

# Minimally invasive versus transapical versus transfemoral aortic valve implantation: A one-to-one-to-one propensity score–matched analysis



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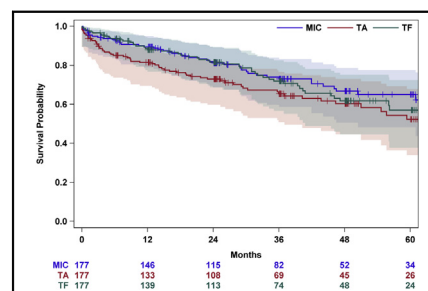
## ABSTRACT

**Objectives:** Although transcatheter aortic valve implantation was the treatment of choice in inoperable and high-risk patients, the effect of transcatheter aortic valve implantation relative to conventional aortic valve replacement via ministernotomy in patients with moderate surgical risk remains unclear.

**Methods:** We consecutively enrolled patients who underwent minimally invasive aortic valve replacements via ministernotomy (n = 1929), transapical (n = 607), and transfemoral (n = 1273) aortic valve implantations from a single center during the period from July 2009 to July 2017. Of those, we conducted a 1:1:1 propensity score matching according to 23 preoperative risk factors.

**Results:** We were able to find 177 triplets (n = 531). The median European System for Cardiac Operative Risk Evaluation II was 3.0% versus 3.4% versus 2.9%, and Society of Thoracic Surgeons Predicted Risk of Mortality was 3.2% versus 3.6% versus 3.4%, respectively. According to the Valve Academic Research Consortium 2 criteria, there were no significant periprocedural differences regarding 30-day mortality (2.3% minimally invasive aortic valve replacement vs 4.5% transapical transcatheter aortic valve implantation vs 1.7% transfemoral transcatheter aortic valve implantation,  $P = .34$ ), stroke (1.1% minimally invasive aortic valve replacement vs 0.6% transapical transcatheter aortic valve implantation vs 1.7% transfemoral transcatheter aortic valve implantation,  $P = .84$ ), or myocardial infarction (0.6% minimally invasive aortic valve replacement vs 0.0% transapical transcatheter aortic valve implantation vs 0.0% transfemoral transcatheter aortic valve implantation,  $P = .83$ ). Both intensive care and hospitalization times were significantly longer in the transapical group. Regarding midterm survival, transapical transcatheter aortic valve implantation was associated with a tendency toward a less favorable outcome (hazard ratio, 1.48; 95% confidence interval, 0.95–2.31;  $P = .17$ ) compared with minimally invasive aortic valve replacement.

**Conclusions:** In this real-world propensity score–matched minimally invasive aortic valve replacement, transapical transcatheter aortic valve implantation, transfemoral transcatheter aortic valve implantation cohort of intermediate-risk patients, early mortality was not significantly different, whereas the rates of periprocedural complications were different depending on the approach. During follow-up, there was a tendency in the transapical transcatheter aortic valve implantation group toward a less favorable survival outcome, although there was no significant difference among the 3 groups. (*J Thorac Cardiovasc Surg* 2018;156:1825–34)



Survival probability in the propensity-matched populations.

## Central Message

There was no significant difference in early mortality after MIC-AVR, TF-TAVI, and TA-TAVI in this PS analysis. The rates and types of early complications were different, depending on the method.

## Perspective

There was no significant difference in mortality or major adverse cardiac and cerebrovascular event among the MIC-AVR, TA-TAVI, and TF-TAVI groups with intermediate risk. Although TAVI is not limited to inoperable patients, our data suggest that we have to carefully choose the most appropriate approach for each individual patient to achieve optimal results.

See Editorial Commentary page 1835.

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**Abbreviations and Acronyms**

AVR	= aortic valve replacement
CI	= confidence interval
HR	= hazard ratio
LBBB	= left bundle branch block
MIC-AVR	= minimally invasive aortic valve replacement
PARTNER	= Placement of Aortic Transcatheter Valves
PMI	= pacemaker implantation
PS	= propensity score
SAVR	= surgical aortic valve replacement
TA	= transapical
TAVI	= transcatheter aortic valve implantation
TEE	= transesophageal echocardiography
TF	= transfemoral
VARC	= Valve Academic Research Consortium

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Progress in the techniques and management of surgical aortic valve replacement (SAVR) has steadily improved outcomes in patients with severe symptomatic aortic valve stenosis. Several studies have also shown various benefits of minimally invasive (MIC) approaches, that is, reduced blood loss, shortened length of hospital stay, preservation of lung function, and more rapid return to functional activity.<sup>1-3</sup> Transcatheter aortic valve implantation (TAVI) has been introduced as an alternative to SAVR in high-risk patients. Because of the rapidly evolving TAVI technology and recent accumulated experiences, the outcomes of TAVI have improved and the incidences of complications such as bleeding and vascular injury have been reduced. The Placement of Aortic Transcatheter Valves (PARTNER) trial has shown similar outcomes after TAVI and SAVR in high-risk patients.<sup>4</sup> Nowadays, TAVI procedures are routinely performed worldwide, even in patients at lower risk, although the role of TAVI has not been clarified for intermediate- or low-risk patients.

To address this issue, we conducted a 1:1:1 propensity score (PS)-matched analysis among 3809 consecutive patients who underwent aortic valve replacement (AVR) via ministernotomy or transapical (TA) or transfemoral (TF) TAVI at our hospital.

**MATERIALS AND METHODS****Patients**

The decision regarding a treatment strategy of MIC-AVR or TAVI, and the access route for TAVI were based on an interdisciplinary consensus by our TAVI team, including cardiac surgeons, cardiologists, and anesthesiologists.

Between July 2009 and July 2017, a total of consecutive 1929 patients underwent MIC-AVR, 607 patients underwent TA-TAVI, and 1273 patients underwent TF-TAVI in our institution. Data collection and analysis were performed under approval by the local institutional review board. Written informed consent was obtained from all patients.

**Procedures**

Details of the MIC-AVR procedure have been described.<sup>3</sup> In brief, MIC-AVR was performed via an upper ministernotomy with cardiopulmonary bypass and mild systemic hypothermia. Skin incision was 7 to 8 cm in length, and an upper sternotomy was performed and extended from the midline into the right fourth intercostal space. Bioprosthetic valves were implanted in all cases. Cardiopulmonary bypass and crossclamp times in the MIC group were 79 minutes (69; 95) and 59 minutes (52; 72) (median [first quartile; third quartile]), respectively.

The surgical and interventional techniques of TA-TAVI and TF-TAVI have been well described and standardized.<sup>5,6</sup> The function of the prosthesis was assessed by transesophageal echocardiography (TEE) and aortography. In patients receiving TAVI, the endotracheal tube was removed immediately after the procedure in the operation room, if appropriate.

Patients with biological valves received warfarin for 3 months postoperatively, and then warfarin was switched to 100 mg acetylsalicylic acid. All patients receiving TAVI received 100 mg of acetylsalicylic acid (indefinitely) and clopidogrel (for 3 months) from the second postoperative day.

**Preoperative Patient Characteristics**

The following 23 preoperative variables were recorded for each patient: age, sex, year of surgery, height, weight, left ventricular ejection fraction, glomerular filtration rate, European System for Cardiac Operative Risk Evaluation II, Society of Thoracic Surgeons Predicted Risk of Mortality version 2.61,<sup>7-9</sup> German Aortic Valve Score,<sup>10</sup> hypertension, previous aortic valve surgery, diabetes mellitus, chronic obstructive pulmonary disease, pulmonary hypertension, preoperative stroke, peripheral arterial occlusive disease stage II or higher, cerebrovascular disease, atrial fibrillation, coronary artery disease, previous myocardial infarction, heart failure classified by New York Heart Association Functional Classification, and priority.

**Categoric and Continuous Outcomes**

The primary objective of this analysis was to determine 30-day and midterm survival in patients undergoing MIC-AVR versus TA-TAVI versus TF-TAVI. Additional categoric outcomes were perioperative complications in accordance with the Valve Academic Research Consortium (VARC)-2 criteria.<sup>11</sup> We also evaluated ventilation time, operative time, duration of intensive care unit stay, and duration of hospitalization. The clinical follow-up was conducted on an outpatient basis or by telephone interview with the treating physicians or hospitals. With respect to midterm follow-up, the median observational time was 766 days, with a first quartile of 376 and a third quartile of 1468 days. The maximum follow-up time was 2931 days.

**Statistical Analysis**

Because the surgical technique was decided on in a nonrandomized fashion, we conducted a matched PS analysis with 1:1:1-matching ratios, as suggested by Rassen and colleagues.<sup>12</sup> A logistic regression model including all the covariates from Table 1 as main effects was used to estimate the PS. Fourteen missing values for glomerular filtration rate were

TABLE 1. Characteristics of patients at baseline

Variable	All patients (n = 3809)					PS-matched sample (n = 531)				
	MIC-AVR (n = 1929)	TA-TAVI (n = 607)	Z	TF (n = 1273)	Z	MIC-AVR (n = 177)	TA-TAVI (n = 177)	Z	TF-TAVI (n = 177)	Z
Age [y, median (Q1; Q3)]	70 (61; 76)	82 (78; 86)	−38.2	83 (79; 86)	−49.1	78 (75; 82)	80 (75; 84)	−1.52	79 (75; 83)	0.02
Female gender [n (%)]	836 (43.3)	328 (54.0)	4.62	737 (57.9)	8.15	94 (53.1)	90 (50.9)	−0.43	87 (49.2)	−0.74
Year of surgery [n (%)]			−0.10		12.7			−0.14		1.05
2009	74 (3.8)	16 (2.6)		22 (1.7)		4 (2.3)	6 (3.4)		2 (1.1)	
2010	146 (7.6)	41 (6.8)		44 (3.5)		15 (8.5)	12 (6.8)		8 (4.5)	
2011	168 (8.7)	49 (8.1)		70 (5.5)		15 (8.5)	13 (7.3)		16 (9.0)	
2012	218 (11.3)	76 (12.5)		98 (7.7)		22 (12.4)	22 (12.4)		22 (12.4)	
2013	273 (14.2)	97 (16.0)		143 (11.2)		27 (15.3)	32 (18.1)		34 (19.2)	
2014	352 (18.3)	113 (18.6)		167 (13.1)		34 (19.2)	32 (18.1)		28 (15.8)	
2015	323 (16.7)	121 (19.9)		228 (17.9)		30 (17.0)	37 (20.9)		31 (17.5)	
2016	236 (12.2)	53 (8.7)		320 (25.1)		18 (10.2)	13 (7.3)		17 (9.6)	
2017	139 (7.2)	41 (6.8)		181 (14.2)		12 (6.8)	10 (5.7)		19 (10.7)	
Height [cm, median (Q1; Q3)]	171 (164; 178)	165 (159; 172)	11.5	165 (160; 172)	13.6	167 (160; 173)	167 (160; 173)	0.18	168 (160; 175)	−0.41
Weight [kg, median (Q1; Q3)]	80 (70; 91)	72 (63; 82)	9.86	73 (63; 84)	12.5	76 (68; 87)	75 (67; 85)	0.13	76 (66; 85)	0.31
LVEF [%, median (Q1; Q3)]	60 (57; 66)	55 (45; 60)	18.0	55 (45; 55)	30.2	58 (50; 62)	59 (50; 60)	−1.11	55 (55; 55)	0.88
GFR [mL/min, median (Q1; Q3)]	80.7 (66.7; 92.4)	56.0 (40.9; 72.4)	22.2	59.3 (43.7; 74.4)	26.9	65.7 (51.3; 79.6)	63.9 (50.9; 77.3)	0.58	68.8 (51.8; 81.2)	−1.14
euroSCORE II [%, median (Q1; Q3)]	1.2 (0.8; 1.9)	6.0 (3.5; 10.3)	−19.8	4.9 (3.0; 8.0)	−25.9	3.0 (1.9; 4.2)	3.4 (2.1; 5.1)	−1.17	2.9 (1.9; 4.2)	0.57
German Aortic Valve score [%; median (Q1; Q3)]	1.2 (0.8; 1.6)	2.9 (2.2; 3.9)	−18.0	2.7 (2.1; 3.8)	−26.1	1.9 (1.7; 2.5)	2.2 (1.8; 2.8)	−1.45	2.0 (1.6; 2.5)	0.99
STS score [%, median (Q1; Q3)]	1.5 (1.0; 2.3)	5.9 (4.0; 9.2)	−23.7	5.0 (3.6; 7.6)	−34.4	3.2 (2.3; 5.0)	3.6 (2.6; 5.0)	−0.37	3.4 (2.5; 4.7)	1.27
Hypertension [n (%)]	1447 (75.0)	549 (90.4)	9.97	1131 (88.9)	10.5	158 (89.3)	157 (88.7)	−0.17	158 (89.3)	0.00
Previous aortic valve surgery [n (%)]	1 (0.1)	13 (2.1)	3.54	42 (3.3)	6.45	1 (0.6)	2 (1.1)	0.58	1 (0.6)	0.00
Diabetes mellitus [n (%)]	362 (18.8)	214 (35.3)	7.73	387 (30.4)	7.43	53 (29.9)	51 (28.8)	−0.23	50 (28.3)	−0.35
COPD [n (%)]	88 (4.6)	105 (17.3)	7.93	156 (12.3)	7.44	22 (12.4)	16 (9.0)	−1.03	19 (10.7)	−0.50
Pulmonary hypertension [n (%)]	177 (9.2)	202 (33.3)	11.9	552 (43.4)	22.2	45 (25.4)	48 (27.1)	0.36	45 (25.4)	0.00

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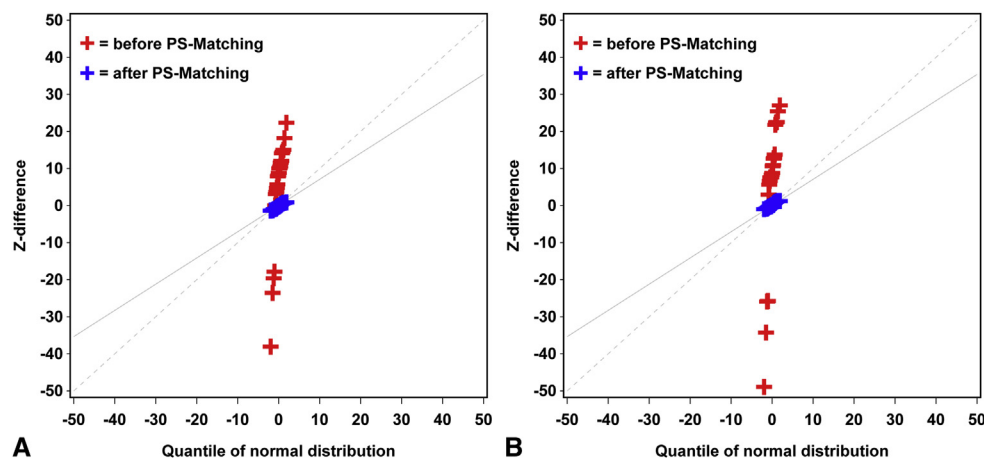
TABLE 1. Continued

Variable	All patients (n = 3809)					PS-matched sample (n = 531)				
	MIC-AVR (n = 1929)	TA-TAVI (n = 607)	Z	TF (n = 1273)	Z	MIC-AVR (n = 177)	TA-TAVI (n = 177)	Z	TF-TAVI (n = 177)	Z
Stroke [n (%)]	37 (1.9)	51 (8.4)	5.55	75 (5.9)	5.44	7 (4.0)	10 (5.7)	0.75	10 (5.7)	0.75
PAOD [n (%)]	60 (3.1)	193 (31.8)	14.9	127 (10.0)	7.40	18 (10.2)	22 (12.4)	0.67	15 (8.5)	−0.55
Cerebrovascular disease [n (%)]	89 (4.6)	140 (23.1)	10.4	217 (17.1)	10.7	23 (13.0)	17 (9.6)	−1.01	26 (14.7)	0.46
Atrial fibrillation [n (%)]	36 (1.9)	167 (27.5)	13.9	406 (31.9)	22.4	22 (12.4)	19 (10.7)	−0.50	20 (11.3)	−0.33
CAD [n (%)]			25.9		25.3			0.39		1.07
1-vessel	171 (8.9)	99 (16.3)		243 (19.1)		26 (14.7)	28 (15.8)		35 (19.8)	
2-vessel	75 (3.9)	83 (13.7)		174 (13.7)		14 (7.9)	21 (11.9)		16 (9.0)	
3-vessel	46 (2.4)	214 (35.3)		292 (22.9)		25 (14.1)	21 (11.9)		26 (14.7)	
Previous MI [n (%)]	58 (3.0)	100 (16.5)	8.66	145 (11.4)	8.63	15 (8.5)	11 (6.2)	−0.82	13 (7.3)	−0.39
NYHA class [n (%)]			14.3		21.6			−0.66		−0.95
I	219 (11.3)	20 (3.3)		27 (2.1)		7 (4.0)	11 (6.2)		13 (7.3)	
II	983 (51.0)	174 (28.7)		288 (22.6)		63 (35.6)	63 (35.6)		64 (36.2)	
III	700 (36.3)	345 (56.8)		862 (67.7)		97 (54.8)	95 (53.7)		91 (51.4)	
IV	27 (1.4)	68 (11.2)		96 (7.5)		10 (5.7)	8 (4.5)		9 (5.1)	
Priority urgent/ emergency [n (%)]	9 (0.5)	14 (2.3)	2.93	19 (1.5)	2.75	3 (1.7)	2 (1.1)	−0.45	1 (0.6)	−1.01

PS, Propensity score; MIC-AVR, minimally invasive aortic valve replacement; TA-TAVI, transcatheter aortic valve implantation; Z, z-difference; TF, transfemoral; Q1, first quartile; Q3, third quartile; LVEF, left ventricular ejection fraction; GFR, glomerular filtration rate; euroSCORE, European System for Cardiac Operative Risk Evaluation; STS, Society of Thoracic Surgeons; COPD, chronic obstructive pulmonary disease; PAOD, peripheral arterial occlusive disease; CAD, coronary artery disease; MI, myocardial infarction; NYHA, New York Heart Association Functional Classification.

imputed by a single multiple imputation step. Matching was performed with an SAS-based (SAS Version 9.3; SAS Institute Inc, Cary, NC) nearest-neighbor matching algorithm as implemented in the

Pharmacoepidemiology Toolbox of Rassen and colleagues.<sup>13</sup> Rassen and colleagues<sup>13</sup> gave no explicit recommendation for choosing the caliper width for matching; so, we used the caliper width (0.35), which



**FIGURE 1.** A, Q-Q plot for judging balance (via z-differences; Table 1) of the 15 preoperative patient variables before and after PS matching when comparing MIC with TA; z-differences from a randomized trial would follow the broken light gray line; z-differences from a perfectly matched PS analysis would follow the solid light gray line. B, Q-Q plot for judging balance (via z-differences; Table 1) of the 15 preoperative patient variables before and after PS matching when comparing MIC with TF; z-differences from a randomized trial would follow the broken light gray line; z-differences from a perfectly matched PS analysis would follow the solid light gray line. PS, Propensity score.

TABLE 2. Primary end points and categoric, continuous, and follow-up outcomes in the propensity score–matched sample

Categoric outcomes						
	PS-matched sample (n = 531)					Global <i>P</i> value for treatment
	MIC (n = 177)	TA (n = 177)	OR [95% CI]	TF (n = 177)	OR [95% CI]	
Mortality <72 h [n (%)]	0 (0)	3 (1.7)	3.85 [0.87 to –]	1 (0.6)	1.00 [0.11 to –]	.31
Mortality <30 d [n (%)]	4 (2.3)	8 (4.5)	2.00 [0.61-7.61]	3 (1.7)	0.75 [0.14-3.63]	.34
Perioperative myocardial infarction [n (%)]	1 (0.6)	0 (0.0)	1.00 [0.00-9.00]	0 (0.0)	1.00 [0.00-9.00]	.83
TIA [n (%)]	1 (0.6)	1 (0.6)	1.00 [0.03-39.0]	1 (0.6)	1.00 [0.03-39.0]	.89
Stroke [n (%)]	2 (1.1)	1 (0.6)	0.50 [0.02-6.57]	3 (1.7)	1.50 [0.22-12.6]	.84
Nondisabling stroke [n (%)]	0 (0)	0 (0)	–	0 (0)	–	–
Disabling stroke [n (%)]	2 (1.1)	1 (0.6)	0.50 [0.02-6.57]	3 (1.7)	1.50 [0.22-12.6]	.84
New pacemaker [n (%)]	10 (5.7)	24 (13.6)	2.55 [1.21-5.69]	34 (19.2)	3.79 [1.86-8.27]	<.001
New ICD [n (%)]	0 (0.0)	2 (1.1)	2.41 [0.46 to –]	4 (2.3)	5.29 [1.29 to –]	.17
Atrial fibrillation [n (%)]	43 (24.3)	24 (13.6)	0.46 [0.25; 0.82]	11 (6.2)	0.19 [0.08-0.38]	<.0001
Other arrhythmia [n (%)]	17 (9.6)	20 (11.3)	1.22 [0.59-2.52]	35 (19.8)	2.60 [1.34-5.22]	.007
Low output syndrome [n (%)]	10 (5.7)	12 (6.8)	1.22 [0.50-3.00]	2 (1.1)	0.19 [0.03-0.80]	.03
Bleeding [n (%)]						
Major	3 (1.7)	5 (2.8)	1.67 [0.39-8.47]	2 (1.1)	0.67 [0.08-4.48]	.61
Life threatening	0 (0.0)	0 (0.0)	–	0 (0.0)	–	–
Acute kidney injury [n (%)]						
Stage 1	5 (2.8)	2 (1.1)	0.40 [0.05-2.03]	0 (0.0)	0.15 [0.00-0.59]	.07
Stage 2	0 (0.0)	1 (0.6)	1.00 [0.11 to –]	0 (0.0)	–	.83
Stage 3	16 (9.0)	14 (7.9)	0.87 [0.41-1.83]	2 (1.1)	0.12 [0.02-0.46]	.003
Vascular complications [n (%)]						
Minor	0 (0)	0 (0)	–	29 (16.4)	41.3 [– to –]	<.0001
Major	0 (0)	0 (0)	–	4 (2.3)	5.29 [1.29 to –]	.03
New-onset complete atrioventricular block [n (%)]	9 (5.1)	21 (11.9)	2.53 [1.14-6.01]	31 (17.5)	4.09 [1.90-9.49]	.001
Continuous outcomes						
	MIC (n = 177)	TA (n = 177)	MD [95% CI]	TF (n = 177)	MD [95% CI]	Global <i>P</i> value for treatment
Ventilation time [h]						
Mean (SD)	22.5 (63.4)	21.5 (67.3)	–1.03 [–12.5-10.4]	1.89 (22.0)	–20.6 [–32.1–9.16]	.0004
Median (Q1; Q3)	9.3 (7.1; 12.4)	6.9 (0.0; 11.9)		0 (0; 0)		
Operative time [min]						
Mean (SD)	166 (36.1)	93 (43.8)	–73 [–80–65]	75 (30.9)	–91 [–99–83]	<.0001
Median (Q1; Q3)	160 (139; 185)	85 (75; 97)		68 (56; 81)		
Duration of ICU stay [d]						
Mean (SD)	3.4 (5.9)	4.7 (6.2)	1.3 [0.2-2.4]	3.3 (4.3)	–0.1 [–1.2-1.1]	.03
Median (Q1; Q3)	1 (1; 3)	3 (1; 5)		2 (2; 4)		
Duration of hospitalization [d]						
Mean (SD)	15.2 (7.8)	18.2 (8.4)	3.0 [1.4-4.7]	12.9 (7.6)	–2.3 [–4.0–0.7]	<.0001
Median (Q1; Q3)	14 (12; 15)	16 (14; 21)		11 (9; 14)		
Follow-up outcome						
	MIC (n = 177)	TA (n = 177)	HR [95% CI]	TF (n = 177)	HR [95% CI]	Global <i>P</i> value for treatment
1-y/2-y/3-y survival probability	89%/81%/74%	81%/73%/65%	1.48 [0.95-2.31]	89%/82%/72%	1.08 [0.68-1.71]	.17

PS, Propensity score; MIC, minimally invasive; TA, transapical; OR, odds ratio; CI, confidence interval; TF, transfemoral; TIA, transient ischemic attack; ICD, implantable cardioverter defibrillator; MD, mean deviation; SD, standard deviation; Q1, first quartile; Q3, third quartile; ICU, intensive care unit; HR, hazard ratio.



**TABLE 3. Echocardiographic valve performance after minimally invasive aortic valve replacement, transapical transcatheter aortic valve implantation, and transfemoral transcatheter aortic valve implantation in the propensity score-matched sample**

	MIC	TA	MD [95% CI]	TF	MD [95% CI]	Global <i>P</i> value for treatment
AVA [cm <sup>2</sup> ]						
Mean (SD)	1.90 (0.40)	1.78 (0.52)	−0.12 [−0.240–0.003]	1.81 (0.42)	−0.09 [−0.20–0.02]	.10
Median (Q1; Q3)	1.80 (1.60; 2.10)	1.60 (1.50; 2.00)		1.80 (1.50; 2.00)		
MPG [mm Hg]						
Mean (SD)	12.0 (4.6)	11.0 (7.7)	−1.00 [−2.34–0.38]	10.2 (5.8)	−1.76 [−3.04–−0.47]	.03
Median (Q1; Q3)	11 (9; 15)	10 (7; 13)		9 (7; 12)		
AI (PVL) [grade I–III]						
AI I [n (%)]	3 (1.7)	34 (22.7)	13.5 [4.55–56.3]	54 (32.3)	22.2 [7.61–91.3]	<.0001
AI ≥2 [n (%)]	1 (0.6)	3 (2.0)	3.20 [0.34–84.4]	23 (13.8)	28.7 [5.09–624]	<.0001

MIC, Minimally invasive; TA, transapical; MD, mean deviation; CI, confidence interval; TF, transfemoral; AVA, aortic valve area; SD, standard deviation; Q1, first quartile; Q3, third quartile; MPG, mean pressure gradient; AI, Aortic insufficiency; PVL, paravalvular leakage.

resulted in good covariate balance on the one hand and a fair number of matched triplets on the other. Balance of risk factors was judged by the recently proposed z-difference,<sup>14</sup> and we sought a minimal mean square error of all 46 z-differences comparing TA-TAVI with MIC-AVR and TF-TAVI with MIC-AVR. The z-difference has the advantage of assessing binary, ordinal, and continuous variables on the same scale. Moreover, plotting z-differences before and after matching in a Q-Q-plot allows balance to be compared with that of a randomized trial and a perfectly matched PS analysis. To measure treatment effects, we calculated odds ratios for binary, differences in means for continuous, and hazard ratios (HRs) for time-to-event outcomes. All analyses adjusted for the PS matching stratum via conditioning, that is conditional exact logistic regression (SAS LOGISTIC procedure with STRATA statement), linear mixed models (SAS MIXED procedure with random effect for the matching stratum), and stratified proportional hazard models (SAS PHREG procedure with STRATA statement) for binary, continuous, and time-to-event outcomes, respectively. The treatment effect was included as a 3-valued categorical covariate in all of these models. Parameter estimates are given for TA-TAVI and TF-TAVI, both with reference to MIC-AVR effect, with their 95% confidence intervals (CIs) and with an overall *P* value for the treatment effect.

### Propensity Score Matching

Table 1 summarizes the preoperative patient variables before and after PS matching. After matching, we found 177 triples not differing in terms of their preoperative risk profile. According to the z-differences in Table 1 and the Q-Q-plots in Figure 1, balance of risk factors dramatically improved after PS matching. In the matched sample, balance is better than in a randomized trial and very close to a perfectly matched PS analysis.

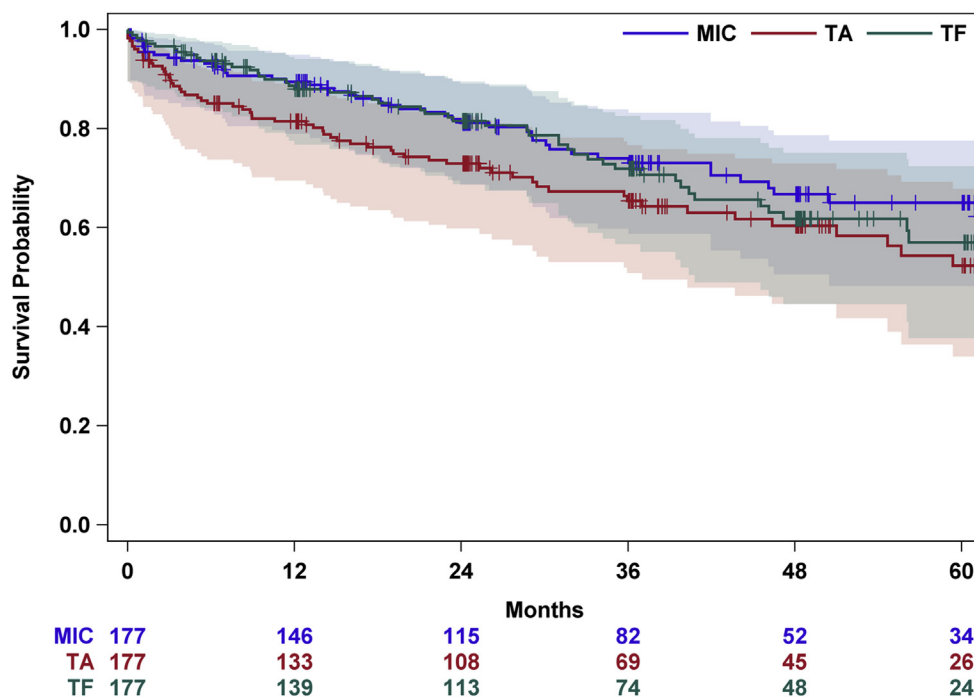
Patients undergoing MIC-AVR received stented prostheses (Perimount Magna, Edwards Lifesciences, Irvine, Calif; 131/177, 74.0%, Perimount Magna Ease, Edwards Lifesciences; 25/177, 14.1%, Hancock II, Medtronic, Minneapolis, Minn; 5/177, 2.8%, Trifecta, St Jude Medical Inc, St Paul, Minn; 14/177, 7.9%) or sutureless prostheses (Perceval, Sorin/LivaNova Group, Saluggia, Italy; 2/177, 1.1%). In the TA-TAVI group, the implanted prostheses were Sapien XT (Edwards Lifesciences; 74/177, 41.8%), Sapien 3 (Edwards Lifesciences; 57/177, 32.2%), or Accurate TA (Symetis, Lausanne, Switzerland; 46/177, 26.0%). In the TF-TAVI group, the implanted prostheses were CoreValve (Medtronic, Minneapolis, Minn; 99/177, 55.9%), Sapien XT (28/177, 15.8%), Sapien 3 (26/177, 14.7%), Accurate TF neo (4/177, 2.3%), or Direct Flow (Direct Flow Medical Inc, Santa Rosa, Calif; 20/177, 11.3%).

### RESULTS

Table 2 depicts the results for the categorical and continuous outcomes in the matched subgroups. In comparison, there were no significant differences regarding periprocedural mortality within 72 hours and 30 days. There were also no significant differences in the proportions of stroke, perioperative myocardial infarction, or bleeding complications. The incidences of postoperative low output syndrome and renal complication (stage 3) were significantly more frequent after MIC-AVR and TA-TAVI than after TF-TAVI. The incidence of new-onset complete atrioventricular block and the need for permanent pacemaker implantation (PMI) were more common after TA-TAVI and TF-TAVI than after MIC-AVR. The incidence of postoperative atrial fibrillation was more frequent after MIC-AVR than after TA-TAVI and TF-TAVI. Other arrhythmias, including complete or incomplete left bundle branch block (LBBB), occurred more frequently after TF-TAVI than after MIC-AVR. Vascular complications occurred only in patients undergoing TF-TAVI (minor complications in 16.4% and major complications in 2.3%) and no patients undergoing MIC-AVR or TA-TAVI. The average operation time was longer in the MIC-AVR group than in both TAVI groups. The average ventilation time was significantly shorter in the TF-TAVI group than in the MIC-AVR and TA-TAVI groups. Both intensive care and hospitalization times were significantly longer in the TA-TAVI group than in the MIC-AVR and TF-TAVI groups.

Table 3 depicts the postoperative aortic valve area, the mean pressure gradient, and the rate of aortic insufficiency through paravalvular leakages by echocardiography at discharge.

Regarding survival experience over the complete follow-up time, there was no significant difference. However, the TA-TAVI procedure showed a tendency toward a less favorable outcome (TA-TAVI HR, 1.48; 95% CI, 0.95–2.31; TF-TAVI HR, 1.08; 95% CI, 0.68–1.71; global *P* value for treatment = .17, ref. MIC-AVR) (Table 2 and Figure 2).



**FIGURE 2.** Kaplan–Meier analysis of overall survival with 95% confidence bands and patients at risk at the respective time points. Results from the proportional hazards model are given as HRs with 95% CIs as an inset. *MIC*, Minimally invasive; *TA*, transapical; *TF*, transfemoral.

## DISCUSSION

The results of our study showed no significant differences in perioperative mortality or major adverse cardiovascular and cerebral complications according to VARC-2 among the MIC-AVR, TA-TAVI, and TF-TAVI groups with intermediate surgical risk.

In the matched sample, we observed no significant difference in the incidence of bleeding complications among the 3 groups. However, considering the more invasive nature of operative AVR and coagulopathy that results from the use of cardiopulmonary bypass, it is an expected result that bleeding complications were more frequent after MIC-AVR than after TAVI. In the PARTNER trial, the incidences of major bleeding complications defined by VARC criteria within 30 days after SAVR, TF-TAVI, and TA-TAVI were 22.7%, 11.3%, and 8.8%, respectively.<sup>15</sup> In the world's first randomized trial, first-generation Edwards SAPIEN valves and delivery systems were used. Over the last couple of years, the field of TAVI has evolved rapidly. The new-generation valve has emerged, and the sheath diameter of delivery system has been significantly reduced. Recently, the outcome of the PARTNER II trial with use of the second-generation Edwards SAPIEN XT was published. Because of the effects of lower-profile delivery system, the risk of major complications such as stroke, vascular, or bleeding complications decreased when compared with the previous trial.

Recent studies have shown better clinical outcomes with MIC-AVR compared with conventional AVR.<sup>1-3</sup> However, MIC-AVR is technically demanding and likely to require longer crossclamp and operation times, which are associated with potential additive risks. We have already reported in a previous article that the average operation and cross-clamp times were slightly longer in the MIC-AVR group than in conventional AVR (161 vs 155 minutes, 58 vs 54 minutes, respectively). However, these differences are not clinically relevant.<sup>3</sup> The procedural advantages of MIC-AVR over TAVI are that a surgeon can directly observe the anatomy of the aortic valve, accurately remove valve leaflets and annular calcifications, and measure the aortic annulus to choose the optimal prosthesis size. Furthermore, if the final result of the implanted prosthesis is found to be inappropriate (eg, paravalvular leakage discovered with TEE), the surgeon can immediately improve it. The incidence of paravalvular leakage can be reduced by direct removal of annular calcification and intraoperative surgical improvement after TEE control. In our study, there was no significant difference in aortic valve area after MIC-AVR, TA-TAVI, and TF-TAVI ( $1.90 \pm 0.40 \text{ cm}^2$  vs  $1.78 \pm 0.52 \text{ cm}^2$  vs  $1.81 \pm 0.42 \text{ cm}^2$ , respectively, global *P* value for treatment = .10). Mean pressure gradient was statistically significantly lower in the TF-TAVI group than in the MIC-AVR group. However, this difference was clinically relevant (MIC-AVR  $12.0 \pm 4.6 \text{ mm Hg}$ , TA-TAVI

11.0  $\pm$  7.7 mm Hg, TF-TAVI 10.2  $\pm$  5.8 mm Hg, global *P* value for treatment = .03). The rate of postoperative aortic insufficiency through the paravalvular leakage was significantly less in the MIC-AVR than in the TA-TAVI and TF-TAVI groups (AI I, 1.7% vs 22.7% vs 32.3%, *P* < .0001; AI  $\geq$  2, 0.6% vs 2.0% vs 13.8%, *P* < .0001, respectively) (Table 3).

Similar to the results of other studies,<sup>16-21</sup> the need for new PMI was more frequent in both TAVI groups compared with the MIC-AVR group in our series. The incidence of atrioventricular conduction injury during TAVI procedure can be caused by the lateral dislocation of annular calcific nodules or by the radial prosthesis-expanding force itself. These stresses to the His bundle in the region of the membranous septum are associated with the occurrence of new conduction abnormalities, specifically new LBBB. The persistent LBBB after TAVI is associated with a lack of improvement in left ventricular ejection fraction, poorer function status at long-term follow-up, and complete atrioventricular block requiring PMI.<sup>16</sup> PMI after TAVI is reported to be associated with certain unfavorable hemodynamic changes, including left ventricular ejection fraction reduction and deterioration of right ventricular function.<sup>17,18</sup> Although the impact of a postprocedural LBBB and PMI on hemodynamic performance may be less important for elderly and inoperable patients, it may affect survival over the long term and quality of life for younger and lower-risk patients.

Several studies have reported the outcomes of TAVI versus SAVR for patients with low or intermediate risk. The NOTION trial was a randomized clinical trial with a total of 280 low-risk patients undergoing TF-TAVI and SAVR. Mortality of these 2 groups was 2.1% versus 3.7% (*P* = .43) at 30 days and 4.9% versus 7.5% (*P* = .38) at 1 year, respectively.<sup>19</sup> It was expected that the lower-risk patients would show more benefits from the less-invasive TAVI procedure than high-risk patients. However, there was no significant difference in mortality at 30 days and 1 year.

The PARTNER II trial was one of the largest randomized trials and assigned 2032 intermediate-risk patients (mean Society of Thoracic Surgeons Predicted Risk of Mortality 5.8%) to TAVI and SAVR. There was no significant difference in mortality at 30 days (3.9% vs 4.1%), 1 year (12.3% vs 12.9%), and 2 years (16.7% vs 18.0%). However, the subgroup analyses showed that the TF-TAVI group had a significantly lower rate of death or disabling stroke than the SAVR group. On the other hand, the outcomes of the transthoracic TAVI group were inferior to the SAVR group. In parallel, we found in our study that the TA-TAVI group had a tendency toward a less favorable outcome over the follow-up period compared with the other groups, although the difference did not reach statistical significance.

Piazza and colleagues<sup>20</sup> analyzed a 3-center PS-matched comparison of the intermediate-risk patients undergoing TF-TAVI and SAVR. They found no significant difference in mortality at 30 days (7.8% vs 7.1%) and 1 year (16.5% vs 16.9%) between the TF-TAVI and SAVR groups. Latib and colleagues<sup>21</sup> analyzed an intermediate-risk PS-matched population (111 pairs) of TF-TAVI and SAVR groups. The mortality was 1.8% at 30 days for both groups and 6.4% (TF-TAVI) versus 8.1% (SAVR) at 1 year (HR, 0.87; 95% CI, 0.32-2.41; *P* = .80).<sup>21</sup> In the latter studies with low- to moderate-risk patients, major vascular complications, the need for PMI, and postprocedural moderate and severe aortic regurgitation were more frequent in the TAVI groups, which was confirmed by our study. Although TAVI is not superior to SAVR for perioperative mortality and major adverse cardiovascular and cerebral events, these data showed that TAVI is safe and effective in low- and intermediate-risk patients.

The decision for TAVI or SAVR has to be based on individual patient characteristics and risk factors and on clinical judgment to avoid high perioperative mortality and morbidity. As attention shifts to lower-risk populations, the question of risk versus benefit has to be considered. Because lower- and intermediate-risk patients will have a longer life expectancy, the complications with an after-effect will have greater impact on quality of life after interventions. The Observational Study of Effectiveness of SAVR-TAVI Procedures for Severe Aortic Stenosis Treatment investigated the outcomes after SAVR and TAVI in low-risk patients. In this study, survival and freedom from major adverse cardiac and cerebrovascular event at 3-year follow-up were significantly better after SAVR than TAVI (83.4% vs 72.0%; HR, 1.59; 95% CI, 1.18-2.13; *P* = .002).<sup>22</sup> Despite the improvement in clinical outcome due to the technical refinement and remarkable progress of the devices, clinical uncertainties still exist, such as the durability of valves,<sup>23</sup> the long-term neurologic influence of the silent stroke, and hemodynamic influence of conduction abnormalities after TAVI. A residual postprocedural paravalvular leakage is also one of the issues of TAVI, which should be resolved before expanding the TAVI indication to lower-risk patients with longer life expectancy. Therefore, we think that MIC-AVR is the first choice for intermediate-risk patients at present, although TF-TAVI was comparable to MIC-AVR in mortality over the midterm follow-up in our study. Heavily calcified aortic valve is one of the risk factors for paravalvular leakages and residual high-pressure gradient after TAVI. These postprocedural unfavorable outcomes can affect the life of patients with only intermediate risk after TAVI. If a patient has contraindications for MIC-AVR, such as porcelain aorta or a high operative risk due to a reoperation, the next option should be TF-TAVI. Although TA-TAVI trended toward a less favorable outcome in the midterm follow-up, TA-TAVI is



still a good option if TF-TAVI is impossible because of severe stenosis or kinking of peripheral arteries.

### Study Limitations

This study is limited as a single-center experience, based on retrospective analysis of our institutional, observational, prospectively collected database. In this study, we did not analyze the impact factors of calcified aorta, hostile chest, chest deformity, or frailty. These factors are not included in the European System for Cardiac Operative Risk Evaluation II and Society of Thoracic Surgeons score, but they can also influence the procedure decision. Each TAVI case was preoperatively evaluated by a multidisciplinary heart team consisting of cardiac surgeons, interventional cardiologists, and anesthesiologists. A heart team, by its nature, may contain some selection bias in making treatment decisions. The present study lacked assessment of patient satisfaction, postoperative hemodynamic improvement, and cost-effectiveness, which are also important outcomes that need to be further researched. PS analysis was used to adjust for differences in preoperative risk factors. This analysis is useful for reducing bias in observational studies. Although we were able to identify well-matched triplets by 23 confounders, we could not match many of the TAVI cases, that is, the baseline characteristics were substantially different.

During peer review, the fact that our PS-matched sample is only a small and nonrepresentative subsample of all operated patients was heavily criticized and considered as the main weakness of our analysis. However, we consider this fact as a strength rather than a weakness because by PS matching (instead of, eg, covariate adjustment for the PS or an inverse probability of treatment weighing estimation) we made sure that the groups to be compared were really comparable, while we certainly anticipated that we would lose a large number of patients.

### CONCLUSIONS

Our PS-adjusted study showed no significant difference in mortality at 30 days, incidence of stroke, or myocardial infarction among MIC-AVR, TF-TAVI, and TA-TAVI. MIC-AVR, TF-TAVI, and TA-TAVI resulted in different periprocedural complications associated with each approach. There was no significant difference in midterm mortality among MIC-AVR, TA-TAVI, and TF-TAVI. Although TAVI is not limited to inoperable patients, our data suggest that we have to carefully choose the most appropriate approach for each individual patient to achieve optimal results.

### Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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**Key Words:** aortic valve replacement, minimally invasive cardiac surgery, propensity score analysis, transcatheter aortic valve implantation

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