Impact of Small Aortic Annuli on the Performance of Transcatheter Aortic Valve Replacement Bioprostheses: An Updated Meta-Analysis of Recent Studies

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A metanalysis of available randomized controlled trials and observational studies comparing self-expanding (SE) and balloon-expandable (BE) bioprostheses in patients with small aortic annulus and aortic stenosis for short- and midterm hemodynamic and clinical outcomes was performed. A total of 21 studies with a total 8,647 patients (SE: n = 4,336 patients vs BE: n = 4,311 patients) were included. SE bioprostheses had a lower postoperative mean gradient at 30 days (Mean Difference [MD] −5.16, 95% confidence interval [CI] 4.7 to 5.5, p <0.001) and at 1 year (MD −6.6, 95%CI 6.1 to 7.03, p <0.001), with a larger indexed effective orifice area (0.17, 95% CI 0.13 to 0.22, p <0.001 and 0.17, 95% CI 0.08 to 0.27, p <0.001) at both time intervals. BE bioprostheses had a higher risk of 30-day and 1-year severe prosthesis-patient mismatch (risk ratio [RR] 1.07, 95% CI 1.04 to 1.09, p <0.001; RR 1.07, 95% CI 1.04 to 1.11, p <0.001). The 30-day and 1 year paravalvular leaks (RR 0.99, 95% CI 0.98 to 0.99, p <0.001; RR 0.89, 95% CI 0.82 to 0.95, p <0.001) and permanent pacemaker implantation (RR 0.97, 95% CI 0.94 to 0.99, p 0.01, I2 = 40%,) were lower in the BE group. BE bioprostheses were associated with a lower risk of in-hospital stroke (RR 0.99, 95% CI 0.98 to 1, p = 0.01). In conclusion, in patients with small aortic annulus and aortic stenosis, SE bioprostheses have superior hemodynamic performance but higher rates of paravalvular leak, permanent pacemaker implantation, and in-hospital stroke. BE bioprostheses were associated with a higher risk of severe prosthesis-patient mismatch. **(Am J Cardiol 2024;229:1−12)**

Keywords: balloon-expandable valves, self-expanding valves, bioprostheses, small aortic annuli, TAVR, meta-analysis

Introduction

Small aortic annulus (SAA) poses significant management concerns in the setting of severe aortic valve stenosis because it strongly predicts a challenging aortic valve replacement (AVR).[1] Patients with SAA eligible for AVR are at a higher risk of prosthesis-patient mismatch (PPM) because they often receive smaller prostheses, resulting in a smaller effective orifice area (EOA) for cardiac output requirements.[2] However, a clear consensus about the cut-off value for defining SAA is missing with heterogeneous definitions.[3] From the surgical experience, an aortic annulus should be defined as small when it could not accommodate a prosthesis size >21 mm or when aortic annulus diameter is <23 mm, measured by echocardiography or by direct sizing.[4]

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The prevalence of SAA ranges from 22% to 44% in the United States and Northern Europe.[4] Female and Asian populations are more likely to present with SAA because of lower body mass index at clinical evaluation.[5]

Despite controversy around its performance, European guidelines recommend the surgical approach as first-line therapy for severe aortic valve stenosis in patients with SAA.[6] Additional techniques, such as aortic root enlargement, have been proposed; however, they are associated with increased procedure complexity and perioperative morbidity and mortality.[7] Conversely, growing evidence supports the comparable and even superior hemodynamic results associated with transcatheter AVR (TAVR), which may represent an alternative for these patients.[8] However, evidence is not conclusive and there is still a gap regarding the comparison between self-expanding (SE) versus balloon-expandable (BE) bioprostheses in these patients.[9] To clarify this issue, this review and meta-analysis aimed to investigate the impact of a SAA on the performance of different prostheses systems.

Methods

The present analysis adheres strictly to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[10] Moreover, it was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO CRD42023463689). Ethical approval was not required for this study-level metanalysis. In addition, patient written informed consent for the study's publication was not received because individual patient information is missing. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Search strategy

We performed comprehensive searches to identify all randomized controlled trials (RCTs) and observational studies that compared short- and midterm clinical and echocardiographic outcomes of patients with severe aortic valve stenosis and SAA who underwent TAVR. Searches were run until April 2024 in the following databases: Ovid MEDLINE, Ovid EMBASE, and The Cochrane Library (Wiley). The search strategy included a combination of the following keywords and Medical Subject Headings: "TAVI," "Transcatheter Aortic Valve Intervention," "TAVR," "Transcatheter aortic valve implantation," "small annulus," "small annuli" and "small aortic annuli," "balloon-expandable," "self-expandable," "BEV," "SEV" (detailed search keywords are listed in Supplementary Table 1).

Study selection and data extraction

Database searches were deduplicated. A total of 3 investigators (G.D.P, R.I., and F.G.) screened the searched database for inclusion and performed data extraction independently. Disagreements were resolved by a fourth author who also checked the extracted data for accuracy (F. D.A.). The selection inclusion criteria were represented as follows: (1) patients aged >18 years with severe aortic valve stenosis and SAA revealed by computed tomography angiography or by echocardiography, (2) patients who underwent TAVR using BE or SE bioprostheses, and (3) short- (30-day) and midterm (1-year) echocardiographic and clinical follow-up. Studies focusing on bicuspid aortic stenosis and SAA or extra-small annulus were excluded (Supplementary List 1).

The publication with the largest cohort was selected for studies with overlapping samples. Animal or in vitro studies, case reports, conference presentations, editorials, reviews and expert opinions were excluded. Full text for the selected studies was pulled for a second round of eligibility screening. Reference lists of articles were also searched to identify other relevant trials.

Data on investigators, year, journal, design, study period, follow-up duration, procedural approach, sample size, patient characteristics, and outcomes were independently extracted by 3 authors (G.D.P, R.I., and F.G.) and verified by a fourth author (F.D.A).

The Cochrane Risk of Bias 2.0 tool assessed the quality of the RCTs,[11] whereas the Risk Of Bias In Non-randomised Studies - of Interventions tool was used for observational studies.[12] Publication bias was assessed using means of funnel plots and the Egger test.

Study definitions

There is no clear agreement on the definition of SAA in previous studies. Therefore, the included studies have used varying definitions, relying on different imaging techniques. Aortic valve annular diameter or perimeter-/area-derived measurements are commonly obtained by echocardiography or by computed tomography angiography. Table 1 lists the summary of the SAA definitions in each study.

Outcomes

In-hospital, 30-day, and 1-year all-cause mortality were the primary end points. The secondary outcomes were cardiovascular death, any stroke, permanent pacemaker implantation (PPI), acute kidney injury (AKI), hemorrhagic events, vascular complications, and in-hospital readmission. Additional echocardiographic outcomes were mean transvalvular gradient (MTG), indexed EOA (iEOA), severe PPM, and at least moderate paravalvular leaks (PVLs). PPM is caused by an imbalance between the EOA of a bioprosthesis and the patient's body surface area. For patients with a body mass index (BMI) <30 kg/m^2, severe PPM is defined as iEOA <0.65 cm^2/m^2, whereas for patients with a BMI >30 kg/m^2, the cutoff for severe PPM is 0.55 cm^2/m^2. In addition, PVL occurs when blood flows around the bioprosthesis because of an incomplete seal.

Statistical analysis

Continuous variables are presented as means (SD) or medians (first and third quartile), whereas categorical variables are expressed as n (%). Statistical pooling for incidence estimates was performed using a restricted maximum likelihood random-effects or Mantel-Haenszel fixed-effects model. Risk ratios (RRs) were chosen as effect sizes, and risk estimates with 95% confidence intervals (CIs) were computed using SPSS v.29 (The Cochrane Collaboration,

Table 1
Characteristics of included studies

First Author	Year	Study Design	Sample size (n)	SE (n)	BE (n)	SAA definition	Devices
Abdelghani et al. CHOICE Trial	2018	Randomized	94	51	43	Mean aortic diameter < 23 mm	CoreValve/ SAPIEN XT
CHOICE-Extend		Non randomized, Prospective	122	44	78		Evolut R/SAPIEN 3
Mosleh et al.	2023	Retrospective	573	236	337	Aortic Valve annuus area < 430 mmq by CTA or 3D TOE	BE: 23 mm SAPIEN 3 SE: 26 mm Evolute R/Evolut PRO
Ferrara et al.	2022	Prospective	131	55	76	Aortic annulus area between 330 and 440 mmq by CTA	BE: 23 mm SAPIEN 3TM SE: ACURATE NeoTM S or M and 26 mm or 29 mm Evolut ProTM
Okuyama et al.	2020	Retrospective	46	13	33	Aortic annulus area < 330 mmq	BE: SAPIEN 3 SE: Evolut R/ Evolute Pro
Jin et al.	2022	Retrospective	1162	233	929	Not Available	BE:23 mm SAPIEN 3 SE: 26 mm – Evolut valve
Okuno et al.	2023	Retrospective, Propensity match	342	171	171	Aortic annulus area < 430 mmq	BE: SAPIEN SE: CoreValve/ Evolut
Leone et al.	2023	Retrospective	1378	1092	286	Annular Perimeter < 72 mm or area < 400 mmq	BE: SAPIEN 3 SE: Evolut R/Pro/ ACURATE Neo/ Portico
Hase et al. (OCEAN-TAVI Registry)	2020	Retrospective, Propensity match	138	69	69	Mean aortic diameter < 23 mm	BE: SAPIEN 3 or SAPIEN XT SE: CoreValve/ Evolut R
Del Trigo et al.	2016	Prospective	62	22	40	Aortic area within 50 mmq by CCTA	BE: SAPIEN XT SE: Portico
Costa et al. OPERA Registry	2022	Propensity match	1174	587	587	Aortic Area/Perimeter < 23 mm	BE: SAPIEN 3 SE: EVOLUT PRO +
Koh et al.	2022	Prospective	123	90	33	Mean aortic diameter < 23 mm	BE: SAPIEN 3/XT SE: CoreValve/Evolut R/ Pro/Portico/Engager
Herrman et al. SMART Trial	2024	Randomized	716	355	361	Annulus Area < 430 mmq	SE: Evolut R/Evolut PRO/ Evolut PRO/Evolut Fx BE: SAPIEN 3/SAPIEN Ultra
Lee et al.	2021	Retrospective	70	45	25	Mean diameter < 23 mm e mean minimal diameter < 21 mm	BE: SAPIEN 3 SE: Evolut R/Pro
Guimaraes et al.	2020	Retrospective, Propensity match	104	52	52	Aortic annulus diameter < 21 mm	BE: SAPIEN XT/3 SE: CoreValve/ Evolut R
Medranda et al.	2022	Retrospective	262	118	144	Aortic annulus area < 430 mmq by CTA	BE: SAPIEN 3 SE: CoreValve/ Evolut Pro/ Pro+
Voigtlaender et al.	2021	Retrospective	1005	717	288	Aortic annulus area < 400 mmq by CTA	BE: SAPIEN 3 SE: Portico /Evolut/ ACURATE Neo
Rogers et al.	2017	Retrospective	62	30	32	Aortic annulus perimeter < 73 mm by CTA	BE: SAPIEN XT/3 SE: CoreValve/Evolut R
Kornyeva et al.	2023	Retrospective, Propensity match	384	192	192	Aortic perimeter < 72 mm or Aortic annulus area < 400 mmq	BE: Not available SE: Evolut R/Pro/ Portico/ ACURATE Neo
Moon et al. (Korean Registry)	2023	Retrospective	68	41	27	Mean diameter < 20 mm by CTA	BE: SAPIEN XT/3 SE: Evolut R/CoreValve
Meguro et al. (Japanese Registry)	2021	Retrospective	193	103	90	Aortic annulus area < 314 mmq	BE: SAPIEN 3 20 mm SE: Evolut R 23 mm

BE = balloon-expandable; CTA = computed tomography angiography; SAA = small aortic annuli; SE = self-expanding; TOE = transesophageal echocardiography.

The Nordic Cochrane Centre, Copenhagen, Denmark). Hypothesis testing for superiority was conducted at the 2-tailed 0.05 level. The I^2 statistic was used to assess heterogeneity, with low heterogeneity defined as 0% to 25%, moderate heterogeneity defined as 25% to 50%, and substantial heterogeneity defined as >50%. When significant heterogeneity was present, a random-effects analysis model was used; otherwise, a fixed-effects analysis model was

used. A sensitivity analysis was performed when significant heterogeneity resulted from the primary analysis. Publication bias was investigated by visual inspection of the funnel plot asymmetry and the Eggers Test. The trim and fill method was performed to identify and correct for funnel plot asymmetry and to adjust the overall effect estimate in the presence of potentially missing studies because of publication bias.

Results

After searching for studies reporting outcomes stratified by valve system, 2 RCTs and 19 observational studies (Supplemental List 1) were included for the quantitative analysis, globally encompassing 8,647 patients with severe aortic stenosis and small annulus who underwent TAVR (PRISMA flow chart in Supplementary Figure 1). Overall, 4,311 patients received BE valves and 4,336 patients received SE valves. The characteristics of the included studies are listed in Table 1, whereas the baseline features of included patients are listed in Table 2. The BE and SE cohorts had comparable preoperative surgical risk as assessed by Society of Thoracic Surgeons predicted risk of mortality score (5.5, interquartile range [IQR] 4.4% to 6.2% vs 5.6, IQR 5% to 6.7%), left ventricular ejection fraction (61, IQR 58% to 63% vs 60, IQR 58% to 62%), and baseline MTG (44, IQR 43 to 49 vs 44, IQR 41 to 49 mm Hg). Similarly, patients with SE vs patients with BE did not differ with respect to aortic annular perimeter (70, IQR 65 to 72 vs 69, IQR 64 to 71 mm) or aortic annular area (373, IQR 349 to 383 vs 364, IQR 342 to 380 mm^2). Additional baseline features are listed in Supplementary Table 3.

The risk of bias assessment for observational studies and RCTs is listed in Supplementary Table 2. The primary end point funnel plot for publication bias evaluation is displayed in Supplementary Figure 2, whereas the results of the main analysis with the Egger's Test are listed in Tables 3 and 4.

All-cause mortality

Pooled results from 5 studies encompassing 3,171 patients (1,215 receiving SE and 1,956 receiving BE) showed no significant difference in terms of in-hospital all-cause death (RR 1, 95% CI 0.99 to 1.01, p = 0.70, I^2 = 0%) (Figure 1). Similarly, the 30-day and 1-year all-cause mortality rates did not differ between the 2 cohorts of patients (2,475 patients: 1,452 receiving SE and 1,023 receiving BE) (RR 1, 95% CI 0.99 to 1.02, p = 0.61, I^2 = 0%) (Figure 1). The pooled results from 13 studies including 6,978 patients (SE: 3,727 patients; BE: 3,251 patients) showed no significant difference in terms of 1-year all-cause mortality between BE and SE bioprostheses (RR 1.02, 95% CI 1 to 1.03, p = 0.07, I^2 = 0%) (Figure 1).

Cardiac death

Pooled results from 4 studies encompassing 1,319 patients (685 receiving SE and 634 receiving BE) showed no significant difference in terms of 30 days cardiac death (RR 1, 95%CI 0.98 to 1.01, p = 0.96, I^2 = 0%) (Figure 2). Similarly, the 1-year cardiac death rates did not differ

Table 2
Overall baseline characteristics of patients

	BE (N=4311)	SE (N=4336)
Baseline characteristics		
Age, y (IQR)	82 (80-83)	82 (81-83)
Female sex, % (IQR)	86 (84-96)	89 (74-94)
BSA, m2 (IQR)	1.71 (1,5-1,77)	1.7 (1,5-1,7)
Diabetes Mellitus, % (IQR)	28 (22-33)	29 (23-34)
Hypertension, % (IQR)	88 (78-89)	85 (74-89)
Hyperlipidemia, % (IQR)	52 (45-66)	59 (51-68)
Coronary Artery Disease, % (IQR)	46 (38-55)	37 (30-53)
Previous PCI, % (IQR)	23 (21-27)	21 (18-25)
Previous MI, % (IQR)	10 (8-14)	10 (9-13)
Peripheral Artery Disease, % (IQR)	14 (9-19)	14 (11-23)
Chronic Obstructive Pulmonary Disease, % (IQR)	12 (7-18)	13 (9-18)
Atrial Fibrillation, % (IQR)	22 (12-26)	22 (18-28)
STS PROM, % (IQR)	5.5 (4.4-6.2)	5.6 (5-6.7)
PRE-PROCEDURAL CHARACTERISTICS		
LVEF % (IQR)	61 (58-63)	60 (58-62)
Pre-operative Mean Gradient, mmHg (IQR)	44 (43-49)	44 (41-49)
Annular Perimeter By CTA, mm (IQR)	70 (65-72)	69 (64-71)
Annular Area By CTA, mm^2 (IQR)	373 (349-383)	364 (342-380)
Post-PROCEDURAL CHARACTERISTICS		
Post-operative Mean Gradient, mmHg (IQR)	**12,2 (11,5-13,7)**	**8 (7.1-9.2)**
Post-operative iEOA, cm2/m2 (IQR)	**0,94 (0,86-1,01)**	**1,07 (0,9-1,2)**

BE = balloon-expandable; BMI = body mass index; BSA = body surface area; CABG = coronary artery bypass graft; CTA = computed tomography angiography; IQR = interquartile range; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; STS = Society of Thoracic Surgeons.

Table 3
Summary of the binary outcomes of the meta-analysis

	SEV vs BEV in SAA patients	
	RR [95%CI]	Egger's Test
In-hospital All cause of mortality	1 [0.99-1.01]	**0.34**
30 days All cause of mortality	1 [0.99-1.02]	**0.78**
1 year All cause of mortality	1.02 [1.00-1.03]	**0.33**
30 days Cardiac Death	1 [0.98-1.01]	**0.88**
1 year Cardiac Death	1 [0-98-1.01]	**0.33**
Periprocedural stroke	0.99 [0.99-1.00]	**0.53**
In-hospital stroke	0.99[0.98-1.01]	**0.31**
1 year stroke	0.99[0.97-1.01]	**0.58**
New Permanent Pacemaker Implantation	0.97[0.94-0.99]	**0.24**
30 days-PVLs	0.99[0.98-0.99]	**0.08**
1 year PVLs	0.89[0.82-0.95]	**0.24**
Severe PPM at 30 days	1.07[1.04-1.09]	**0.09**
Severe PPM at 1 year	1.07 [1.04-1.11]	**0.75**
Vascular complications	0.99[0.98-1]	**0.5**
Major Bleedings	0.99[0.98-1]	**0.42**
1 year Rehospitalization	1[0.98-1.01]	**0.94**

BEV = balloon-expanding valves; PPM = prosthesis-patient mismatch; PVL = paravalvular leak; SAA = small aortic annulus; SEV = self-expanding valves.

Table 4
Summary of the continuous outcomes of the meta-analysis with adjustment using the trim and fill method

	SEV vs BEV in SAA patients		
	MD[95%CI]	Egger's Test	MD [95%CI] adjusted using Trim and Fill Method
MTG at 30 days, mmHg	-4.33[3.67-4.99]	**<0.05**	-5.16[4.7-5.6]
MTG at 1 year, mmHg	-6.18[5.06-7.13]	**<0.05**	- 6.6 [6-7.3]
iEOA at 30 days, mmHg	0.17[0.13-0.22]	**0.2**	-
iEOA at 1 year, mmHg	0.17[0.08-0.27]	**0.3**	-

BEV = balloon-expanding valves; iEOA = indexed effective orifice area; MTG = mean transvalvular gradient; SAA = small aortic annulus; SEV = self-expanding valves.

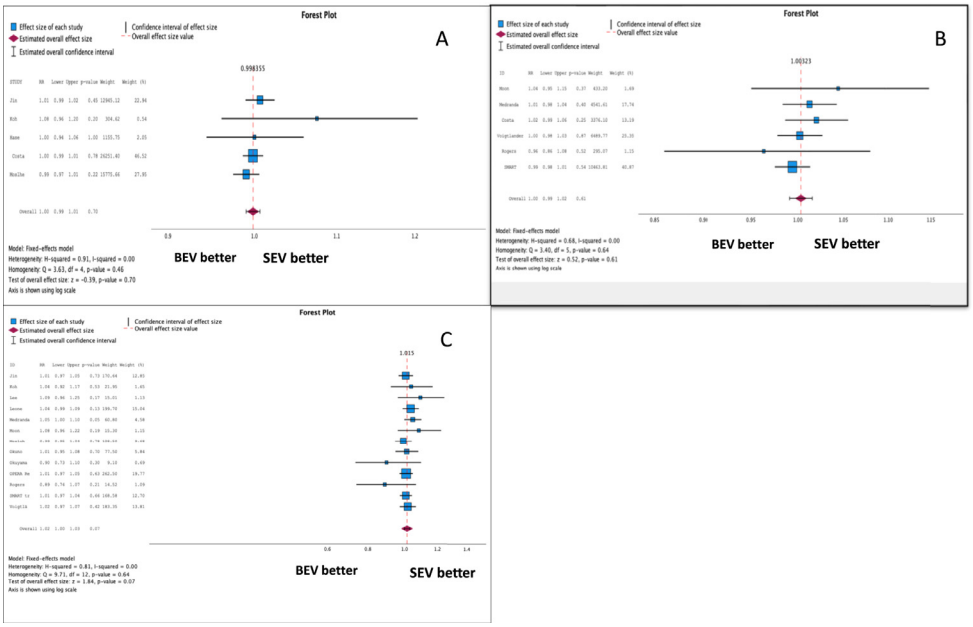

Figure 1. In-hospital (*A*), 30-day (*B*), and 1-year (*C*) all-cause death.

between the 2 cohorts of patients (2,559 patients: 1,708 receiving SE and 851 receiving BE) (RR 1.00, 95% CI 0.98 to 1.01, p = 0.78, I^2 = 6%) (Figure 2).

Any stroke

The analysis showed no significant differences between SE and BE in terms of periprocedural strokes (RR 0.99, 95% CI 0.99 to 1, p = 0.14, I^2 = 0%) (Figure 3). However, the risk of in-hospital stroke was higher in patients with SEV than those with BEV (RR 0.99, 95% CI 0.98 to 1, p = 0.01) (Figure 3). Conversely, after 1 year, the risk of any stroke was comparable between the 2 groups of treatment (RR 0.99, 95% CI 0.97 to 1.01, p = 0.38, I^2 = 18%) (Figure 3).

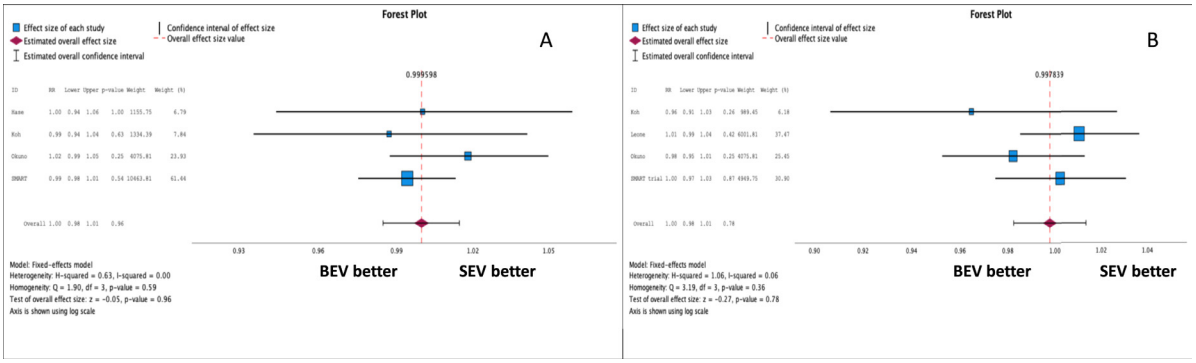

Figure 2. The 30-day (*A*) and 1-year (*B*) cardiac death.

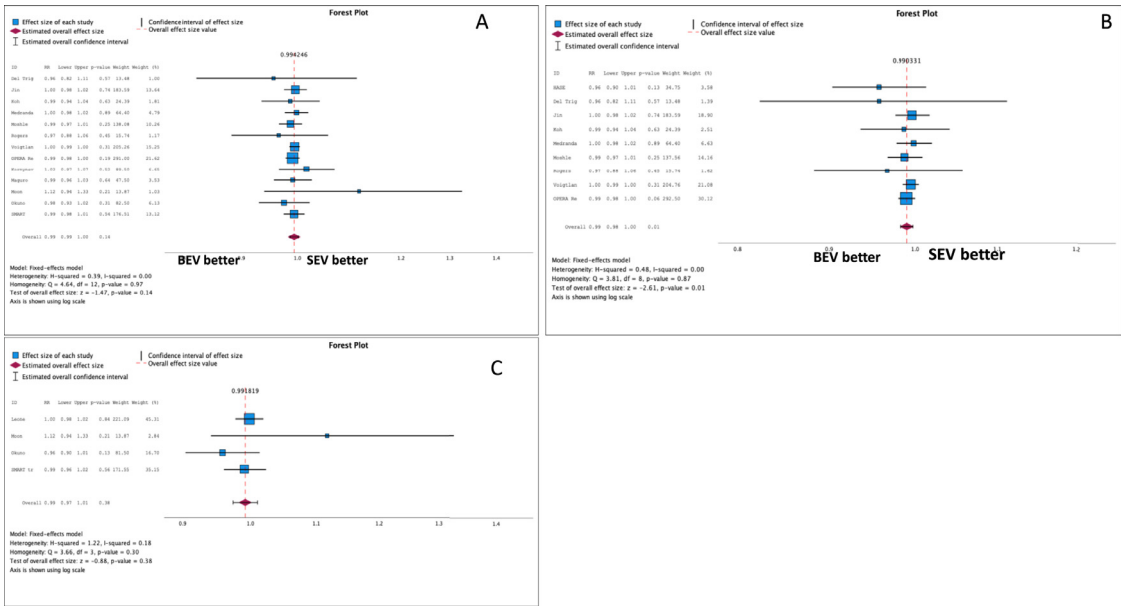

Figure 3. Periprocedural (*A*), in-hospital (*B*), and 1-year (*C*) any stroke.

Major bleedings

The pooled results from 14 studies encompassing 6,890 patients (SE: 3,714 patients; BE: 3,266 patients) showed no significant risk difference in terms of major bleedings between patients receiving SE or BE valves (RR 0.99, 95% CI 0.98 to 1, p = 0.06, I^2 = 0%) (Supplementary Figure 3).

Vascular complications

There was no significant difference in terms of postprocedural vascular complications between the SE and the BE arms (RR 0.99, 95% CI 0.98 to 1, p = 0.08, I^2 16%) (Supplementary Figure 4).

AKI

The analysis showed no significant differences between the SE and BE groups in terms of AKI for patients with SAA (RR 1, 95% CI 1 to 1.01, p = 0.87, I^2 = 0%) (Supplementary Figure 5).

PPI

The pooled results from 18 studies encompassing 7,889 patients (SE: 4,169 patients; BE: 3,720 patients) showed that PPI were more frequently required in patients with SE than those who with BE (RR 0.95, 95% CI 0.93 to 0.98, p = 0.001, I^2 = 53%) (Figure 4). Significant heterogeneity was observed. The results were not affected after the removal of 3 outliers (RR 0.97, 95% CI 0.94 to 0.99, p = 0.01, I^2 = 40%) (Figure 4).

PVLs

PVLs occurred more frequently in patients received SE bioprostheses than those who received BE bioprostheses at 30 days (RR 0.99, 95% CI 0.98 to 1, p = 0.04, I^2 = 33%) (Figure 5). The results were not affected after the removal of 2 studies, which introduced moderate heterogeneity (RR 0.99, 95% CI 0.98 to 0.99, p <0.001, I^2 = 0%) (Figure 5). Similarly, after 1 year, the analysis showed no significant difference between the SE and BE groups in terms of all PVLs (RR 0.93, 95% CI 0.83 to 1.06, p =0.28) (Figure 5).

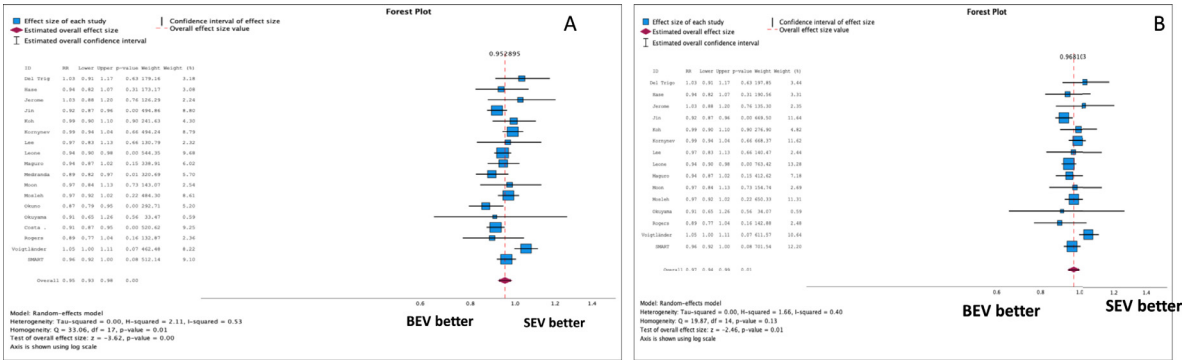

Figure 4. Permanent pacemaker implantation: primary analysis (*A*) and sensitivity analyses (*B*).

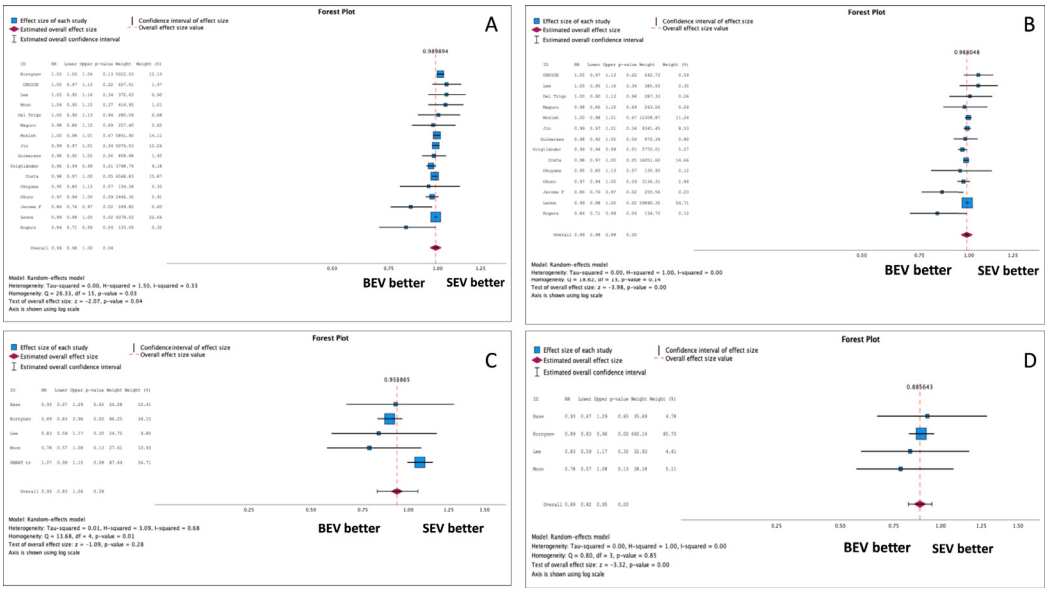

Figure 5. Paravalvular leaks at 30 days: primary analysis (*A*) and sensitivity analyses (*B*) and paravalvular leaks at 1 year: primary analysis (*C*) and sensitivity analyses (*D*).

Significant heterogeneity was reported (I^2 = 68%). After observing the funnel plot and removing the outlier study, the level of heterogeneity decreased (I^2 = 0) and SE bioprostheses were associated with more frequent PVLs than BE bioprostheses (RR 0.89, 95% CI 0.82 to 0.95, p <0.001) (Figure 5).

Severe PPM

The pooled results from 17 studies with a total of 7,085 patients (SE: 4,221 patients, BE: 2,864) showed that SE valves were associated with a lower risk of 30-day severe PPM than BE valves (RR 1.06, 95% CI 1.03 to 1.08, p = 0.001) (Figure 6). Significant heterogeneity was documented (I^2 = 57%). After removing the outlier studies, the level of heterogeneity decreased (RR 1.07, 95% CI 1.04 to 1.09, p <0.001, I^2 = 22%) (Figure 6); however, the result was preserved. Supplementary Figure 6 shows the significant clinical impact of BMI on the occurrence of severe PPM (β coefficient = 0.7, p = 0.007)

Similarly, after 1 year, severe PPM occurred less frequently in patients received SE than those who received BE bioprostheses (RR 1.07, 95% CI 1.04 to 1.11, p <0.001, I^2 = 54%) (Figure 6).

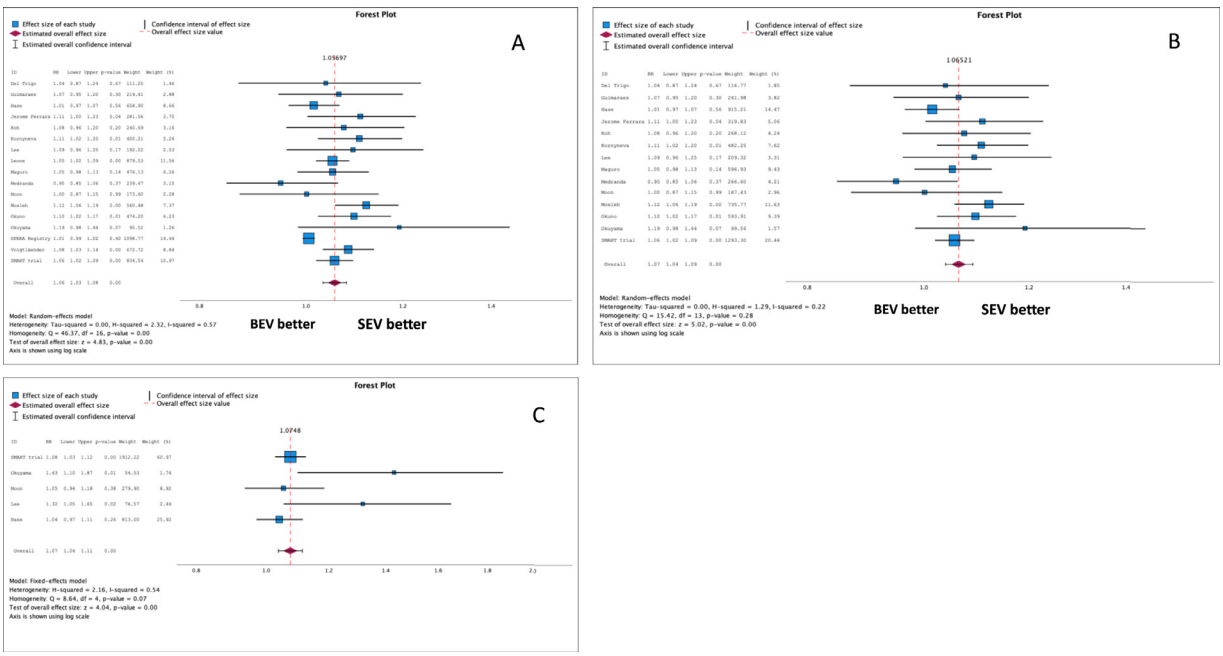

Figure 6. Severe PPM at 30 days: primary (*A*) and sensitivity analyses (*B*) and severe PPM at 1 year (*C*).

One-year hospital readmission

There was no significant differences between SE and BE valve systems in terms of 1 year hospital readmission (RR 1, 95% CI 0.98 TO 1.01, p = 0.51, I^2 = 0%) (Supplementary Figure 7).

MTG

The pooled results from 20 studies, globally encompassing 7,491 patients (SE 3,994 patients; BE: 3,497 patients) showed that SE bioprostheses had lower 30-day mean transvalvular gradient than BE ones (MD 4.33, 95% CI 3.67 to 4.99, p <0.001) (Figure 7). A significant heterogeneity was registered (I^2 = 86%). A sensitivity analysis was performed, removing the outliers studies. The level of the heterogeneity progressively decreased and, after inspecting the asymmetry of the funnel plot, we adjusted the level of association using the trim and fill method (MD 5.16, 95% CI 4.7 to 5.5, p <0.001, I^2 = 32%) (Figure 7). The funnel plot adjusted using the trim and fill method is reported in Supplementary Figure 8.

Similarly, after 1 year, SE bioprostheses had lower a MTG than BE ones (MD 6.18, 95% CI 5.06 to 7.30, p <0.001, I^2 83%) (Figure 7). A sensitivity analysis was performed removing the outliers studies. The level of the heterogeneity progressively decreased and, after inspecting the asymmetry of the funnel plot, we adjusted the level of association using the trim and fill method (MD 6.6, 95%CI 6.1 to 7.03, p <0.001, I^2 = 0%) (Figure 7). The funnel plot adjusted using the trim and fill method is reported in Supplementary Figure 9.

iEOA

The pooled results from 12 studies encompassing 5,044 patients (SE: 3,264 patients; BE: 1,780) showed that SE bioprostheses had 30-day larger iEOA than BE ones (MD 0.15, 95% CI 0.11 to 0.20, p <0.00, $I^2$83%) (Figure 8). After the removal of outliers studies, the results were not affected (MD 0.17, 95% CI 0.13 to 0.22, p <0.001, I^2 = 18%) (Figure 8).

After 1 year, SE bioprostheses were confirmed to have larger iEOA than BE ones (MD 0.24, 95% CI 0.10 to 0.37, p <0.001) (Figure 8). The results were not affected after removing the outlier study (MD 0.17, 95% CI 0.08 to 0.27, p <0.001, I^2 = 41%) (Figure 8).

Discussion

Our meta-analysis aimed to assess the clinical impact of transcatheter heart valve choice on patients with SAA who underwent TAVR. Including 21 studies with 8,647patients, our study, to date and to the best of our knowledge, represents the largest meta-analysis on this topic. The main results could be summarized as follows: (1) SE bioprostheses resulted in improved short and midterm hemodynamic parameters compared with BE ones. Specifically, SE were associated with a larger postoperative iEOA, a smaller MTG and a lower risk of severe PPM. (2) BE valves were associated lower in-hospital stroke rates than SE valves. (3) SE bioprostheses were associated with increased risks of PVLs and PPI. (4) Finally, the midterm major cardiovascular events did not differ significantly between patients with SE or BE bioprostheses.

In patients with SAA, often women,[5] annular sizing is crucial during preoperative planning to avoid complications because it significantly impacts short-term hemodynamic and midterm clinical outcomes.[13] Emerging data from larger clinical trials found that TAVR may have better hemodynamic results than the surgical approach.[3] A thinner stent frame, the supra-annular design, and the systematic oversizing of the transcatheter bioprostheses could be the possible reasons.[14] Although TAVR appears more suitable in patients with SAA, the current studies on the outcomes for specific TAVR valve systems remains unclear, and results from

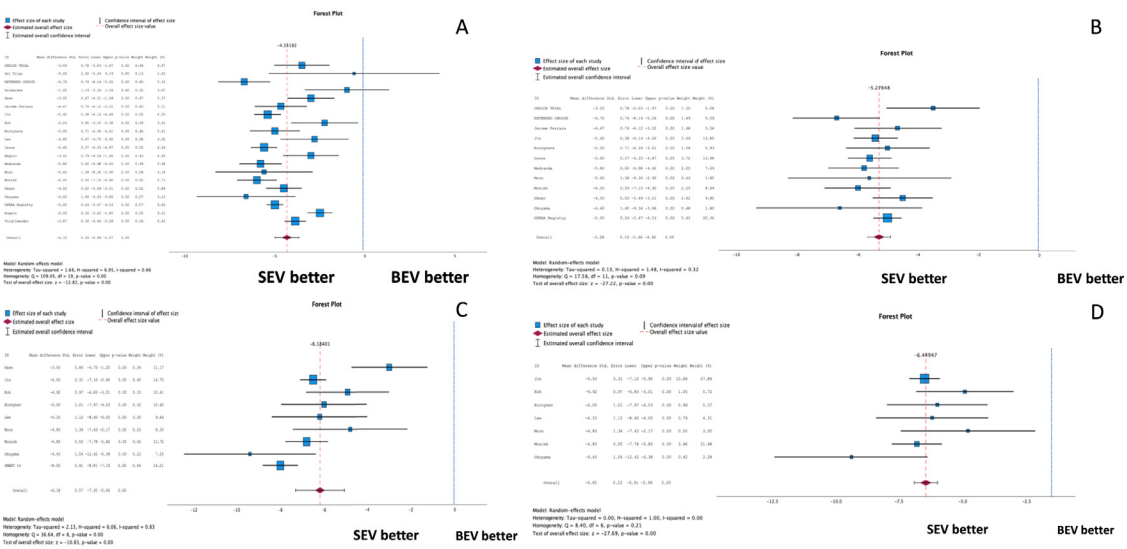

Figure 7. Mean transvalvular gradient at 30 days: primary (*A*) and sensitivity analyses (*B*); mean transvalvular gradient at 1 year: primary (*C*) and sensitivity (*D*) analyses. The CI was adjusted using the trim and fill method.

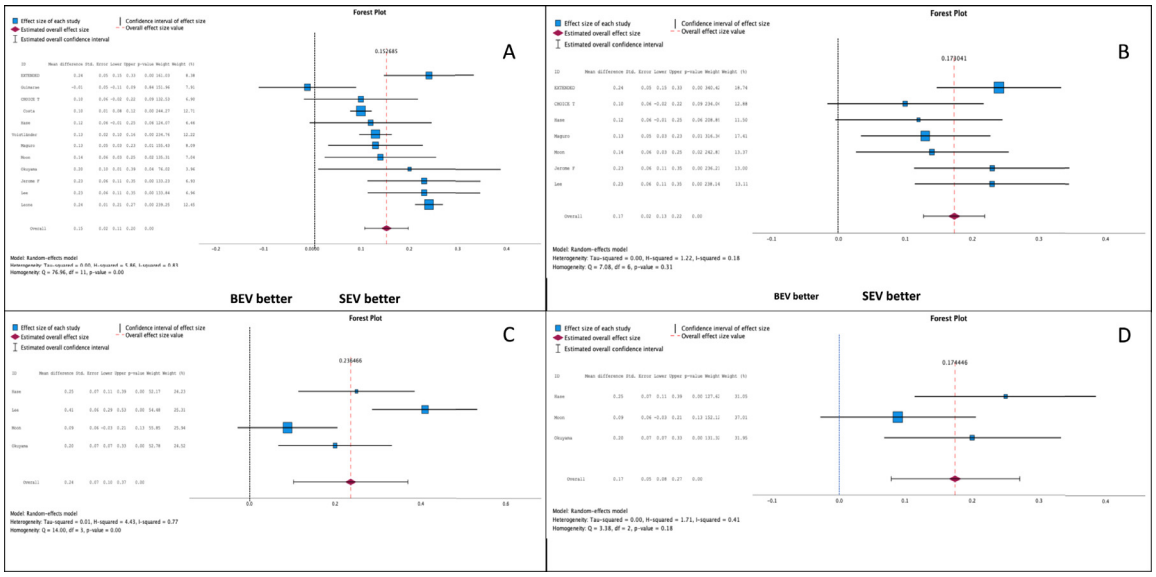

Figure 8. Indexed effective orifice area at 30 days: primary (*A*) and sensitivity (*B*) analyses; indexed effective orifice area at 1 year: primary (*C*) and sensitivity analyses (D).

prospective randomized trials are eagerly awaited. In the most recent VIVA trial, TAVR was demonstrated to be not inferior to the surgical approach; however, a clear benefit of SE over BE bioprostheses did not emerge. The low number of patients enrolled did not allow us to draw definite conclusions on the best type of valve systems.[14]

Our analysis showed that SE bioprostheses had better hemodynamic performance, resulting in larger postoperative iEOA and lower MTG. These findings are consistent with previous studies in patients with and without small aortic annuli, including the CHOICE[15] and SOLVE-TAVI[16] trials and the TAVI-SMALL[17] and FRANCE-TAVI[18] registries. In addition, a recent study by Tirado-Conte et al[19] comparing SE and BE bioprostheses in patients with extra SAA confirmed our results. The intra-annular position of BE may increase the turbulence and the blood flow stress. On the contrary, the supra-annular leaflet position of some SE (EVOLUT or ACURATE Neo in particular) may limit the additional constraints because of native annulus combined with leaflets and stent, resulting in larger EOA than intra-annular transcatheter bioprostheses. In addition, oversizing can often be achieved to a higher degree with SE and has been shown to be protective toward development of PPM in SE but not BE.[20] The latter factors might, at least, in part, explain the difference in hemodynamic parameters between the 2 valve systems.[13] Similarly, our study confirmed that patients who received BE are at higher risk of developing severe PPM. Although clinical significance of PPM, particularly, when severe, has been suggested by recent studies; the limitations in the definition of PPM and echocardiographic measurement of EOA need to be recognized.[21]

Indeed, the clinical impact of PPM seems more significant after surgical AVR than TAVR.[22] Nevertheless, it is worth noting that, among other factors, the impact of PPM in TAVR patients was studied in the short to medium term only,[23] whereas long-term data for patients who underwent surgical AVR are available. In addition, differences in the methods used to define PPM (predicted or measured) may explain the variation in clinical outcomes observed in studies comparing surgical AVR and TAVR.[24]

In the early phase after TAVR, the frequent occurrence of PVL has been a concern because it is an independent predictor of mortality.[25] In our analysis, SE resulted in higher risk of postoperative PVLs than those with BE. This is likely because of the less represented outer skirts in SE, the weaker radial strength of the nitinol frame, the angle between the left ventricular outflow tract and ascending aorta, and deep implantation, making it difficult to form a tight seal.[26] Our findings contrast with the CoreValve Pivot trial[27] and other observational studies, showing that moderate/severe PVLs frequency was lower at 1 year than at discharge.[28] The nitinol framework might continue to expand after deployment, allowing it to conform better to surrounding structures.[28] Moreover, PVLs clinically impact mortality in the long term.[29] Indeed, according to the FRANCE-TAVI Registry, the impact of PVLs on mortality becomes evident beyond 1 year.[30] Postoperative conduction abnormalities leading to PPI are a concerning complication, especially considering the expanded use of TAVR in younger or low-risk surgical patients.[31] Our study confirmed the increased risk of who underwent PPI after SE bioprostheses implantation also in patients with SAA, as found in previous studies.[9] The stent design, ideal implantation depth, and radial force exerted on the left ventricular outflow tract are potential causes of injury to the conduction system.[13]

The higher in-hospital stroke incidence results were in line with the OPERA-REGISTRY substudy[32] and with previous studies.[16,33] Predilation and postdilation procedures are frequently performed in SE bioprosthesis implantation and, together with recapturing maneuvers, could explain this finding.

Our metanalysis has several important limitations. First, only 2 RCTs were included, whereas others were

observational studies. Second, there was heterogeneity in the studies because of varying SAA definitions, differences in the patients' risk profiles, and different observation periods, which influences the reliability of the results. Third, most studies did not provide data regarding each specific valve implanted, making it impossible to compare different-sized bioprostheses. Fourth, confounding factors such as concomitant PVLs may influence results on PPM. In conclusion, the longest follow-up to date is only 1 year, requiring the need for additional studies to show the potential impact of PPM on late adverse events.

Conclusion

In patients with a SAA treated with TAVR, SE bioprostheses have a better hemodynamic performance than BE bioprostheses. Patients with SE bioprostheses have a larger iEOA, lower MTG, and less severe PPM but a higher risk of PVL and PPI. BE bioprostheses were associated with a lower risk of in-hospital stroke. Further RCTs with longer-term follow-up are required to investigate whether specific valve properties will yield survival benefits in this context.

Declaration of competing interest

Dr. Thomas Pilgrim reports research, travel or educational grants to the institution without personal remuneration from Biotronik, Boston Scientific, Edwards Lifesciences, and ATSens; speaker fees and consultancy fees to the institution from Biotronik, Boston Scientific, Edwards Lifesciences, Abbott, Medtronic, Biosensors, and Highlife. Dr. Kay Woon Ho received speaker fees from Edwards Lifesciences, Medtronic, and Abbott Vascular. The remaining authors have no competing interest to declare.

CRediT authorship contribution statement

Gianluca Di Pietro: Writing – original draft, Formal analysis, Conceptualization. **Riccardo Improta:** Writing – original draft. **Francesco Bruno:** Writing – review & editing. **Ovidio De Filippo:** Writing – review & editing. **Pier Pasquale Leone:** Writing – review & editing. **Marco Nebiolo:** Writing – review & editing. **Federico Giacobbe:** Writing – review & editing. **David Caporusso:** Writing – review & editing. **Lucia Ilaria Birtolo:** Writing – review & editing. **Alfonso Ielasi:** Writing – review & editing. **Abdel-Wahab Mohamed:** Writing – review & editing. **Kay Woon Ho:** Writing – review & editing. **Kentaro Meguro:** Writing – review & editing. **Jerome Ferrara:** Writing – review & editing. **Ron Waksman:** Writing – review & editing. **Thomas Pilgrims:** Writing – review & editing. **Raymond G. McKay:** Writing – review & editing. **Moritz Seiffert:** Writing – review & editing. **Mancone Massimo:** Writing – review & editing. **Gaetano Maria De Ferrari:** Writing – review & editing. **Fabrizio D'Ascenzo:** Writing – original draft, Formal analysis, Conceptualization.

Data Availability

The data underlying this article are available in the article and in its online supplementary material.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2024.07.026.

1. Nakashima M, Watanabe Y. Transcatheter aortic valve implantation in small anatomy: patient selection and technical challenges. *Interv Cardiol* 2018 May;13:66–68.
2. Fiore A, Gueldich M, Folliguet T. Sutureless valves fit/perform well in a small aortic annulus. *Ann Cardiothorac Surg* 2020;9:414–416.
3. Freitas-Ferraz AB, Tirado-Conte G, Dagenais F, Ruel M, Al-Atassi T, Dumont E, Mohammadi S, Bernier M, Pibarot P, Rodés-Cabau J. Aortic stenosis and small aortic annulus. *Circulation* 2019;139:2685–2702.
4. Coutinho GF, Correia PM, Paupério G, de Oliveira F, Antunes MJ. Aortic root enlargement does not increase the surgical risk and short-term patient outcome? *Eur J Cardiothorac Surg* 2011;40:441–447.
5. Leone PP, Gohar A, Pagnesi M, Mangieri A, Stefanini G, Cacia M, Cozzi O, Barbanti M, Teles R, Adamo M, Taramasso M, De Marco F, Giannini F, Ohno Y, Saia F, Buono A, Ielasi A, Pighi M, Ribichini F, Maffeo D, Bedogni F, Kim WK, Maisano F, Tamburino C, Van Mieghem NM, Colombo A, Reimers B, Latib A, Regazzoli D, TAVI-SMALL Investigators. Clinical outcomes in women and men with small aortic annuli undergoing transcatheter aortic valve implantation: a multicenter, retrospective, propensity score-matched comparison. *Int J Cardiol* 2023;379:16–23.
6. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, Capodanno D, Conradi L, De Bonis M, De Paulis R, Delgado V, Freemantle N, Gilard M, Haugaa KH, Jeppsson A, Jüni P, Pierard L, Prendergast BD, Sádaba JR, Tribouilloy C, Wojakowski W, ESC/EACTS Scientific Document Group. 2021 ESC/EACTS Guidelines for the management of valvular heart disease [published correction appears in *Eur Heart J* 2022;43:2022]. *Eur Heart J* 2022;43:561–632.
7. Dhareshwar J, Sundt TM, Dearani JA, Schaff HV, Cook DJ, Orszulak TA. Aortic root enlargement: what are the operative risks? *J Thorac Cardiovasc Surg* 2007;134:916–924.
8. Rodés-Cabau J, Pibarot P, Suri RM, Kodali S, Thourani VH, Szeto WY, Svensson LG, Dumont E, Xu K, Hahn RT, Leon MB. Impact of aortic annulus size on valve hemodynamics and clinical outcomes after transcatheter and surgical aortic valve replacement: insights from the PARTNER Trial. *Circ Cardiovasc Interv* 2014;7:701–711.
9. D'Ascenzo F, Bruno F, Baldetti L, De Filippo O, Marengo G, Breviario S, Melillo F, Thyregod HGH, Thiele H, Sondergaard L, Popma JJ, Kodali S, Franchin L, Annaratone M, Marruncheddu L, Gallone G, Crimi G, La Torre M, Rinaldi M, Omedè P, Conrotto F, Salizzoni S, De Ferrari GM. Aortic valve replacement vs. balloon-expandable and self-expandable transcatheter implantation: a network meta-analysis. *Int J Cardiol* 2021;337:90–98.
10. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
11. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:l4898.
12. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hróbjartsson A, Kirkham J, Jüni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu

L, Santaguida PL, Schünemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JP. Robins-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016;355:i4919.
13. Costa G, Buccheri S, Barbanti M, Picci A, Todaro D, Di Simone E, La Spina K, D'Arrigo P, Criscione E, Nastasi M, Sgroi C, Tamburino C. Outcomes of three different new generation transcatheter aortic valve prostheses. *Catheter Cardiovasc Interv* 2020;95:398–407.
14. Rodés-Cabau J, Ribeiro HB, Mohammadi S, Serra V, Al-Atassi T, Iñiguez A, Vilalta V, Nombela-Franco L, Sáez de Ibarra Sánchez JI, Auffret V, Forcillo J, Conradi L, Urena M, Moris C, Muñoz-Garcia A, Paradis JM, Dumont E, Kalavrouziotis D, Maria Pomerantzeff P, Rosa VEE, Pezzute Lopes M, Sureda C, Diaz VAJ, Giuliani C, Avvedimento M, Pelletier-Beaumont E, Pibarot P, VIVA (Transcatheter Aortic Valve Replacement Versus Surgical Aortic Valve Replacement for Treating Elderly Patients With Severe Aortic Stenosis and Small Aortic Annuli) Trial Investigators. Transcatheter or surgical aortic valve replacement in patients with severe aortic stenosis and small aortic annulus: a randomized clinical trial. *Circulation* 2024;149:644–655.
15. Abdel-Wahab M, Landt M, Neumann FJ, Massberg S, Frerker C, Kurz T, Kaur J, Toelg R, Sachse S, Jochheim D, Schäfer U, El-Mawardy M, Robinson DR, Richardt G, CHOICE Investigators. 5-year outcomes after TAVR with balloon-expandable versus self-expanding valves: results from the CHOICE randomized clinical trial. *JACC Cardiovasc Interv* 2020;13:1071–1082.
16. Thiele H, Kurz T, Feistritzer HJ, Stachel G, Hartung P, Eitel I, Marquetand C, Nef H, Doerr O, Lauten A, Landmesser U, Abdel-Wahab M, Sandri M, Holzhey D, Borger M, Ince H, Öner A, Meyer-Saraei R, Wienbergen H, Fach A, Frey N, König IR, Vonthein R, Rückert Y, Funkat AK, de Waha-Thiele S, Desch S. Comparison of newer generation self-expandable vs. balloon-expandable valves in transcatheter aortic valve implantation: the randomized SOLVE-TAVI trial. *Eur Heart J* 2020;41:1890–1899.
17. Regazzoli D, Chiarito M, Cannata F, Pagnesi M, Miura M, Ziviello F, Picci A, Reifart J, De Marco F, Bedogni F, Adamo M, Curello S, Teles R, Taramasso M, Barbanti M, Tamburino C, Stefanini GG, Mangieri A, Giannini F, Pagnotta PA, Maisano F, Kim WK, Van Mieghem NM, Colombo A, Reimers B, Latib A, TAVI-SMALL Investigators. Transcatheter self-expandable valve implantation for aortic stenosis in small aortic annuli: the TAVI-SMALL registry. *JACC Cardiovasc Interv* 2020;13:196–206.
18. Van Belle E, Vincent F, Labreuche J, Auffret V, Debry N, Lefèvre T, Eltchaninoff H, Manigold T, Gilard M, Verhoye JP, Himbert D, Koning R, Collet JP, Leprince P, Teiger E, Duhamel A, Cosenza A, Schurtz G, Porouchani S, Lattuca B, Robin E, Coisne A, Modine T, Richardson M, Joly P, Rioufol G, Ghostine S, Bar O, Amabile N, Champagnac D, Ohlmann P, Meneveau N, Lhermusier T, Leroux L, Leclercq F, Gandet T, Pinaud F, Cuisset T, Motreff P, Souteyrand G, Iung B, Folliguet T, Commeau P, Cayla G, Bayet G, Darremont O, Spaulding C, Le Breton H, Delhaye C. Balloon-expandable versus self-expanding transcatheter aortic valve replacement: a propensity-matched comparison from the France-TAVI registry. *Circulation* 2020;141:243–259.
19. Tirado-Conte G, Rodés-Cabau J, Oteo JF, Pan M, Muñoz E, Witberg G, Cheema AN, Alpieri A, Lopez D, Amat-Santos IJ, Akodad M, Ojeda S, Serra V, Garcia-Blas S, Alfonso F, De Backer O, Asmarats L, Muñoz A, Hamdan A, Toggweiler S, Del Valle R, Salido L, Cruz-González I, Estevez-Loureiro R, Martin Alfaro LE, Gheorge L, Dabrowski M, Berenguer A, Arzamendi D, Saia F, Webb JG, Sondergaard L, Nombela-Franco L. Transcatheter aortic valve implantation in patients with extra-small aortic annuli. *EuroIntervention* 2023;19:e340–e351.
20. Leone PP, Regazzoli D, Pagnesi M, Costa G, Teles R, Adamo M, Taramasso M, De Marco F, Mangieri A, Kargoli F, Ohno Y, Saia F, Ielasi A, Ribichini F, Maffeo D, Kim WK, Maisano F, Van Mieghem NM, Colombo A, Reimers B, Latib A, TAVI-SMALL Investigators. Prosthesis-patient mismatch after transcatheter implantation of contemporary balloon-expandable and self-expandable valves in small aortic annuli. *Catheter Cardiovasc Interv* 2023;102:931–943.
21. Leone PP, Regazzoli D, Pagnesi M, Sanz-Sanchez J, Chiarito M, Cannata F, Van Mieghem NM, Barbanti M, Tamburino C, Teles R, Adamo M, Miura M, Maisano F, Kim WK, Bedogni F, Stefanini G, Mangieri A, Giannini F, Colombo A, Reimers B, Latib A, TAVI-SMALL Investigators. Predictors and clinical impact of prosthesis-patient mismatch after self-expandable TAVR in small annuli. *JACC Cardiovasc Interv* 2021;14:1218–1228.
22. Kalavrouziotis D, Rodés-Cabau J, Bagur R, Doyle D, De Larochellière R, Pibarot P, Dumont E. Transcatheter aortic valve implantation in patients with severe aortic stenosis and small aortic annulus. *J Am Coll Cardiol* 2011;58:1016–1024.
23. Herrmann HC, Daneshvar SA, Fonarow GC, Stebbins A, Vemulapalli S, Desai ND, Malenka DJ, Thourani VH, Rymer J, Kosinski AS. Prosthesis-patient mismatch in patients undergoing transcatheter aortic valve replacement: from the STS/ACC TVT registry. *J Am Coll Cardiol* 2018;72:2701–2711.
24. Sá MPBO, Cavalcanti LRP, Sarargiotto FAS, Perazzo ÁM, Rayol SDC, Diniz RGS, Sá FBCA, Menezes AM, Lima RC. Impact of prosthesis-patient mismatch on 1-year outcomes after transcatheter aortic valve implantation: meta-analysis of 71,106 patients. *Braz J Cardiovasc Surg* 2019;34:318–326.
25. Kodali SK, Williams MR, Smith CR, Svensson LG, Webb JG, Makkar RR, Fontana GP, Dewey TM, Thourani VH, Pichard AD, Fischbein M, Szeto WY, Lim S, Greason KL, Teirstein PS, Malaisrie SC, Douglas PS, Hahn RT, Whisenant B, Zajarias A, Wang D, Akin JJ, Anderson WN, Leon MB, PARTNER Trial Investigators. Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N Engl J Med* 2012;366:1686–1695.
26. Piazza N, de Jaegere P, Schultz C, Becker AE, Serruys PW, Anderson RH. Anatomy of the aortic valvar complex and its implications for transcatheter implantation of the aortic valve [published correction appears in *Circ Cardiovasc Interv* 2008;1:e1]. *Circ Cardiovasc Interv* 2008;1:74–81.
27. Popma JJ, Adams DH, Reardon MJ, Yakubov SJ, Kleiman NS, Heimansohn D, Hermiller J, Hughes GC, Harrison JK, Coselli J, Diez J, Kafi A, Schreiber T, Gleason TG, Conte J, Buchbinder M, Deeb GM, Carabello B, Serruys PW, Chenoweth S, Oh JK, CoreValve United States Clinical Investigators. Transcatheter aortic valve replacement using a self-expanding bioprosthesis in patients with severe aortic stenosis at extreme risk for surgery. *J Am Coll Cardiol* 2014;63:1972–1981.
28. Ko TY, Kao HL, Chen YC, Lin LC, Liu YJ, Yeh CF, Huang CC, Chen YH, Chen YS, Lin MS. Temporal change in paravalvular leakage after transcatheter aortic valve replacement with a self-expanding valve: impact of aortic valve calcification. *Acta Cardiol Sin* 2020;36:140–147.
29. Généreux P, Head SJ, Hahn R, Daneault B, Kodali S, Williams MR, van Mieghem NM, Alu MC, Serruys PW, Kappetein AP, Leon MB. Paravalvular leak after transcatheter aortic valve replacement: the new Achilles' heel? A comprehensive review of the literature. *J Am Coll Cardiol* 2013;61:1125–1136.
30. Deharo P, Leroux L, Theron A, Ferrara J, Vaillier A, Jaussaud N, Porto A, Morera P, Gariboldi V, Iung B, Lefevre T, Commeau P, Gouysse M, du Chayla F, Glatt N, Cayla G, Le Breton H, Benamer H, Beurtheret S, Verhoye JP, Eltchaninoff H, Gilard M, Collet JP, Dumonteil N, Collart F, Modine T, Cuisset T, France-TAVI and STOP-AS Investigators. Long-term prognosis value of paravalvular leak and patient-prosthesis mismatch following transcatheter aortic valve implantation: insight from the France-TAVI registry. *J Clin Med* 2022;11:6117.
31. Holmes DR Jr, RA Nishimura, Grover FL, Brindis RG, Carroll JD, Edwards FH, Peterson ED, Rumsfeld JS, Shahian DM, Thourani VH, Tuzcu EM, Vemulapalli S, Hewitt K, Michaels J, Fitzgerald S, Mack MJ, STS/ACC TVT Registry. Annual outcomes with transcatheter valve therapy: from the STS/ACC TVT registry. *J Am Coll Cardiol* 2015;66:2813–2823.
32. Scotti A, Sturla M, Costa G, Saia F, Pilgrim T, Abdel-Wahab M, Garot P, Gandolfo C, Branca L, Santos IA, Mylotte D, Bedogni F, De Backer O, Nombela Franco L, Webb J, Ribichini FL, Mainardi A, Andreaggi S, Mazzapicchi A, Tomii D, Laforgia P, Cannata S, Fiorina C, Fezzi S, Criscione E, Lunardi M, Poletti E, Mazzucca M, Quagliana A, Montarello N, Hennessey B, Mon-Noboa M, Akodad M, Meier D, De Marco F, Adamo M, Sgroi C, Reddavid CM, Valvo R, Strazzieri O, Motta SC, Frittitta V, Dipietro E, Comis A, Melfa C, Calì M,

Sammartino S, Laterra G, Thiele H, Sondergaard L, Tamburino C, Barbanti M, Latib A. Evolut PRO and Sapien ULTRA performance in small aortic annuli: the OPERA-TAVI registry. *JACC Cardiovasc Interv* 2024;17:681–692.

33. Vlastra W, Chandrasekhar J, Muñoz-Garcia AJ, Tchétché D, de Brito FS, Barbanti M, Kornowski R, Latib A, D'Onofrio A, Ribichini F, Baan J, Tijssen JGP, Trillo-Nouche R, Dumonteil N, Abizaid A, Sartori S, D'Errigo P, Tarantini G, Lunardi M, Orvin K, Pagnesi M, Del Valle R, Modine T, Dangas G, Mehran R, Piek JJ, Delewi R. Comparison of balloon-expandable vs. self-expandable valves in patients undergoing transfemoral transcatheter aortic valve implantation: from the CENTER-collaboration. *Eur Heart J* 2019;40:456–465.