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STRUCTURAL

Transcatheter Versus Surgical Aortic Valve Replacement in Patients With Complex Coronary Artery Disease

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ABSTRACT

OBJECTIVES The aim of this study was to compare, in a cohort of patients with complex coronary artery disease (CAD) and severe aortic stenosis (AS), the clinical outcomes associated with transfemoral transcatheter aortic valve replacement (TAVR) (plus percutaneous coronary intervention [PCI]) versus surgical aortic valve replacement (SAVR) (plus coronary artery bypass grafting [CABG]).

BACKGROUND Patients with complex CAD were excluded from the main randomized trials comparing TAVR with SAVR, and no data exist comparing TAVR + PCI vs SAVR + CABG in such patients.

METHODS A multicenter study was conducted including consecutive patients with severe AS and complex CAD (SYNTAX [Synergy Between PCI with Taxus and Cardiac Surgery] score >22 or unprotected left main disease). A 1:1 propensity-matched analysis was performed to account for unbalanced covariates. The rates of major adverse cardiac and cerebrovascular events (MACCE), including all-cause mortality, nonprocedural myocardial infarction, need for new coronary revascularization, and stroke, were evaluated.

RESULTS A total of 800 patients (598 undergoing SAVR + CABG and 202 undergoing transfemoral TAVR + PCI) were included, and after propensity matching, a total of 156 pairs of patients were generated. After a median follow-up period of 3 years (interquartile range: 1-6 years), there were no significant differences between groups for MACCE (HR for transfemoral TAVR vs SAVR: 1.33; 95% CI: 0.89-1.98), all-cause mortality (HR: 1.25; 95% CI: 0.81-1.94), myocardial infarction (HR: 1.16; 95% CI: 0.41-3.27), and stroke (HR: 0.42; 95% CI: 0.13-1.32), but there was a higher rate of new coronary revascularization in the TAVR + PCI group (HR: 5.38; 95% CI: 1.73-16.7).

CONCLUSIONS In patients with severe AS and complex CAD, TAVR + PCI and SAVR + CABG were associated with similar rates of MACCE after a median follow-up period of 3 years, but TAVR + PCI recipients exhibited a higher risk for repeat coronary revascularization. Future trials are warranted. (J Am Coll Cardiol Intv 2021;14:2490–2499)

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Transcatheter aortic valve replacement (TAVR) is an alternative to surgical aortic valve replacement (SAVR) for patients 65 years of age or older with symptomatic severe aortic stenosis (AS) (1,2). In light of the promising results obtained with TAVR compared with SAVR in low-risk patients (3,4), an expansion of TAVR toward the treatment of younger patients with AS and low surgical risk is expected in the upcoming years. However, a substantial number of patients treated for severe AS in a real-world setting would have been ineligible for the aforementioned randomized trials (5), and the decision-making process in such cases remains controversial.

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A high prevalence of concomitant coronary artery disease (CAD) has been reported in the TAVR population, with up to 25% of TAVR recipients undergoing percutaneous coronary intervention (PCI) during the preprocedural work-up or at the time of the TAVR procedure (6). Additionally, CAD severity and completeness of revascularization may have an impact on clinical outcomes following TAVR (6). The presence of concomitant complex CAD has been a common exclusion criterion in most randomized studies (3,4) and remains one of the most important features limiting the generalizability of the results of trials comparing TAVR versus SAVR to the general AS population. Scarce data exist on the clinical outcomes associated with SAVR compared with TAVR in the presence of complex CAD, and whether to perform a fully percutaneous approach by means of TAVR plus PCI or a surgical-based procedure with coronary artery bypass grafting (CABG) at the time of SAVR remains controversial. Thus, we sought to compare, in a large cohort of patients with complex CAD and severe AS, the clinical outcomes associated with TAVR + PCI versus SAVR + CABG.

METHODS

This was a multicenter study including consecutive patients with severe AS and complex CAD who underwent either transfemoral TAVR (data derived from 14 centers across North America and Europe) or SAVR (data derived from a single center in North America) between 2007 and 2019. Data regarding medical history, procedural details, and clinical outcomes were recorded in a dedicated database. In-hospital medical records as well as national and regional public health registries were used to ensure accurate follow-up. The decision to perform either surgery or percutaneous treatment was taken individually by the heart team at each center. The study was performed in accordance with the ethics committee of each participating center and all patients provided informed consent for the procedures.

Severe AS was defined according to current guidelines when at least 1 of the following features was present: aortic valve area <1 cm^2, indexed aortic valve area <0.6 cm^2/m^2, peak transaortic valve velocity >4 m/s, or transaortic mean gradient >40 mm Hg (7). Complex CAD was considered as either significant (>50%) unprotected left main CAD or the presence of an anatomical SYNTAX (Synergy Between PCI with Taxus and Cardiac Surgery) score higher than 22 (4). The SYNTAX score was calculated for each patient on the basis of the coronarography preceding CABG or PCI. For patients undergoing TAVR + PCI, all PCIs took place either within 3 months before TAVR or at the time of the TAVR procedure, whereas for patients undergoing SAVR + CABG, all coronary bypass procedures were performed at the time of SAVR. All patients received before TAVR or at the time of SAVR the best revascularization deemed feasible by the heart team, and no staged coronary procedures were planned.

CLINICAL OUTCOMES. The primary outcome was a composite of major adverse cardiac and cerebrovascular events (MACCE) including all-cause mortality, nonprocedural myocardial infarction, need for new coronary revascularization, and stroke at follow-up. The secondary outcomes included the individual components of the combined primary endpoint. The events were defined according to Valve Academic Research Consortium-2 criteria and acute coronary syndrome guidelines (8,9). Type 2 non-ST-segment elevation myocardial infarctions (those settings with oxygen demand and supply imbalance unrelated to acute coronary atherothrombosis triggered by situations such as sustained tachyarrhythmia, severe hypertension, respiratory failure, severe anemia,

ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

CABG = coronary artery bypass grafting

CAD = coronary artery disease

MACCE = major adverse cardiac and cerebrovascular event(s)

PCI = percutaneous coronary intervention

PS = propensity score

SAVR = surgical aortic valve replacement

STS = Society of Thoracic Surgeons

TAVR = transcatheter aortic valve replacement

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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TABLE 1 Baseline Characteristics of the TAVR + PCI and SAVR + CABG Groups

	Unmatched Population			
	TAVR + PCI (n = 202)	SAVR + CABG (n = 598)	*P* Value	Standardized Difference
Age, y	81.8 ± 7.8	74 ± 8.3	0.001	0.94
Female	77 (38.1)	149 (24.9)	0.001	0.28
BMI, kg/m^2	26.7 ± 4.3	28.1 ± 5.1	0.001	−0.29
COPD	35 (17.3)	54 (9.0)	0.001	0.24
Diabetes mellitus	66 (32.7)	252 (42.1)	0.02	−0.17
Hypertension	157 (77.7)	521 (87.1)	0.02	−0.24
Previous MI	60 (29.7)	215 (36)	0.11	−0.08
Prior valve surgery	13 (7.5)	0 (0.0)	0.001	0.29
Prior pacemaker	17 (8.4)	31 (5.2)	0.09	0.13
Prior atrial fibrillation	58 (28.7)	112 (18.7)	0.003	0.21
Peripheral vascular disease	32 (15.8)	113 (18.9)	0.33	−0.06
Glomerular filtration rate, mL/min/1.73 m^2	53.6 ± 23	63.8 ± 23.2	0.001	−0.42
NYHA functional class			0.001	
I and II	68 (33.7)	358 (59.9)		
III and IV	134 (66.3)	240 (40.1)		0.54
STS mortality	6.3 ± 6.2	4.3 ± 4.1	0.001	0.37
SYNTAX score	25.6 ± 8.6	27.1 ± 7.4	0.02	−0.20
Left main disease	120 (59.4)	308 (51.5)	0.05	0.19
LVEF, %	52.7 ± 12.9	53.7 ± 12.5	0.51	−0.07
AVA, cm^2	0.65 ± 0.19	0.77 ± 0.17	0.001	−0.60
Moderate/severe MR	45 (22.3)	102 (17.1)	0.10	0.15
Moderate/severe AR	11/79 (13.9)	101 (16.8)	0.52	−0.08

Values are mean ± SD or n (%).

AR = aortic regurgitation; AVA = aortic valve area; BMI = body mass index; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MR = mitral regurgitation; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; SAVR = surgical aortic valve replacement; STS = Society of Thoracic Surgeons; SYNTAX = Synergy Between PCI With Taxus and Cardiac Surgery; TAVR = transcatheter aortic valve replacement.

hypotension, or shock) were not included in the analysis. Clinical follow-up was performed according to the clinical practice of each center at 1 and 12 months after procedure and yearly thereafter.

STATISTICAL ANALYSIS. Continuous variables are expressed as mean ± SD or median (interquartile range) and categorical variables as absolute numbers and percentages. Comparisons were performed using Student's *t*-test for normally distributed continuous variables, and the Mann-Whitney *U* test was used for continuous variables not normally distributed. The chi-square and Fisher exact tests were used to compare categorical variables as appropriate. Propensity score (PS) matching was used to adjust for differences in baseline characteristics and potential confounders that may lead to biased estimates of treatment outcomes. A PS was calculated for each patient to estimate the propensity for being included in a specific treatment group (TAVR + PCI vs SAVR + CABG). This was done by means of a multivariate logit regression including the following covariates: age, sex, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, prior myocardial infarction, prior valvular cardiac surgery, peripheral vascular disease, atrial fibrillation, New York Heart Association functional class at the time of procedure, estimated glomerular filtration rate, left ventricular ejection fraction, moderate or severe mitral regurgitation at baseline, unprotected left main disease, anatomical SYNTAX score, and Society of Thoracic Surgeons (STS) Predicted Risk of Mortality score. A 1-to-1 nearest neighbor matching algorithm without replacement, with a caliper of 0.2, was performed to identify PS-matched pairs. Adequate balance of covariate distribution between the matched groups was numerically assessed using standardized means differences before and after propensity matching and graphically assessed using box and cumulative probability plots for raw and propensity-matched data (Supplemental Figures 1 and 2). Cox regression analyses were performed in the propensity-matched population to compare 5-year rates for the primary and secondary outcomes according to the treatment received (TAVR + PCI vs SAVR + CABG), and HRs with their 95% CIs were reported (all HRs are reported as TAVR + PCI vs SAVR + CABG, with values >1 indicating a higher risk for the percutaneous group). Kaplan-Meier estimates and the log-rank test were used to compare and graphically display outcomes between groups. *P* values <0.05 were considered to indicate statistical significance for all statistical tests. Finally, to evaluate the presence of unobserved, unbalanced confounders leading to biased results, an alternative outcome (first noncardiac readmission related to pneumonia, cancer, or bone fracture), which should not be affected by the treatment under study, was investigated.

All analyses were performed using Stata version 14.0 software (StataCorp).

RESULTS

A total of 806 patients presented with severe AS and complex CAD and were included. Among them, 604 (74.9%) and 202 (25.1%) patients underwent SAVR + CABG and transfemoral TAVR + PCI, respectively. A total of 6 patients (1%) in the SAVR + CABG group were lost of follow-up, whereas all patients had a clinical follow-up in the TAVR + PCI group. Therefore, 598 (74.8%) and 202 (25.2%) patients were ultimately included in the SAVR + CABG and TAVR + PCI groups, respectively. All coronary bypass grafts were performed concomitantly during the index SAVR surgery, whereas the median time between PCI and TAVR was 34 days (interquartile range: 11-71 days).

Baseline clinical characteristics for the nonmatched cohorts are displayed in **Table 1**, while the characteristics for the propensity-matched cohorts are presented in **Table 2**. In the overall population, patients in the TAVR + PCI group were older ($P = 0.001$), were more frequently women ($P = 0.001$), and exhibited higher STS scores ($P = 0.001$). The main procedural characteristics regarding coronary revascularization and aortic valve replacement features are displayed in **Tables 3 and 4** for the matched TAVR + PCI and SAVR + CABG groups, respectively. The main procedural characteristics for the unmatched populations are summarized in Supplemental Tables 1 and 2.

After PS matching, a total of 156 pairs were formed, and the baseline covariates were well balanced between groups (**Table 2**). The mean STS score was 5.8% ± 5.1% and 5.7% ± 4.3% for the TAVR + PCI and SAVR + CABG groups, respectively ($P = 0.97$). A total of 51 patients (32.7%) in the propensity-matched TAVR group exhibited severely calcified ascending aortas. After a median follow-up period of 3 years (interquartile range: 1-6 years), the incidence of MACCE (the primary endpoint) was 15.7 events per 100 patient-years for the TAVR + PCI group and 10.3 events per 100 patient-years for the SAVR + CABG group (HR: 1.33; 95% CI: 0.89-1.98; $P = 0.15$) (**Table 5**). The Kaplan-Meier estimates for MACCE at 5-year follow-up are shown in the **Central Illustration**. The MACCE rates at 5-year follow-up were 52.1% and 38.2% in the TAVR + PCI and SAVR + PCI groups, respectively (log-rank $P = 0.15$). The incidence of all-cause mortality in the PS-matched cohort was 11.6 and 8.4 deaths per 100 patient-years for the TAVR + PCI and SAVR + CABG groups, respectively (HR: 1.25; 95% CI: 0.81-1.94; $P = 0.30$) (**Table 5**). The Kaplan-Meier estimates for all-cause mortality at 5-year follow-up are shown in **Figure 1A**. The mortality rate at 5 years was slightly higher in the TAVR + PCI group (38.1%) compared with the SAVR + CABG group (32.2%), without statistically significant differences (log-rank $P = 0.30$). A total of 12 patients (7.6%) underwent repeat coronary revascularization at follow-up, with a higher incidence among TAVR + PCI versus SAVR + CABG patients (3.3 vs 0.7 events per 100 patient-years; HR: 5.38; 95% CI: 1.73-16.7; $P = 0.003$) (**Table 5**). The Kaplan-Meier estimates for repeat revascularization at 5-year follow-up are shown in **Figure 1B**, and the reasons underlying the need for new coronary revascularization are displayed in Supplemental Table 3. The 5-year repeat revascularization rates were 24.4% and 4.1% in the TAVR + PCI and SAVR + CABG groups, respectively (log-rank $P = 0.002$). There were no significant differences between the TAVR + PCI and SAVR + CABG groups for the endpoint of myocardial infarction (1.9 vs 1.5 events per 100 patient-years; HR: 1.16; 95% CI: 0.41-3.27; $P = 0.78$). The Kaplan-Meier estimates for myocardial infarction events at 5-year follow-up are shown in **Figure 1C**. The 5-year myocardial infarction rates were 11.2% and 10.1% for the TAVR + PCI and SAVR + CABG groups, respectively (log-rank $P = 0.78$). A total of 16 patients (5.1%) in the PS-matched cohort experienced stroke during the study period, with the majority of events (n = 9 [56.3%]) occurring during the first 30 days after procedure. The stroke rates were 1.3 and 1.7 events per 100 patient-years for the TAVR + PCI and SAVR + CABG groups, respectively (HR: 0.42; 95% CI: 0.13-1.32; $P = 0.14$) (**Table 5**). The Kaplan-Meier estimates for stroke events at 5-year follow-up are shown in **Figure 1D**. The 5-year stroke rates were 2.9% and 7.2% in the TAVR + PCI and SAVR + CABG groups, respectively (log-rank $P = 0.13$).

Table 6 and Supplemental Figure 3 show the results of a 30-day landmark analysis conducted to further examine the incidence of the selected endpoints after the periprocedural period. In this subanalysis, the rates of the composite primary endpoint, all-cause

TABLE 2 Baseline Characteristics of the Propensity Score–Matched Population

	Matched Population			
	TAVR + PCI (n = 156)	SAVR + CABG (n = 156)	*P* Value	Standardized Difference
Age, y	79.5 ± 8	79 ± 6.7	0.51	0.09
Female	66 (33.5)	71 (36)	0.60	−0.03
BMI, kg/m^2	27.1 ± 4.6	26.9 ± 5	0.57	0.08
COPD	33 (16.8)	35 (17.8)	0.79	−0.04
Diabetes mellitus	72 (36.5)	63 (32)	0.34	0.09
Hypertension	167 (84.8)	163 (82.7)	0.59	0.03
Previous MI	68 (34.5)	72 (36.5)	0.67	−0.04
Prior valve surgery	3 (1.5)	3 (1.5)	1.00	0.00
Prior pacemaker	13 (8.3)	9 (5.8)	0.38	0.10
Prior atrial fibrillation	54 (27.4)	54 (27.4)	1.00	0.00
Peripheral vascular disease	51 (25.9)	47 (23.9)	0.64	0.08
Glomerular filtration rate, mL/min/1.73 m^2	55.1 ± 24	53.5 ± 19	0.47	0.02
NYHA functional class			0.99	−0.11
I and II	82 (40.6)	80 (41.6)		
III and IV	115 (59.4)	117 (58.4)		
STS mortality, %	5.8 ± 5.1	5.7 ± 4.3	0.97	0.004
SYNTAX score	26.3 ± 8.1	26.9 ± 7.5	0.50	−0.07
Left main involvement	87 (55.8)	89 (57.1)	0.81	−0.03
LVEF, %	52.1 ± 13.2	52.9 ± 12.9	0.59	−0.06
AVA, cm^2	0.66 ± 0.19	0.72 ± 0.19	0.01	−0.31
Moderate/severe MR	36 (23.1)	37 (23.7)	0.89	−0.02
Moderate/severe AR	8/62 (12.9)	24 (15.4)	0.61	−0.08

Values are mean ± SD or n (%).
Abbreviations as in **Table 1**.

TABLE 3 Procedural Details for the Propensity Score–Matched TAVR + PCI Cohort

Type of TAVR	
BEV	95 (60.9)
SEV	61 (39.1)
Old-generation THV (SAPIEN, SAPIEN XT, or CoreValve)	68 (43.6)
Prosthesis size	
<26 mm	37 (23.7)
≥26 mm	119 (76.3)
Post-TAVR mean transvalvular gradient, mm Hg	9.7 ± 4.3
Post-TAVR mean gradient >20 mm Hg	3 (0.7)
Post-TAVR severe patient-prosthesis mismatch (index EOA <0.65 cm^2/m^2)	13/80 (16.3)
Post-TAVR moderate/severe AR	12 (7.8)
Number of diseased coronary vessels	
1	26 (16.7)
2	61 (39.1)
3	69 (44.2)
Left main disease	87 (55.8)
SYNTAX score	26.3 ± 8.1
SYNTAX score terciles	
Second tercile (>22 and ≤32)	66 (42.3)
Third tercile (>32)	53 (34)
Type of PCI	
DES	130 (83.3)
BMS	24 (15.4)
DEB	1 (0.65)
Plain old balloon angioplasty	1 (0.65)
Number of vessels treated	
1	77 (49.4)
2	62 (39.7)
3	17 (10.9)
Number of lesions treated	
1	77 (49.4)
2	49 (31.4)
3	21 (13.5)
4	9 (5.8)
Use of rotational atherectomy	21 (13.5)
Use of cutting balloon	25 (16)
Number of stents implanted	2.2 ± 1.4
Total length of stent, mm	42.9 ± 34
At least one bifurcation lesion	86 (55.1)
At least one ostial lesion	77 (49.4)
At least one chronic total occlusion	55 (35.3)
Complete revascularization	78 (50)

Values are n (%) or mean ± SD.

BEV = balloon-expandable valve; BMS = bare-metal stent(s); DEB = drug-eluting balloon; DES = drug-eluting stent(s); EOA = effective orifice area; SEV = self-expandable valve; THV = transcatheter heart valve; other abbreviations as in Table 1.

mortality, and new coronary revascularization were significantly higher for the TAVR + PCI group, whereas there were no statistically significant differences for myocardial infarction or stroke events.

Data regarding an alternative outcome including noncardiac readmissions related to pneumonia, cancer, or bone fracture are shown in Supplemental Table 4. No differences between groups were observed regarding this noncardiac readmission composite outcome. Data on cardiac rehospitalization (of any cause) are presented in Supplemental Table 5. A higher rate of cardiac rehospitalization was observed in TAVR + PCI recipients.

DISCUSSION

The main findings of our study can be summarized as follows: in a large cohort of consecutive patients with severe AS and complex CAD (SYNTAX score >22 and/or left main disease): 1) TAVR + PCI and SAVR + CABG were associated with similar rates of MACCE after a median follow-up period of 3 years (**Central Illustration**); 2) there was an increased risk for repeat coronary revascularization in the TAVR + PCI group; and 3) in a landmark analysis excluding the periprocedural (initial 30 days) period, the rates of MACCE and all-cause mortality were higher in the TAVR + PCI (vs SAVR + CABG) group.

The treatment of CAD in patients undergoing TAVR remains a controversial topic, partially because of the lack of definite data on the need to revascularize hemodynamically significant coronary lesions found in the preprocedural TAVR work-up. The benefit of coronary revascularization in patients with stable ischemic heart disease is contentious (10). However, a recent meta-analysis reported lower rates of nonprocedural myocardial infarction and unstable angina readmission after coronary revascularization in patients in stable condition with CAD (11), and current guidelines recommend revascularizing severe (>70%) coronary lesions located in proximal coronary segments before TAVR (12). Therefore, pre-TAVR revascularization has been common practice at most TAVR centers to date. Also, it has been well established that the presence of complex CAD (eg, multivessel disease, involvement of the left main coronary artery) has a significant negative impact on patient outcomes independent of the presence of angina-like symptomatology, and previous studies have suggested a potential benefit of coronary revascularization (CABG, PCI) versus medical treatment alone in such cases (13,14). Also, it has been demonstrated that the benefit of PCI in multivessel stable CAD is greater when achieving complete revascularization (15). Although most previous TAVR studies included patients with less complex CAD (mean SYNTAX score < 14) (6), all patients included in our study had severe complex CAD.

Randomized trials comparing TAVR and SAVR for the treatment of severe AS in low- and intermediate-risk patients included patients with CAD, with rates ranging between 4% and 22% (3,4,16,17). These trials showed either the superiority or noninferiority of TAVR compared with SAVR, but only patients with

noncomplex CAD were included. Thus, the SYNTAX score for recent low-risk TAVR versus SAVR trials (PARTNER [Placement of Aortic Transcatheter Valves] 3 and Evolut Low Risk [Evolut Surgical Replacement and Transcatheter Aortic Valve Implantation in Low-Risk Patients]) was as low as about 2 for the TAVR and SAVR groups. Interestingly, a subanalysis of the PARTNER 3 trial showed that unlike the overall superiority results of TAVR compared with SAVR, the combined primary endpoint (death, stroke, or rehospitalization) was not statistically different between TAVR and SAVR in those patients with CAD requiring coronary revascularization (either PCI or CABG). However, a small number of patients (TAVR, n = 32; surgery, n = 58) were included in that subanalysis (3). These findings may raise concern about differences in clinical course between both strategies when CAD is present.

Data regarding left main revascularization and TAVR are limited. Although one observational study reported the feasibility of left main percutaneous revascularization pre-TAVR, this was based on a very high risk cohort (mean STS score 8.1) with limited follow-up (18). Controversial results exist regarding surgical versus percutaneous left main revascularization outside the severe AS clinical setting, and clinical guidelines recommend both therapies in cases of low SYNTAX scores (<23), with a surgical approach favored for more complex scenarios (SYNTAX score >23) (13). Recent clinical trials have shown that in patients with unprotected left main disease, the rates of new revascularization and target vessel failure were higher for PCI compared with CABG (19,20), with controversial results regarding mortality events. Additionally, the BEST (Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients With Multivessel Coronary Artery Disease) trial showed a higher rate of repeat revascularization following PCI compared with CABG in patients with multivessel CAD (21). Our findings are therefore in line with those previously reported in CABG versus PCI trials for left main and multivessel CAD, with the percutaneous approach associated with higher rates of new revascularization procedures. However, it must be outlined that the rate of new coronary revascularization (25% at 5 years) is relatively low considering the burden of CAD observed in this subpopulation.

Recent PCI vs CABG trials for complex CAD did not demonstrate significant differences between treatment groups with respect to stroke events (19-21). However, previous SAVR versus TAVR trials revealed significant differences between groups regarding cerebrovascular events, favoring the transcatheter

TABLE 4 Procedural Details of the Propensity Score–Matched SAVR + CABG Cohort

Type of SAVR	
Bioprosthesis	154 (98.7)
Mechanical	2 (1.3)
Prosthesis size	
<26 mm	141 (90.4)
≥26 mm	15 (9.6)
Post-SAVR mean transvalvular gradient, mm Hg	13.5 ± 4.8
Post-SAVR mean gradient >20 mm Hg	12 (7.7)
Post-SAVR severe patient-prosthesis mismatch (index EOA <0.65 cm^2/m^2)	35/140 (25)
Post-SAVR moderate/severe AR	1 (0.6)
Number of diseased coronary vessels	
1	1 (0.6)
2	66 (42.3)
3	89 (57.1)
Left main disease	89 (57.1)
SYNTAX score	26.9 ± 7.5
SYNTAX score terciles	
Second tercile (>22 and ≤32)	71 (45.5)
Third tercile (>32)	52 (33.3)
At least 1 chronic total occlusion	59 (37.8)
Number of grafts performed	
1	0
2	42 (26.9)
3	100 (64.1)
4	11 (7)
5	2 (1.3)
6	1 (0.7)
Use of left internal mammary artery	140 (89.7)
Complete revascularization	151 (96.8)
Concomitant mitral valve intervention	12 (7.7)
Mitral valve replacement	11 (7.1)
Mitral valve repair	1 (0.6)
Concomitant tricuspid valve intervention	
Tricuspid valve replacement	0
Tricuspid valve repair	0
Concomitant ascending aortic surgery	6 (3.8)
Time of extracorporeal circulation, min	144 ± 35

Values are n (%) or mean ± SD.
Abbreviations as in Tables 1 and 3.

TABLE 5 Incidence and Survival Estimate for the Primary and Secondary Outcomes in the Propensity Score–Matched Population

	TAVI + PCI	SAVR + CABG	HR (95% CI)	*P* Value
Primary endpoint[a]				
MACCE	15.7	10.3	1.33 (0.89-1.98)	0.15
Secondary endpoints[a]				
All-cause mortality	11.6	8.4	1.25 (0.81-1.94)	0.30
New coronary revascularization	3.3	0.7	5.38 (1.73-16.7)	0.003
Myocardial infarction	1.9	1.5	1.16 (0.41-3.27)	0.78
Stroke	1.3	1.7	0.42 (0.13-1.32)	0.14

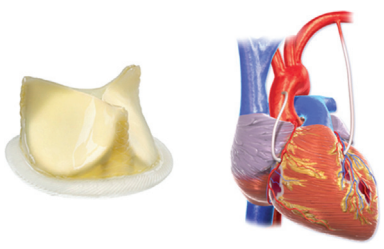
[a]Incidences are expressed as events per 100 patient-year.
MACCE = major adverse cardiac and cerebrovascular event(s); other abbreviations as in Table 1.

CENTRAL ILLUSTRATION **Study Flowchart and Main Findings**

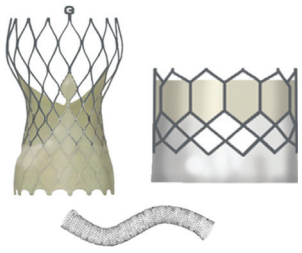
800 patients with severe aortic stenosis and complex coronary artery disease (SYNTAX score >22 or unprotected left main disease)

598 (74.8%) SAVR + CABG

202 (25.2%) Transfemoral TAVR + PCI



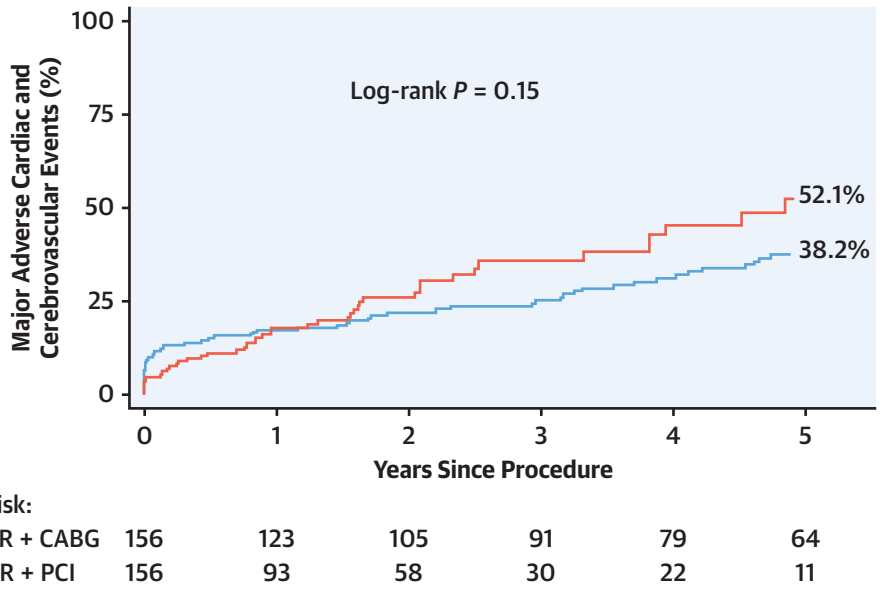
1:1 Propensity-matching



156 patients SAVR + CABG

156 patients TAVR + PCI

Primary endpoint: All-cause death, myocardial infarction, stroke, or new coronary revascularization

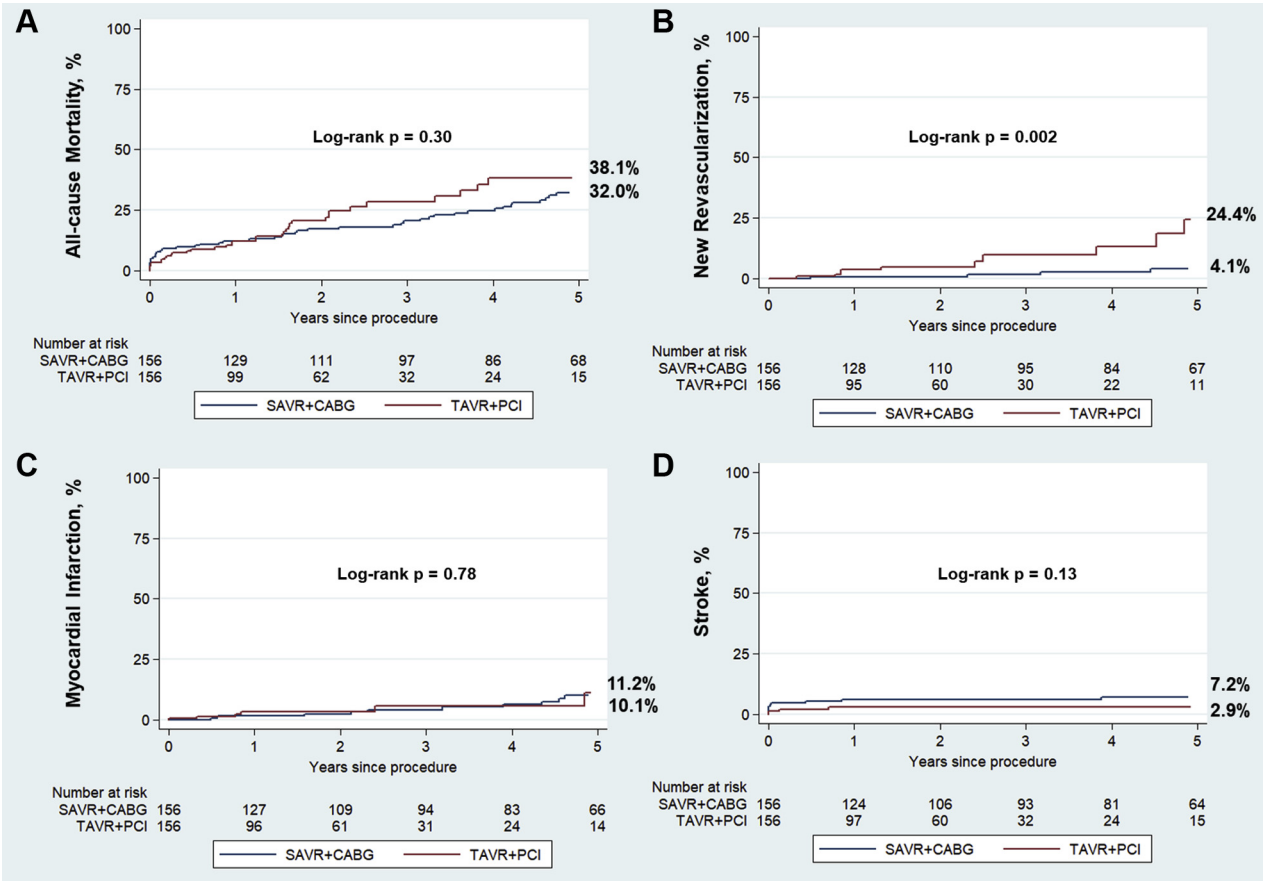


Alperi, A. et al. J Am Coll Cardiol Intv. 2021;14(22):2490–2499.

A series of 800 patients with severe aortic stenosis and severe coronary artery disease undergoing either surgical aortic valve replacement (SAVR) plus coronary artery bypass grafting (CABG) or transfemoral transcatheter aortic valve replacement (TAVR) plus percutaneous coronary intervention (PCI) was evaluated. After 1:1 propensity matching, a total of 156 pairs of matched patients were obtained. The primary endpoint of all-cause mortality, myocardial infarction, stroke, or new coronary revascularization was similar between groups.

approach in moderate- to low-risk patients (3,17). Interestingly, the higher rates of stroke in the surgical groups were driven mainly by early (periprocedural/30-day) events. In our PS-matched cohort there was a trend toward a higher risk for stroke for the SAVR + CABG group, and in accordance with previous SAVR versus TAVR trials, this was due primarily to a higher incidence of postprocedural stroke in surgical patients. It should be outlined that unlike isolated CABG, for which interventions can be performed off-pump when deemed appropriate and feasible by the surgical team, all SAVR + CABG interventions must be

FIGURE 1 **Kaplan-Meier Cumulative Incidence Estimates for the Secondary Endpoints**



Kaplan-Meier cumulative incidence estimates at 5-year follow-up for **(A)** all-cause mortality, **(B)** new coronary revascularization, **(C)** myocardial infarction, and **(D)** stroke. CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

performed under extracorporeal circulation, with longer pump times compared with isolated SAVR or CABG. This could have played a role in the higher stroke rate observed in our study (similar to some previous SAVR vs TAVR trials), as opposed to what has been reported in CABG versus PCI studies.

It should be noted that in the TAVR + PCI group, neither the presence of significant valve disease beyond the aortic valve nor the presence of ascending aorta dilation or aneurysm was addressed, whereas these concomitant pathologies were treated in a proportion of patients in the SAVR + CABG subgroup (Table 4). Additionally, postprocedural valve performance was different between groups; while the rates of significant residual aortic regurgitation were higher for the TAVR + PCI group, the mean gradient and the rate of severe prosthesis-patient mismatch were numerically lower in this group. Finally, the rate of complete revascularization was lower for the TAVR + PCI group, probably in relation to the complexity of the concomitant CAD with a significant proportion of chronic total occlusions. Overall, all

TABLE 6 **Incidence and Survival Estimates for the Primary and Secondary Outcomes in the Propensity Score–Matched Population in a Landmark Analysis Starting at 30 Days After the Procedure**

	TAVI + PCI	SAVR + CABG	HR (95% CI)	*P* Value
Primary endpoint[a]				
MACCE	13.4	7.7	1.96 (1.26-3.04)	0.003
Secondary endpoints[a]				
All-cause mortality	10	6.8	1.64 (1.03-2.64)	0.04
New coronary revascularization	3.3	0.7	5.38 (1.73-16.7)	0.004
Myocardial infarction	1.5	1.5	1.00 (0.34-3.01)	0.99
Stroke	0.6	0.7	0.76 (0.13-4.31)	0.75

[a]Incidences are expressed as events per 100 patient-year.
Abbreviations as in Tables 1 and 5.

these could have affected clinical outcomes and may be partially responsible for the better clinical course observed in the SAVR + CABG subgroup in the 30-day landmark analysis, once the procedural related comorbidity is largely overcome. However, because of the observational nature of the study, unnoticed baseline conditions that were unbalanced between groups should always be considered. Future studies are needed to determine the feasibility and potential benefit of concomitant mitral or tricuspid percutaneous procedures for patients with multiple valve disease undergoing TAVR, as well as the clinical course of those patients with complex CAD in whom complete revascularization is achieved.

STUDY LIMITATIONS. The study had an observational design, and although the data were collected prospectively, the present analysis was of retrospective nature. There was no independent event adjudication committee for this study. Also, although the baseline covariates included in the PS were well balanced between groups, some features that could have an impact on outcomes, such as frailty status or pulmonary artery pressure, were not systematically assessed. Therefore, the potential presence of unnoted unmatched covariates between both treatment subgroups should raise caution when interpreting the results of this study. However, as shown in Supplemental Table 4, there were no differences between treatment groups regarding noncardiac rehospitalization for pneumonia, cancer, or bone fracture. This would support a lack of significant bias related to the presence of unnoticed noncardiovascular confounders. The inclusion of early-generation transcatheter valve systems may have negatively affected the results. Additionally, the use of a single surgical center raises unanswerable questions about differing selection processes and surgical technique among various centers. Finally, the sample size was limited for the evaluation of some relatively infrequent outcomes (eg, stroke or myocardial infarction), and a type II statistical error could not be excluded in such cases. Larger studies specifically designed to assess the issue of the optimal treatment for patients with severe AS and concomitant complex CAD are needed to shed more light on this issue.

CONCLUSIONS

In patients with severe AS and complex CAD, TAVR + PCI was associated with a similar risk for all-cause mortality and MACCE compared with SAVR + CABG after a median follow-up period of 3 years. However, TAVR + PCI recipients exhibited a higher risk for repeat coronary revascularization over the follow-up period, and higher rates of all-cause mortality and MACCE were observed in the TAVR + PCI group in a landmark analysis excluding the periprocedural (initial 30 days) period. These results may inform future randomized trials and, while waiting for definite data on this topic, would suggest that a surgical strategy (SAVR + CABG) may be considered a more suitable approach for intermediate- to low-risk patients presenting with severe AS and complex concomitant CAD, whereas a full percutaneous approach may be a better option for high-risk and inoperable patients.

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PERSPECTIVES

WHAT IS KNOWN? The presence of concomitant complex CAD has been a common exclusion criterion in most randomized studies comparing SAVR and TAVR, and a high prevalence of concomitant CAD has been reported in the TAVR population.

WHAT IS NEW? Patients with complex CAD and severe AS undergoing TAVR and PCI did not have a higher risk for MACCE or all-cause death compared to patients undergoing SAVR and CABG, but they exhibited a higher rate of new coronary revascularization.

WHAT IS NEXT? Randomized trials including patients with severe AS and complex CAD must be conducted to further evaluate the most suitable interventional strategy in this population.

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KEY WORDS aortic stenosis, coronary artery disease, surgical aortic valve replacement, transcatheter aortic valve replacement

APPENDIX For supplemental tables and figures as well as the case report form, please see the online version of this paper.