Sutureless versus transcatheter valves in patients with aortic stenosis at intermediate risk: A multi-institutional European study

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ABSTRACT

Background: Recent randomized controlled trials showed comparable short-term outcomes of transcatheter aortic valve implantation versus surgical aortic valve replacement in intermediate and low-risk patients. However, independent studies comparing transcatheter aortic valve implantation results versus surgical aortic valve replacement at 5 years showed worsening outcomes in patients treated with transcatheter aortic valve implantation. The aim of this study was to analyze mid- to long-term outcomes of patients with isolated aortic stenosis and an intermediate-risk profile who underwent aortic valve replacement using a sutureless valve versus transcatheter aortic valve implantation.
Methods: This retrospective multi-institutional European study investigated 2,123 consecutive patients with isolated aortic stenosis at intermediate risk profile treated with sutureless aortic valve replacement (824 patients) or transcatheter aortic valve implantation (1,299 patients) from 2013 to 2020. After 1:1 propensity score matching, 2 balanced groups of 517 patients were obtained. Primary endpoints were as follows: 30 days, late all-cause, and cardiac-related mortality. Secondary endpoints included major adverse cardiocerebrovascular events (all-cause death, stroke/transient ischemic attack, endocarditis, reoperation, permanent pacemaker implantation, and paravalvular leak grade ≥2).
Results: Median follow-up was 4.3 years (interquartile range 1.1−7.4 years). Primary endpoints were as follows—30-day mortality sutureless aortic valve replacement: 2.13% versus transcatheter aortic valve implantation: 4.64% (*P* = .026), all-cause mortality sutureless aortic valve replacement: 36.7% ± 7.8% vs transcatheter aortic valve implantation: 41.8% ± 8.2% (*P* = .023), and cardiac-related mortality sutureless aortic valve replacement: 10.2% ± 2.8% vs transcatheter aortic valve implantation: 19.2% ± 3.5%;(*P* = .00043) at follow-up. Secondary endpoints were as follows—major adverse cardiocerebrovascular events in the sutureless aortic valve replacement group: 47.2% ± 9.0% versus transcatheter aortic valve implantation: 57.3% ± 7.5% (*P* < .001). In particular, the incidence of permanent pacemaker implantation (sutureless aortic valve replacement: 6.38% versus transcatheter aortic valve implantation: 11.8% [*P* = .002]) and paravalvular leak ≥2 (sutureless aortic valve replacement: 0.97% versus transcatheter aortic valve implantation: 4.84% [*P* = .001]) was significantly higher in transcatheter aortic valve implantation group. At Multivariable Cox regression analysis, paravalvular leak ≥2 (hazard ratio: 1.63%; 95% confidence interval: 1.06−2.53, *P* = .042) and permanent pacemaker implantation (hazard ratio: 1.49%; 95% confidence interval: 1.02−2.20, *P* = .039) were identified as predictors of mortality.
Conclusion: Sutureless aortic valve replacement showed a significantly lower incidence of all-cause mortality, cardiac-related death, permanent pacemaker implantation, and paravalvular leak than transcatheter aortic valve implantation. Moreover, permanent pacemaker implantation and paravalvular leak negatively affected survival in patients treated for isolated aortic stenosis.

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Introduction

Transcatheter aortic valve implantation (TAVI) has become a safe and reliable tool for treating aortic stenosis, not only in patients at high surgical risk.[1] Given the amount of data derived from randomized studies,[2-6] the latest TAVI indications have been expanded to include a wider subset of patients.[7,8]

Although the outcomes of patients at low and intermediate risk treated with TAVI versus surgical aortic valve replacement (sAVR) have been considered comparable at short- and mid-term,[2-5] there is a lack of data about long-term outcomes. Recently, outcomes of the PARTNER II trial at 5 years showed a tendency toward better results in the surgical group,[6] thus suggesting complications such as paravalvular leak (PVL) (more frequently seen in the TAVI group) may hamper long-term survival. In addition, "real-world" data, derived from the 5-years outcomes of the OBSERVANT study, showed that patients at intermediate risk treated with TAVI had higher mortality and rate of valve-related complications compared to sAVR.[9] However, these studies compared TAVI versus conventional stented aortic bioprostheses.

First introduced in 2008, sutureless valves (SU-AVR) represent the latest advancement in technology for patients requiring sAVR and have demonstrated a good safety profile associated with a significant reduction of cross-clamping and cardiopulmonary bypass (CPB) times.[10] In addition, the rapid implantation technique facilitates AVR in a minimally invasive approach, giving an additional advantage.[11] For these reasons, SU-AVR may offer potential advantages in early and late outcomes when compared to standard bioprostheses,[12,13] and previous studies have already outlined intermediate-risk patients treated by SU-AVR had a significantly lower mortality at 60 months when compared to TAVI.[14,15]

The present European multi-institutional study sought to investigate and compare the mid- and long-term outcomes of patients with isolated aortic stenosis and intermediate risk profile treated with SU-AVR versus TAVI.

Methods

Data were collected retrospectively from 5 European Centers, including 2,123 consecutive patients who underwent SU-AVR (824 patients) or TAVI (1,299 patients) for isolated aortic stenosis between 2013 and 2020. The University of Brescia, as the coordinator center, received approval for the study from the Institutional Review Board and Ethical Committee (NP 1870). Inclusion criteria were as follows: patients with isolated aortic valve stenosis and Society of Thoracic Surgeons scores ranging from 4% to 8% (intermediate risk). Exclusion criteria were concomitant surgical or transcatheter procedure, bicuspid valve type 0 (Sievers), and previous aortic valve replacement/previous TAVI (valve-in-valve procedures).

The therapeutic strategy (surgery versus TAVI) was defined by a multidisciplinary heart team, which included cardiologists, cardiac surgeons, and anesthesiologists.

SU-AVR: Surgical technique

The sutureless valve Perceval S (LivaNova UK Company, London, United Kingdom) was used in all patients scheduled for surgical AVR. The implantation technique was carried out as previously described.[16]

Surgical access included conventional full sternotomy (261 patients, 31.7%). In contrast, a minimally invasive approach, either by upper "J"-shaped mini-sternotomy or right mini-thoracotomy, was performed in 442 patients (53.6%) and 121 patients (14.7%), respectively, under normothermic CPB. Cardioplegia was administered with a single shot of crystalloid solution. Intraoperative transesophageal echocardiography was routinely performed to assess proper valve positioning. After surgery, patients remained in the intensive care unit ward for monitoring for at least 24 hours.

TAVI

Transcatheter aortic valve implantation was performed using the transfemoral (TF) approach in most patients (1,032/1,299, 79.4%), followed by transapical approach (TA) (198/1299, 15.2%) or other transvascular approaches (69/1,299, 5.3%). Implanted devices included both self-expandable (Evolut R, Evolut Pro, Medtronic, Minneapolis, MN; 958/1,299, 73.7%; ACURATE TA, Boston Scientific, Marlborough, MA; 65/1,299, 5.0%; ACURATE neo/neo2 - Boston Scientific, Marlborough, MA; 56/1,299, 3.0%) and balloon-expandable bioprosthesis (Sapien XT/Sapein 3, Edwards Lifesciences, Irvine, CA; 236/1,299, 18.1%). Valve function was evaluated using intraprocedural echocardiography. After the procedure, patients underwent intensive rhythm monitoring for 24 hours in the coronary care unit.

Statistical analysis

Distribution normality was analyzed with the Kolmogorov-Smirnov test. Continuous variables were compared using an independent Student's *t* test with a 2-tailed distribution if normally distributed. The Mann-Whitney *U*-test was used for not normally distributed variables. Categorical variables were compared using χ2 analysis or the Fisher exact test as needed. To balance baseline characteristics between the groups, propensity score matching with a ratio of 1:1 was performed using the nearest-neighbor method without replacement and a caliper of 0.06. Included variables were chosen from the significantly different baseline variables between the 2 groups that were clinically relevant. To avoid multicollinearity, the variance inflation factor (VIF) was measured for every variable in the propensity model. A VIF value >5 indicates a potentially severe correlation between a given predictor variable and other predictor variables in the model. The matched standardized differences of each covariate in the matched cohorts were <10% (Figure 1), the area under the receiver operating characteristic curve was 0.79, and no multicollinearity issues were detected with VIF in the propensity model (ie, all values were <5). Preoperative characteristics are listed in detail in Table I. The survival differences between the 2 groups were depicted and compared using the Kaplan–Meier method and log-rank tests. The univariable and multivariable Cox proportional hazard regression models were used to investigate the effect of late endpoints (ie, stroke/transient ischemic attack [TIA], endocarditis, reoperation, permanent pacemaker implantation [PPI], and PVL grade ≥2) and non-TF TAVI on all-cause mortality; variables such as PVL and PPI were tested as time-dependent variables. The proportional hazard (PH) assumption was tested using the Schoenfeld individual test to assess if hazard effects remained constant over time. The analysis was performed using R (version 3.6.2; R Foundation for Statistical Computing, Vienna, Austria).

End points and definition

Patient outcomes were defined according to the guidelines for reporting mortality and morbidity after cardiac interventions,[17] whereas prosthesis outcomes were defined according to the Valve Academic Research Consortium 3 criteria.[18] In particular, cardiac-related mortality was defined as any death related to heart failure, cardiogenic shock, bioprosthetic valve dysfunction,
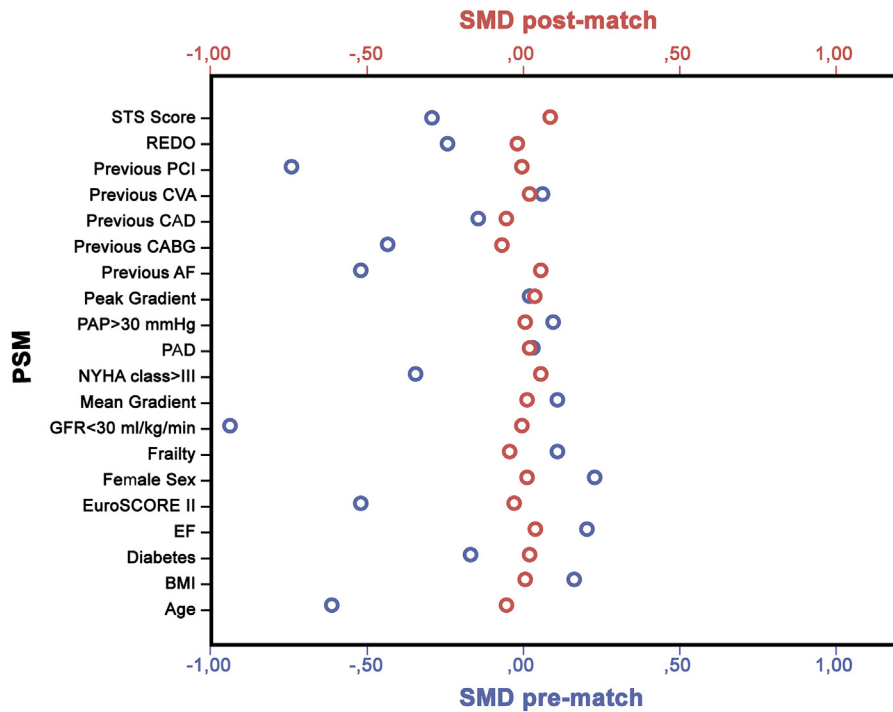
Figure 1. Propensity score Love plot. *AF*, atrial fibrillation; *BMI*, body mass index; *CABG*, coronary artery bypass grafting; *CAD*, coronary artery disease; *CVA*, cerebrovascular accident; *EF*, ejection fraction; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *GFR*; *NYHA*, New York Heart Association; *PAD*, peripheral artery disease; *PCI*, percutaneous coronary intervention; *PSM*, propensity score matching; *REOP*, reoperation; *SMD*, standard mean difference; *STS*, Society of Thoracic Surgeons.

Table I
Preoperative characteristics pre-match and post-match

	SU-AVR unmatched		TAVI unmatched		P value	SUA-VR matched		TAVI matched		P value
	N (824)	% (IQR)	N (1,299)	% (IQR)		N (517)	% (IQR)	N (517)	% (IQR)	
Age, median (IQR), y	80	(76–83)	84	(87–79)	< .001	81	(78–84)	82	(77.4–85)	.139
Euroscore II, median (IQR)	6.2	(4–6)	5.8	(4.68–9)	< .001	6.0	(4–6.63)	5.5	(4.3–7.5)	.067
STS score, median (IQR)	6.0	(4–6)	5.74	(4.27–7)	< .001	6.0	(4–6)	5.9	(4.0–7.1)	.289
Ejection fraction, median (IQR)	60.0	(50–63)	56	(45–60)	< .001	60.0	(50–63)	6.00	(50–65)	.644
BMI, median (IQR)	26.5	(24.0–29.8)	25.9	(23.1–29.0)	< .001	26	(23.8–28.5)	26	(23.2–29.5)	.855
Female sex	549	66.6%	728	56.0%	< .001	323	62.5%	319	61.7%	.797
Hypertension	676	82.0%	1090	83.9%	.295	424	82.0%	432	83.6%	.510
Diabetes	245	29.7%	486	37.4%	< .001	160	30.9%	165	31.9%	.738
CRF, GRF <30 ml/Kg/min	49	5.9%	218	16.8%	< .001	22	4.3%	22	4.3%	1.000
COPD (FEV₁ <60%)	182	22.1%	253	19.5%	.137	114	22.0%	99	19.2%	.249
PAD	190	23.1%	339	26.1%	.227	125	24.2%	129	24.9%	.773
PAPS >30 mm Hg	255	30.1%	365	28.1%	.032	148	28.6%	154	29.8%	.682
Previous CVA (stroke/TIA)	61	7.4%	80	6.2%	.153	41	7.9%	35	6.8%	.475
Atrial fibrillation	95	11.5%	377	29.2%	< .001	87	16.8%	76	14.7%	.348
Cad	224	27.2%	457	35.2%	< .001	148	28.6%	161	31.1%	.377
Redo	63	7.6%	190	14.6%	< .001	43	8.3%	45	8.7%	.824
Previous CABG	27	3.3%	148	11.4%	< .001	21	4.0%	27	5.2%	.375
Previous PCI	72	8.7%	327	25.2%	< .001	74	14.3%	68	13.1%	.588
NYHA ≥class III	499	60.5%	1005	77.4%	< .001	347	67.1%	343	66.3%	.791
Frailty	222	26.9%	415	31.9%	.014	146	28.2%	156	30.2%	.490
Bicuspid valve	41	4.4%	37	2.8%	.011	21	4.0%	13	2.5%	.162
Peak transvalvular gradient, mm Hg	80	(67–85)	78	(68–86)	< .001	80	(69–86)	78	(68–86)	.078
Mean transvalvular gradient, mm Hg	48	(49.2–42)	46	(40–52)	< .001	48	(42–50)	46	(41–55)	0.176
EOA, cm²	0.7	(0.4–0.9)	0.6	(0.5–0.8)	.025	0.7	(0.7–0.7)	0.7	(0.5–0.8)	.157

BMI, body mass index; *CABG*, coronary artery bypass grafting; *CAD*, coronary artery disease; *COPD*, chronic obstructive pulmonary disease; *CRF*, chronic renal failure; *CVA*, cerebrovascular accident; *EOA*, effective orifice area; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *FEV₁*, forced expiratory volume at 1 second; *GFR*, glomerular filtration rate; *NYHA*, New York Heart Association; *PAD*, peripheral artery disease; *PAPs*, pulmonary artery pressure systolic; *PCI*, percutaneous coronary intervention; *REDO*, reoperation; *SMD*, standard mean difference; *STS*, Society of Thoracic Surgeons; *SU-AVR*, sutureless aortic valve replacement, *TAVI*, transcatheter aortic valve implant.

myocardial infarction, tamponade, arrhythmia or conduction system disturbances, cardiovascular infection, or other clear cardiac cause.[18]

Frailty was defined as the presence of ≥2 of the following criteria: 5-meter walk test time of >6 seconds, serum albumin level of <3.5 g/dL, and a Katz Activities of Daily Living total score of ≤4.

Echocardiography was performed preoperatively at the time of patient discharge and 12-month follow-up. Patients were followed prospectively by clinical evaluation, including at least 1 physical examination per year. Follow-up was 100% completed, and the data were collected from institutional databases and analyzed by the coordinating center.

The primary endpoints of the study included the following: (1) 30-day mortality, (2) late all-cause mortality, and (3) late cardiac-related mortality. The secondary endpoint was the incidence of major adverse cardiovascular and cerebrovascular events (MACCE), which included the following: all-cause death, stroke/TIA, endocarditis, reoperation, PPI, and PVL grade ≥2.[17]

Results

Operative results

Operative results were reported in Table II. Sutureless valves were successfully implanted in 813 patients (98.7%). Failures were reported in 11 patients—3 patients had sizing mismatch or valve malpositioning, whereas in the remaining cases, a significant PVL, central leak, migration, or dislodgement occurred. A sutured bioprosthesis was implanted in all of these latter cases.

Transcatheter aortic valve implantation was successfully performed in 1,265 patients (97.4%), and device failure occurred in 34 patients (2.6%). Valve embolization or dislodgement was reported in 13 patients. Among these, 9 patients had a second valve implantation, whereas 4 required surgical conversion. Annular rupture and coronary obstruction, both requiring surgical conversion, were reported in 2 and 3 patients, respectively, whereas a significant PVL requiring a valve-in-valve procedure was performed in 21 patients. Among the 9 patients requiring conversion to surgery, 5 patients died, with a mortality rate of 55.5%.

Postoperative results

Thirty-day mortality was significantly lower in the matched SU-AVR group (SU-AVR = 2.1% vs TAVI = 4.6%; P = .026, Table III). Furthermore, 30-day mortality was higher in the non-TF TAVI subgroup compared to TF TAVI (non-TF TAVI = [6/86] 6.9% vs TF-TAVI = [18/431] 4.1%, P = .259). However, there was no significant difference in 30-day mortality of SU-AVR versus TF-TAVI (2.1% vs 4.1%, P = .067). Transfusion of at least 2 units of red blood cells was significantly lower in patients receiving TAVI in the unmatched and matched cohorts (matched: SU-AVR = 27.8% vs TAVI = 9.7%; P < .001). The incidence of peripheral vascular complications was significantly higher in the TAVI group (matched SU-AVR: 0.8% vs TAVI 5.6%, P < .001). Incidences of PPI and PVL grade ≥ II were significantly higher in the TAVI group when compared to SU-AVR in both the matched and unmatched cohorts (matched PPI: SU-AVR = 6.4% vs TAVI = 11.8%; P = .002; matched PVL: SU-AVR = 0.9% vs TAVI = 4.8%; P < .001, Table III).

A significantly lower incidence of acute kidney injury (AKI) was reported in the SU-AVR group (SU-AVR = 2.1% vs TAVI = 4.4%; P = .036, Table III), whereas no differences were found in postoperative dialysis (SU-AVR = 1.0% vs TAVI = 2.4%; P = .087, Table III).

Comparison of postoperative hemodynamic performances of SU-AVR versus TAVI did not show any significant difference in terms of peak gradient, mean gradient, and effective orifice area (peak gradient matched SU-AVR: 21.8 ± 6.5 mmHg vs TAVI 22.4 ± 6.4 mmHg; P = .424; mean gradient matched SU-AVR: 10.6 ± 6.2 mmHg vs TAVI: 10.8 ± 6.5, P = .786; effective orifice area matched SU-AVR: 1.55 ± 0.3 vs TAVI: 1.52 ± 0.4, P = .224).

Mid- and long-term outcomes

The median follow-up was 4.3 years (IQR 1.1–7.4 years). Incidence of all-cause death at 9-year follow-up was significantly lower in the SU-AVR group both in unmatched and matched cohorts (matched 9-year all-cause death: SU-AVR 36.7%, 95% CI: 28.9%–44.5% vs TAVI = 41.8%, 95% CI: 33.6%–50.0%, P = .023) (Figure 2, A and B). Regarding cardiac-related mortality, at 9-year follow-up, it was significantly lower in the SU-AVR group both in unmatched and matched cohorts (matched 9-year cardiac-related death: SU-AVR 10.2%, 95% CI: 4.5%–15.5% vs TAVI = 19.2%, 95% CI: 12.1%–25.8%, P = .00043) (Supplementary Figure S1, A and B).

Cox regression analysis showed a significantly lower risk of mortality in patients receiving sutureless valves when compared to TAVI both in matched and unmatched populations (matched: hazard ratio [HR]: 1.37, 95% CI: 1.04–1.81; P = .024; unmatched: HR: 1.50, 95% CI: 1.24–1.81), P < .001). Schoenfeld individual test showed that the PH assumption was not violated in the matched groups (P = .366), confirming the reliability of the survival analysis.

Likewise, time-to-event analysis (Kaplan–Meier) for MACCEs showed a significantly lower incidence of MACCEs in the

Table II
Operative outcomes

	SU-AVR unmatched		TAVI unmatched		P value	SU-AVR matched		TAVI matched		P value
	N (824)	% (IQR)	N (1,299)	% (IQR)		N (517)	% (IQR)	N (517)	% (IQR)	
Non-elective Procedure	40	4.9	15	1.1	< .001	19	3.7%	14	2.7%	.376
MAV >48 h	18	2.2	18	1.4	.178	13	2.1%	16	3.1%	.572
ICU stay, median IQR, d	1	(0–2)	1	(0–2.5)	.045	1	(0–1.5)	1	(0–2)	.258
Valve diameter, median (IQR)	23	(23–25)	26	(23–28)	< .001	23	(23–25)	26	(23–29)	< .001
Echocardiogram at discharge										
EF ,% median (IQR)	56	(50–62)	54	(51–60)	.145	55	50–61	56	54–60	.654
Peak transvalvular gradient, mean ± SD, mm Hg,	23.2	9.3	22.9	8.4	.217	21.8	±6.5	22.4	±6.4	.424
Mean transvalvular gradient, mmHg, mean ± SD, mm Hg,	11.1	5.7	10.6	4.9	.108	10.6	±6.2	10.8	±6.5	.786
EOA, mean ± SD, cm^2	1.52	0.4	1.53	0.3	.451	1.55	0.03	1.52	0.04	.224
PVL >grade II	7	0.84%	43	3.3%	< .001	5	0.97%	25	4.8%	< .001
Moderate-severe PPM	64	7.7%	131	10.1%	.055	31	5.9%	43	8.3%	.147

CPB, cardiopulmonary bypass; *EF*, ejection fraction; *EOA*, effective orifice area; *ICU*, intensive care unit; *MAV*, mechanical-assisted ventilation; *PPM*, patient–prosthesis mismatch; *PVL*, perivalvular leak; *SU-AVR*: sutureless aortic valve replacement; *TAVI*, transcatheter aortic valve implant.

Table III
Early outcomes

Outcome	SU-AVR unmatched		TAVI unmatched		P value	SU-AVR matched		TAVI matched		P value
	N (824)	%	N (1,299)	%		N (517)	%	N (517)	%	
30-d mortality	15	1.8	67	5.1	< .001	11	2.1	24	4.6	.026
Stroke/TIA	18	2.3	44	3.4	.156	8	1.5	14	2.7	.596
Perioperative AMI	0	0.0	6	0.5	.182	0	0.0	2	0.4	.031
Perioperative PBRC	187	22.7	147	11.3	< .001	140	27.1	51	9.9	< .001
Bleeding requiring surgical revision	26	3.2	18	1.4	.005	21	4.1	10	1.9	.044
AKI	20	2.4	81	6.2	< .001	11	2.1	23	4.4	.036
CVVH	7	0.9	31	2.4	.014	5	1.0	12	2.3	.087
PPI	48	5.8	137	10.5	< .001	33	6.4	61	11.8	.002
Peripheral vascular complications	8	1.0	63	4.8	< .001	4	0.8	29	5.6	< .001

AKI, acute kidney injury; AMI, acute myocardial infarction; AVB, atrioventricular block; CVVH, continuous venous-venous hemofiltration; PBRC, packed red blood cell; PPI, permanent pacemaker implantation; SU-AVR, sutureless valves aortic valve replacement; TAVI, transcatheter aortic valve implant; TIA, transient ischemic attack.

SU-AVR group both in the matched and unmatched cohorts (matched MACCEs: SU-AVR = 47.2%, 95% CI, 38.2%–56.2% vs TAVI= 57.3%, 95% CI, 49.8%–64.8%, P < .001) (Figure 3, A and B). Cox regression analysis showed a significantly lower risk of MACCEs in patients receiving sutureless valves when compared to TAVI both in matched and unmatched populations (matched: HR: 1.55, 95% CI: 1.21–1.98; P < .001; unmatched: HR: 1.50, 95% CI: 1.24–1.81, P < .001). The Schoenfeld individual test showed that the PH assumption was not violated in matched and unmatched populations (matched P value = .814, unmatched P value = .062), confirming the reliability of the statistical analysis.

Incidence of stroke/TIA at follow-up was higher in the TAVI group (matched 9-year stroke/TIA, SU-AVR 11.7%, 95% CI 4.4%–19.0% vs TAVI= 14.5%, 95% CI 8.9%–20.1%, P = .029).

At 9 years, the cumulative incidence of PVL grade≥ II and PPI was higher in the TAVI group when compared to SU-AVR (PVL: TAVI group = 7.7% vs SU-AVR group = 1.9%, P < .001) (PPI: TAVI = 16.8% vs SU-AVR = 10.0%, P < .001).

In the surgical group, 5 patients underwent redo-operation using a surgical approach in 2 cases, whereas a valve-in-valve procedure was performed in 3 patients. Otherwise, in the TAVI group, 11 patients underwent reintervention—the valve-in-valve procedure was performed in 9 patients, and 2 patients underwent sAVR.

Cox regression multivariable analysis (matched cohorts) identified PVL grade≥ II and PPI as independent predictors of all-cause death (PVL ≥2: HR: 1.63; 95% CI: 1.06–2.53, P = .042) (HR: 1.49; 95% CI: 1.02–2.20, P = .039) (Table IV).

Discussion

Over the past decade, several randomized controlled trials (RCTs) have tried to shed light on the fate of patients with aortic stenosis.[2-4] The results of these studies deeply influenced the development of the current guidelines, leading to the extension of TAVI indication to intermediate and low-risk patients.[7,8]

Nevertheless, long-term outcomes of patients undergoing TAVI are scant, and concerns remain about transcatheter valve durability and the clinical impact of postprocedural complications such as PPI and PVL.

The main findings of the present multi-institutional study are as follows: (1) patients with isolated aortic stenosis with an intermediate risk profile treated with SU-AVR had significantly lower 30-day and long-term all-cause mortality when compared to patients treated with TAVI; (2) at 9-year follow-up, SU-AVR patients had a significantly lower incidence of MACCEs due to a lower incidence of PPI, PVL, and stroke; (3) PVL grade ≥2 and postprocedural PPI have been identified as independent predictors of mortality at multivariable analysis.

Our findings regarding 30-day mortality in patients at intermediate risk who underwent isolated aortic valve replacement by SU-AVR (2.1%) were consistent with previously reported multi-institutional observational studies investigating a similar subset of patients.[13,19,20] Conversely, it was lower if compared to results in the surgical arms of PARTNER II (4.1%) and SURTAVI (3.9%) trials.[2,4] In these studies, several factors might have influenced the higher mortality rate reported in the surgical group despite randomization—inclusion criteria and patients' selection at the entry point (a small percentage of patients enrolled out of the total number treated) might have
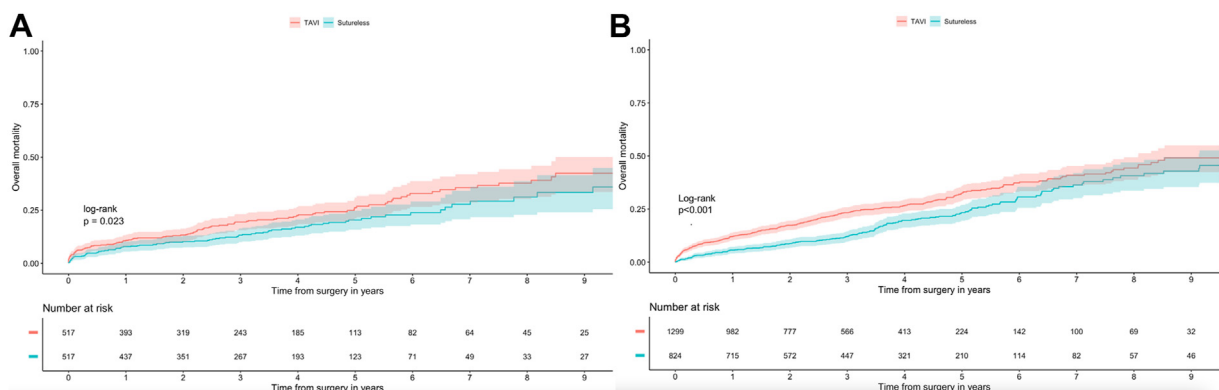

Figure 2. (A) All-cause death matched sample. (B) All-cause death in the unmatched sample.
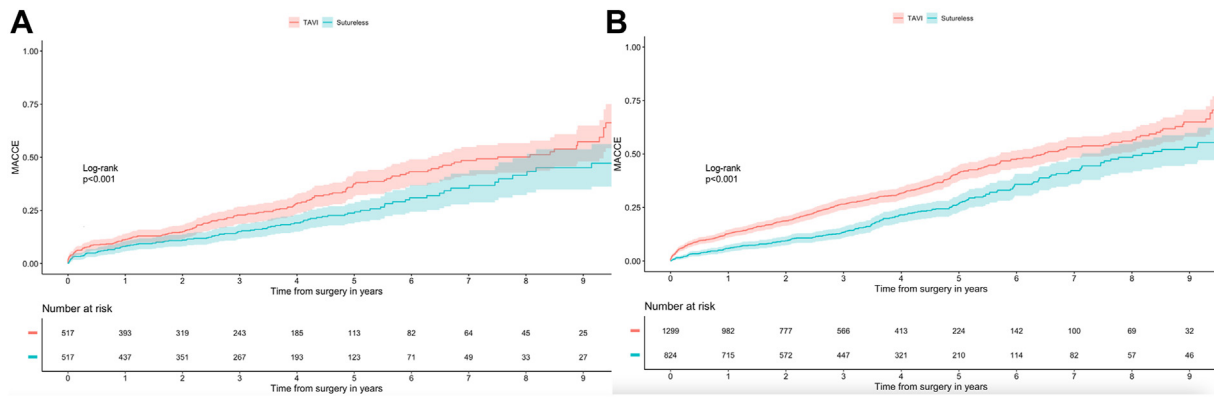
Figure 3. (A) Major adverse cardiovascular and cerebrovascular event–matched sample (all-cause death, stroke/transient ischemic attack, bleeding, myocardial infarction, aortic regurgitation grade II, endocarditis, reintervention, and pacemaker implant). (B) Major adverse cardiovascular and cerebrovascular events in the unmatched sample (all-cause death, stroke/transient ischemic attack, bleeding, myocardial infarction, aortic regurgitation grade II, endocarditis, reintervention, and PM implant). *MACCE*, major adverse cardiovascular and cerebrovascular events.

themselves underpowered the study and introduced confounding factors. Furthermore, risk factors, such as redo operations, concomitant cardiac procedures, and patent internal thoracic artery grafts, may encumber more surgical patients' results than TAVIs, introducing potential selection biases.[21] Patients enrolled in the PARTNER II and SURTAVI trials had an unusually high rate of previous coronary artery bypass grafts (PARTNER II: 25.6%, SURTAVI: 17%), not representing a "real-world" cohort of patients undergoing surgical AVR.[2,4] As a matter of fact, redo sAVR operation with a patent mammary artery has a very high surgical risk, with hospital mortality ranging from 4% to 16%.[21] In addition, in the PARTNER II trial, 9.1% of patients undergoing surgery received an associated surgical procedure, which, per se, carries an increased surgical risk.[2]

The low mortality rate registered in the surgical arm of the present study might also be influenced by the use of a sutureless valve technology, which significantly reduced aortic cross-clamping and CPB times, postoperative complications, and the need for rehospitalization, especially in patients who underwent minimally invasive surgery.[10,22,23]

In the present study, 30-day mortality in the TAVI group (overall TAVI: 4.6%; TF TAVI: 4.1% vs non-TF TAVI: 6.9%) was consistent with results reported in the GARY registry and PARTNER II trial (GARY: TV-TAVI = 5.1%; TA-TAVI = 7.7%) (PARTNER II: TF-TAVI = 3.0%; TA-TAVI = 6.8%).[2,24] Besides, the rate of TA-TAVI enrolled in our study was comparable to those of the PARTNER II trial (present study vs PARTNER II: 15.2% vs 17.2%, respectively).[2]

We reported a significant difference between SU-AVR and TAVI in terms of 30-day mortality (2.1% vs 4.6%, respectively, P = .026), although, similarly to previous studies,[2,4] no differences were

reported between SU-AVR and TF-TAVI for the same outcome. However, 30-day mortality remained significantly higher in non-TF TAVI compared to surgery. These findings should be carefully interpreted in perspective with long-term results.

In fact, there was a significantly lower all-cause death rate at 9 years in the SU-AVR group when compared to TAVI (SU-AVR = 36.7%, 95% CI 28.9%–44.5% vs TAVI = 41.8%, 95% CI 33.6%–50.0%, P = .023). Of note, the TAVI mortality rate was consistent with what has been previously reported in the literature—Chakos and Barbanti reported long-term all-cause mortality in TAVI patients of 48% and 44.5%, respectively.[9,25] Moreover, our findings were also consistent with the 5-year outcomes of the TAVI group in the PARTNER II trial, reporting an all-cause death in the TAVI group of 46%.[6] Besides, in this study, we reported a considerably lower mortality rate in the surgical (SU-AVR) cohort than in PARTNER II trials (42.1%), and this was consistent with outcomes of sAVR reported in the OBSERVANT study (mortality 35.8%).[9] Considering the elevated median age of the population, the risk of death due to both cardiac and all-cause death is increased compared to younger patients. Even if all-cause death represents a completely objective endpoint, it may be independent of the intervention and has a higher incidence than disease-specific death. Therefore, caution should be paid to the interpretation of the results of the study.

A recently published meta-analysis analyzing data from RCTs comparing sAVR and TAVI advocated a significantly higher risk of all-cause mortality and re-hospitalization in TAVI patients compared to sAVR beyond 2-year follow-up. These results suggested short-term advantages of TAVI were mitigated by a worsening in outcomes after 2 years of follow-up, with the higher

Table IV
Cox regression analysis for all-cause death

Cox Regression for all-cause death						
	Univariable			Multivariable		
	HR	95% CI	P value	HR	95% CI	P value
PPI (TVC)	1.35	1.05–1.68	.048	1.49	1.02–2.2	.039
PVL >grade II (TVC)	1.77	1.1–2.44	.024	1.63	1.06–2.53	.042
Endocarditis	2.55	0.82–8.00	.108			
Stroke/TIA	1.05	0.46–2.36	.913			
Reoperation	0.91	0.23–3.65	.891			
Non-TF TAVI	1.24	1.01–1.47	.034			

PPI, permanent pacemaker implantation; *PVL*, perivalvular leak; *TAVI*, transcatheter aortic valve implantation; *TF*, transfemoral; *TIA*, transient ischemic attack; *TVC*, time-varying covariate.

incidence of procedural complications of transcatheter valves (vascular complication, PPI, and PVL) a determinant risk factor affecting long-term outcomes. In our series, PVL at discharge was significantly lower in SU-AVR when compared to TAVI (PVL ≥II: SU-AVR = 0.97% vs TAVI = 4.8%) as well as the incidence of PPI (SU-AVR: 6.4% vs TAVI: 11.8%, $P < .001$). These results for SU-AVR and TAVI are consistent with those reported in the literature.[2-4,10,26,27] The Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry and PARTNER II trial reported that significant PVL was an independent predictor of mortality at follow-up.[2,27] Faroux and Biner et al reported conduction disturbances requiring PPI after TAVI as an independent predictor of mortality. Accordingly, we confirmed these findings (PVL ≥2: HR: 1.63%; 95% CI: 1.06–2.53, $P = .042$) (PPI: HR: 1.49%; 95% CI:1.02–2.20, $P = .039$).[2,27-30]

In adjunct, Sinning et al identified PVL as a determinant for postoperative AKI development after TAVI[28]: "The hemodynamic changes resulting from significant acute aortic regurgitation hamper diastolic renal blood flow, and lead to deterioration of renal function, especially in patients with low left ventricular ejection fraction."[28] The higher incidence of PVL in the TAVI group might explain the higher rate of postoperative AKI in this study (SUAVR = 2.1% vs TAVI = 4.4%, $P = .026$), thus acting as an additive risk factor negatively affecting long-term outcomes.

Finally, the incidence of stroke has been identified as a significant factor impacting both quality of life and postoperative survival[31]; thus, it was included in the composite end point of the PARTNER II and SURTAVI trials.[2,4] The current study found an incidence of stroke comparable with data from the GARY registry on 18,100 patients reported by Beyersdorf et al (sAVR = 1.6% vs TAVI = 1.4%, $P = .786$),[32] giving an incidence of stroke in the surgical cohort considerably lower when compared with PARTNER II and SURTAVI (sAVR PARTNER II = 6.1%, sAVR SURTAVI = 5.6%). The discrepancy between "real-world" outcomes (registries, independent studies) and RCTs underlines the importance of study design and patients' selection at the RCTs' entry point to avoid selection biases related to the presence of risk factors with different weights in the 2 arms.

Study limitations

The present study has the limitation of any non-randomized observational study. The lack of randomization may lead to some selection biases. The propensity score matching methodology may eliminate most of these biases, but some residual confounding factors may persist. The absence of an independent echocardiography core laboratory, the use of older generations of TAVIs, and the use of multiple transcatheter heart valve devices represented a further limitation of the study.

In conclusion, this propensity-matched analysis of sutureless aortic valve significantly improved early, mid-, and long-term outcomes when compared to TAVI in patients at intermediate risk profile according to primary (30-day mortality, 9-year all-cause, and cardiac-related death) and secondary endpoints (MACCEs). Moreover, this study confirmed what was already reported in the literature: PVL and PPI negatively affect survival after TAVI.

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Conflict of interest/Disclosure

Supplementary materials

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