or CoreValve	Medial sternotomy	High risk patients
Miceli	2016	Italy	2008–2013	PSM	37	37	Perceval	Sapien	Right mini- thoracotomy	High risk patients considered for TAVI
Muneretto	2015	Italy	2007–2014	PSM	204	204	Perceval	Stented/stentless bioprosthesis	Mini J-sternotomy	Intermediate-high risk patients only
Santarpino	2015	Germany	2010–2015	PSM	102	102	Perceval	Sapien, Sapien XT or Sapien 3	NR	High frailty and euroSCORE >20% underwent TAVI

MI, minimal incision; NR, not recorded; PC, prospective cohort; PSM, propensity score matched, SUAVR, sutureless aortic valve replacement; TAVI, transcatheter aortic valve implantation

Table 2 Quality assessment of included studies

Assessment	Biancari	D'Onofrio	Kamperidis	Miceli	Muneretto	Santarpino
Clear definition of study population	Yes	Yes	Yes	Yes	Yes	Yes
Clear definition of outcomes and outcome assessment	Yes	Yes	Yes	Yes	Yes	Yes
Independent assessment of outcome parameters	No <sup>a</sup>					
Sufficient duration of follow-up	No	Yes	Yes	Yes	Yes	Yes
No selective loss during follow-up	Yes	Unclear	Unclear	Unclear	Unclear	Unclear
Important confounders and prognostic factors identified	Yes	Yes	Yes	Yes	Yes	Yes

<sup>a</sup>, lack of blinding during outcome assessment, not independently assessed by multiple investigators.

#### study is presented in Table 2.

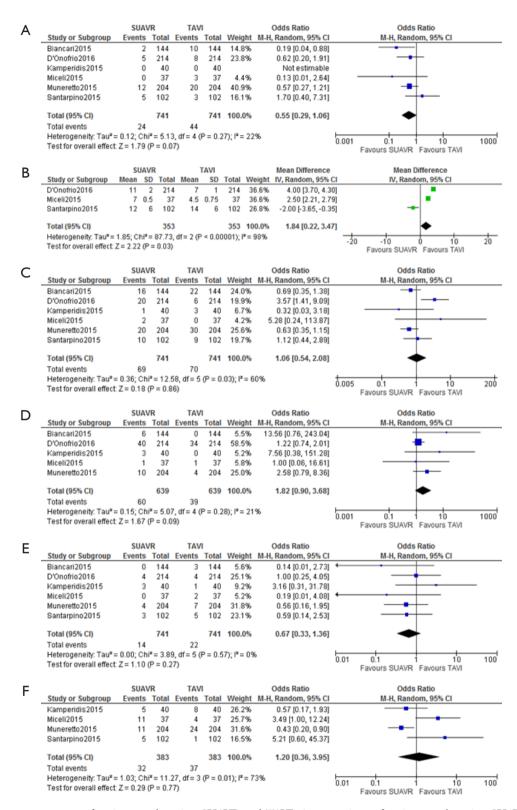
The baseline characteristics of patients undergoing SUAVR compared to TAVI are shown in *Table 3*. Pooled meta-analysis for SUAVR *vs.* TAVI showed no significant differences at baseline for age (mean difference -0.16; 95% CI: -0.90-0.57, P=0.66), gender (OR =0.91; 95% CI: 0.74-1.13, P=0.41), diabetes mellitus (OR =1.02, 95% CI: 0.79-1.32, P=0.90), hypertension (OR =1.01; 95% CI: 0.62-1.65, P=0.97), renal insufficiency (OR =0.88; 95% CI: 0.69-1.12, P=0.30), recent myocardial infarction (OR =0.94; 95% CI: 0.48-1.84, P=0.86), chronic obstructive pulmonary disease (OR =0.95, 95% CI: 0.74-1.22, P=0.70), peripheral vascular disease (OR =1.11, 95% CI: 0.80-1.53, P=0.54), and pulmonary hypertension (OR =0.99, 95% CI: 0.72-1.36, P=0.94). However, TAVI patients had a significantly higher

log EUROscore than SUAVR by a single point (mean difference 1.00; 95% CI: 0.13–1.87, P=0.02).

Table 4 shows the postoperative outcomes of the 6 studies comparing SUAVR and TAVI. Pooled meta-analysis of postoperative outcomes comparing SUAVR and TAVI are shown in *Figure 2*. The perioperative mortality rate showed a non-significant trend favouring improved survival with SUAVR over TAVI (OR =0.55; 95% CI: 0.29–1.06, P=0.07). Patients who underwent SUAVR had a significantly increased length of hospital stay (mean difference 1.84; 95% CI: 0.22–3.47, P=0.03). There was a trend towards major bleeding or bleeding requiring re-exploration in patients who underwent SUAVR compared to TAVI (OR =1.82; 95% CI: 0.90–3.68, P=0.09). There was no significant difference in need for pacemaker implantation (P=0.86),

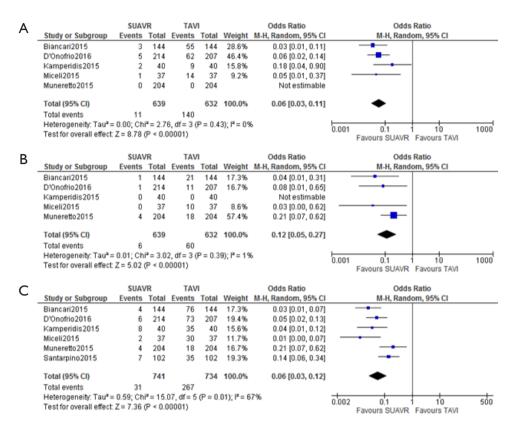
Table 3 Pat	Table 3 Patient characteristics	eristics																				
40	Age		Male	ile	log EuroScore	Score	MD	4	보		LVEF (%)	(%)	Ē		Prior M	Σ	СОРD	Q	PVD	ρ	Pulmonary HT	ary HT
Study	SUAVR TAVI	1	SUAVR TAVI	TAVI	SUAVR	TAVI	SUAVR	TAVI	SUAVR	TAVI	SUAVR	TAVI	SUAVR	TAVI	SUAVR	TAVI	SUAVR	TAVI	SUAVR	TAVI	SUAVR	TAVI
Biancari	79.4±5 79	9.0±6	56/144	54/144	79.4 $\pm 5$ 79.0 $\pm 6$ 56/144 54/144 4.1 $\pm 3^{a}$ 3.6 $\pm 3^{a}$	3.6±3ª	RN	NR	RN	RN	RN	RN	46/144 48/144		5/144 3/144	3/144	38/144 35/144	35/144	NR	NR	92/144	92/144
D'Onofrio	D'Onofrio 77.4±5 77.7±8 76/214 75/214 10.5±6 12.4±9	7.7±8	76/214	75/214	10.5±6	12.4±9	59/214 58/214	58/214	NR	NR	57.7±9 :	57.7±9 58.2±10	67/214 70/214	70/214	NR	RN	39/214 36/214		46/214	46/214 48/214 168/214 170/214	168/214	170/214
Kamperidis	Kamperidis 79±5 79±6		40/40	40/40	40/40 40/40 15.9±11 15.5±8	15.5±8	RN	NR	RN	NR	59.9±10 59.7±10	59.7±10	NR	NR	NR	RN	NR	NR	NR	NR	NR	NR
Miceli	79±5 78	3.8±7	13/37	15/37	79±5 78.8±7 13/37 15/37 16.1±11 15/7±9	15/7±9	10/37	7/37	32/37	31/37	52.6±10 50.6±8	50.6±8	NR	NR	NR	NR	8/37	11/37	11/37	9/37	10/37	9/37
Muneretto	79±4	80±2	99/204	113/204	99/204 113/204 18.9±6 19.5±7			62/204	57/204 62/204 138/204 129/204 55.1±7 54.6±7	129/204	55.1±7	54.6±7	31/204 44/204	44/204	12/204 15/204	15/204	49/204 56/204		40/204 43/204	43/204	NR	NR
Santarpino 80±4 79±7 42/102 44/102 17±14 18±11 40/102 37/102 88/102	80±4 7	7±0	42/102	44/102	17±14	18±11	40/102 ;	37/102		94/102	58±9	54±14	34/102 33/102		1/102 1/102		22/102 24/102	24/102	27/102 16/102	16/102	NR	NR
P-value	0.66		0.41		0.02		0.13		0.97		0.24		0.30		0.86		0.70		0.54		0.94	
<sup>a</sup> , log Euros <sup>i</sup> vascular dis	<sup>4</sup> , log Euroscore II; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HT, hypertension; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NR, not recorded; PVD, peripheral vascular disease; RI, renal insufficiency; SUAVR, sutureless aortic valve replacement; TAVI, transcatheter aortic valve implantation.	PD, chr nal insi	onic obst ufficiency	tructive <sub>f</sub>	pulmonary 3, sutureles	disease is aortic	; DM, dia valve rep	betes m laceme	sease; DM, diabetes mellitus; HT, hypertension; LVEF, left ventricular ej aortic valve replacement; TAVI, transcatheter aortic valve implantation.	, hyperte anscath	snsion; LVI eter aortic	EF, left ve valve im	ntricular ∈ plantation	ejection fi	raction; 1	dl, myoc	ardial infi	arction; 1	NR, not re	ecorded;	PVD, per	ipheral

Study	Perioperative mortality	ative lity	Hospital stay (d)	oital (d)	Pacemaker Implantation	naker tation	Major bleeding <sup>b</sup>	Major leeding <sup>b</sup>	Stroke/TIA	ATT/€	AKI	U	Any	Any PVR	Mild	Mild PVR	}-boM PV	Mod-severe PVR	1-y surv	1-year survival <sup>c</sup>	2-year surviva	2-year survival <sup>c</sup>
	SUAVR TAVI	TAVI	SUAVR	TAVI	SUAVR TAVI SUAVR TAV	TAVI	SUAVR	TAVI	SUAVR	TAVI	SUAVR	TAVI	SUAVR	TAVI	SUAVR	TAVI	SUAVR	TAVI	SUAVR	TAVI	SUAVR	TAVI
Biancari	2/144 10/144	0/144	NR	RN	NR 16/144 22/144 6/144	22/144	6/144	0/144	0/144	3/144	NR	NR	4/144	76/144	3/144	55/144	1/144	21/144	NR	NR	NR	NR
Kamperidis 0/40 0/40	0/40	0/40	NR	NR	1/40 3/40	3/40	3/40	0/40	3/40	1/40	5/40	8/40	8/40	35/40	2/40	9/40	0/40	0/40	NR	NR	37/40	35/40
Muneretto $12/204^a 20/204^a$	12/204ª 2	0/204ª	NR	NR	20/204	30/204	NR 20/204 30/204 10/204	4/204	4/204	7/204	11/204	24/204	4/204	18/204	0/204	0/204	4/204	18/204	198/204	184/204	18/204 198/204 184/204 194/204	162/204
Santarpino 5/102 3/102 12±6 14±6 10/102 9/102	5/102	3/102	12±6	14±6	10/102	9/102	NR	NR	3/102	5/102	5/102	1/102	7/102	35/102	NR	NR	NR	NR	NR	NR	101/102	95/102
D'Onofrio	5/214 <sup>a</sup> 8/214 <sup>a</sup>	3/214ª	11±5	7±2	11±5 7±2 20/214 6/214	6/214		40/214 34/214	4/214	4/214	NR	NR	6/214	73/207	5/214	62/207	1/214	11/207	11/207 202/214 194/214	194/214	NR	NR
Miceli	0/37 3/37	3/37		4.5±2	7±2 4.5±2 2/37 0/37	0/37	1/37	1/37	0/37	2/37	11/37	4/37	2/37 <sup>d</sup>	30/37 <sup>d</sup>	1/37	14/37	0/37	10/37	34/37	29/37	34/37	24/37
<sup>1</sup> , 30-day mortality; <sup>b</sup> , major bleeding or bleeding requiring re-exploration; <sup>c</sup> , calculated by multiplying the percentage of patients who survived at 1 and 2 years by the total number of patients; <sup>d</sup> , includes trivial paravalvular regugitation. AKI, acute kidney injury; Mod, moderate; PVR, paravalvular leak; SUAVR, sutureless aortic valve replacement; TAVI, transcatheter aortic valve implantation; TA,	nortality; <sup>b</sup> , rivial parav	major alvular u	bleeding regurgita:	j or ble tion. A	eeding n Kl, acute	equiring kidney	j re-expl injury; N	loration; 1od, mo	°, calcu derate; P	lated by 'VR, par	y multiply avalvular I	ing the peak; SU	percenta; AVR, sutu	ge of pat ıreless ac	ients wh rtic valve	o survive	ed at 1 a nent; TAV	nd 2 yea 1, transca	rs by the ather ao	total nur rtic valve	mber of p implantativ	atients; on; TIA,



**Figure 2** Short-term outcomes of patients undergoing SUAVR and TAVI. A comparison of patients undergoing SUAVR and TAVI in terms of (A) perioperative mortality; (B) length of hospital stay; (C) need for pacemaker implantation; (D) re-exploration for bleeding; (E) incidence of stroke/TIA and (F) incidence of acute kidney injury.

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**Figure 3** The incidence of paravalvular regurgitation for patients undergoing SUAVR and TAVI. Rates of paravalvular leak were stratified into (A) mild paravalvular leak; (B) moderate-severe paravalvular leak and (C) any paravalvular leak.

incidence of stroke and transient ischemic attacks (P=0.27) and acute kidney injury (P=0.77).

The incidence of paravalvular leak was significantly greater in TAVI patients compared to SUAVR (*Figure 3*) (OR =0.06; 95% CI: 0.03–0.12, P<0.01). In particular, SUAVR had lower incidences of mild paravalvular regurgitation (OR =0.05; 95% CI: 0.03–0.11, P<0.01) and moderate-severe paravalvular regurgitation (OR =0.12; 95% CI: 0.05–0.27, P<0.01).

Five of the 6 studies reported intermediate follow-up and were used to determine the survival rate at 1 and 2 years (27-31). 3 studies reported the percentage of patients who survived at 1 year (27,29,30) and 4 studies reported the percentage of patients who survived at 2 years (28-31). TAVI patients had 140% increased odds of dying at 1 year compared to SUAVR (OR =2.40; 95% CI: 1.40–4.11, P<0.01). The risk increased even greater with further follow-up, with 360% increased odds of fatality in TAVI vs SUAVR at 2-year follow up (OR =4.62; 95% CI: 2.62–8.12, P<0.01).

#### Discussion

Our findings suggest that SUAVR is a suitable alternative for TAVI in the intermediate to high risk patients with severe aortic stenosis. Although SUAVR is associated with a higher incidence of bleeding and prolonged lengths of hospital stay, there are significantly decreased rates of all grades of paravalvular regurgitation. Takagi and Umemoto (23) performed a meta-analysis which showed acceptable short term outcomes for SUAVR compared to TAVI. Our study updates the analysis with larger patient numbers and longer follow-up. We also attempt to minimize selection bias by including propensity score matched studies only. We found no significant difference in perioperative mortality, however SUAVR was associated with reduced mortality rates at 1- and 2- year follow-up. It is likely that the mortality benefit of SUAVR may be more apparent with longer follow up duration. Furthermore, our study stratifies the incidence of paravalvular leak by severity, and we have shown that SUAVR reduces all grades of regurgitation.

Similar to conventional aortic valve replacement, SUAVR requires valve excision and annular decalcification, but avoids the use of permanent sutures at the decalcified annulus (19,33). Herein lies the potential to reduce operative trauma by minimizing manipulation and facilitating minimally invasive approaches. The faster deployments and reduced procedural time has been associated with a lower rate of transfusion of packed red blood cells, shorter intensive care unit and hospital stay, and reduced hospital costs (34). Furthermore, the idea of minimal invasiveness regarding the surgical incision is complemented by reduced manipulation inside the aortic root, compared with a conventional sutured valve prosthesis implantation. Current guidelines (4) and data from Placement of Aortic Transcatheter Valve (PARTNER) (Cohort B) (2) confirm the benefits of TAVI in inoperable or extreme high-risk surgical patients and the indication for conventional valve replacement in patients at intermediaterisk or low-risk patients.

Minimally invasive SUAVR may be considered an alternative to TAVI in patients with high surgical risk. One of the major limitations of TAVI is the high incidence of paravalvular leak, which is quoted at 70–90% (35-37). This is particularly important as paravalvular regurgitation is associated with increased mortality (38). A reduction in aortic regurgitation after SUAVR is potentially the major advantage of SUAVR over TAVI. Techniques have been developed in an attempt to minimize paravalvular leak in TAVI but with significant complications. Post-dilation has been associated with higher risks of stroke (39) and fatal aortic root injury (40). Regurgitation after TAVI is largely due to a non-uniform compression of the calcified native valve against the aortic wall after deployment of the stent prosthesis. The ridges of calcium hinder adequate stent expansion and subsequent paravalvular spaces are created for possible leaks (37). In contrast, surgery allows for the calcified native valve to be excised and the new prosthesis sutured flush against the aortic annulus, which ameliorates potential paravalvular spaces (37).

Previous studies have shown superior outcomes for SUAVR over TAVI. Biancari showed that SUAVR is associated with lower rates of paravalvular leak and 30-day mortality. However, as the authors suggested, these differences could be attributed to the marked differences in baseline characteristics of patients undergoing SUAVR and TAVI. This is largely due to the indications for TAVI, which are high risk patients who would not be otherwise fit for conventional surgery (2,4). Therefore, studies have employed propensity score matching in an attempt to ameliorate the selection bias when comparing SUAVR and TAVI. Miceli et al. (29) found 1 year survival rates of 91.6% vs. 78.6% at 1 year and 91.6% vs. 66.2% at 2-years after propensity score matching, with no significant differences at baseline between the two groups. Similarly, D'Onofrio et al. (27) also found a 1 year survival rates favouring SUAVR (94.2% vs. 91.6%). However, both studies had non-significant findings, largely due to inadequate sample sizes and high drop out rates. Our results suggest that SUAVR is associated with better 1- and 2- year survival rates. Although this result can be partially explained by the slightly higher euroSCORE in the patients who underwent TAVI, the improved survival is likely a true finding. Similarly, Muneretto (30) found SUAVR to have significantly superior survival outcomes at 2 years (94.9% vs. 79.5%). The authors also concluded that TAVI was an independent predictor for all-cause mortality.

TAVI was initially designed as an alternative for high risk patients and was shown to be non-inferior to conventional surgical aortic valve replacement in this specific subset of patients (2,38). Such encouraging results led to the inclusion of the transcatheter approach in the most up-to-date guidelines and consensus statements on valvular heart disease as an additional therapeutic option for high-risk or inoperable patients (4,41). However, the benefits of TAVI in intermediate risk patients has not been as well elucidated, with CESANA IDEM trials currently being conducted to address this question. Furthermore, of the 4 studies (27-29,31) with intermediate follow-up that recruited high risk patients for TAVI, there were no significant difference in 1- and 2- year mortality. However, when considering intermediate-high risk patients, Muneretto et al. found significantly better survival rates for SUAVR at 1 and 2 years (30). Overall it is difficult to conclude which method has superior intermediate survival rates because differences in patient population likely play an important factor. However, it is likely that SUAVR may be more appropriate for intermediate risk patients. This difference may be explained by 2 key factors: firstly, propensity score matching may not account for all differences at baseline as these studies were non-randomised and in our pooled analysis, the log EUROscore was higher in TAVI by a single point; secondly the dramatically reduced incidences of paravalvular regurgitation may also be responsible for the reduced morality rates.

## Limitations

This meta-analysis has several key limitations and must be interpreted with care. Firstly, we were not able to control for heterogeneity between studies. Although we only included studies with propensity score matching, the lack of randomization can subject the studies to selection bias, which were uncontrolled for. Secondly, there has been limited number of studies examining long term outcomes of SUAVR. Currently our results are limited to short term outcomes and estimated intermediate mortality rates. The role of TAVI versus SUAVR or minimally invasive AVR in the setting of reoperation remains unclear, although a recent review of the literature suggests that both methods are feasible (42). Long-term outcomes of SUAVR will be in part addressed by a multi-center international registry (43). Future directions include a prospective multi-center randomized controlled trial comparing TAVI and SUAVR in intermediate-risk and higher-risk patients with aortic stenosis.

## Conclusions

Our findings suggest that SUAVR remains an alternative to TAVI in the intermediate-high risk patients with severe aortic stenosis. The main advantage for SUAVR, likely lies in the lower rates of paravalvular regurgitation when compared to TAVI. Future studies are needed to compare long term outcomes in randomized trials of intermediatehigh risk patients.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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