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ORIGINAL ARTICLE

Clinical Impact of Myocardium at Risk in Transcatheter Aortic Valve Implantation

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BACKGROUND: The best management of coronary artery disease in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation (TAVI) is debated. We investigated the clinical impact of the residual extent of myocardium at risk in patients undergoing TAVI.

METHODS: Patients enrolled in the REVASC-TAVI (Management of Myocardial Revascularization in Patients Undergoing TAVI With Coronary Artery Disease) international multicenter registry were stratified according to the myocardium jeopardized by coronary artery disease using the British Cardiovascular Intervention Society Jeopardy Score (BCIS-JS) after a planned coronary revascularization. A planned revascularization included percutaneous coronary interventions performed before TAVI, during TAVI, or within 1 month after TAVI. The study population was divided according to the residual BCIS-JS (rBCIS-JS): patients with extensive residual myocardial at risk (rBCIS-JS >4 group) and patients without extensive residual myocardial at risk (rBCIS-JS ≤4 group). The primary study end point was the composite of all-cause death, nonfatal myocardial infarction, nonfatal stroke, and rehospitalization for heart failure at 2 years.

RESULTS: Among the 2407 patients enrolled, 294 pairs of patients were selected by propensity matching and compared. At 2-year follow-up, the incidence of the primary end point was higher in patients with rBCIS-JS >4 compared with patients with rBCIS-JS ≤4 (37.5% versus 23.0%, *P*=0.004). A significantly lower rate of myocardial infarction was reported in patients with BCIS-JS ≤4 (8.2% versus 2.6%, *P*=0.011). At multivariate analysis, rBCIS-JS >4 (hazard ratio, 1.43 [95% CI, 1.11–1.84]; *P*=0.005) independently predicted 2-year major adverse cardiac and cerebrovascular events.

CONCLUSIONS: In patients with concomitant coronary artery disease and severe aortic stenosis, the residual myocardial risk significantly affects TAVI outcomes. In particular, a rBCIS-JS >4 is associated with higher rates of major adverse cardiac and cerebrovascular events at 2 years.

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Key Words: aortic valve stenosis ■ heart failure ■ humans ■ incidence ■ stroke

WHAT IS KNOWN

- Coronary artery disease is common in patients undergoing transcatheter aortic valve implantation, but the best approach to revascularization in this setting remains unclear.
- Recent studies have yielded mixed results: 1 trial showed no benefit from routine pretranscatheter aortic valve implantation percutaneous coronary intervention, whereas another reported improved outcomes with percutaneous coronary intervention limited to significant lesions, leaving no consensus on managing coronary artery disease in transcatheter aortic valve implantation.

WHAT THE STUDY ADDS

- A residual British Cardiovascular Intervention Society Jeopardy Score above 4 was an independent predictor of adverse clinical outcomes at 2 years, underscoring the prognostic importance of residual myocardial ischemic burden in this population.
- These findings highlight the importance of a tailored coronary revascularization strategy before or around transcatheter aortic valve implantation to optimize prognosis.

Nonstandard Abbreviations and Acronyms

AS	aortic stenosis
BCIS-JS	British Cardiovascular Intervention Society Jeopardy Score
CAD	coronary artery disease
FFR	fractional flow reserve
HF	heart failure
HR	hazard ratio
MI	myocardial infarction
PCI	percutaneous coronary intervention
PSM	propensity score matching
rBCIS-JS	residual British Cardiovascular Intervention Society Jeopardy Score
REVASC-TAVI	Management of Myocardial Revascularization in Patients Undergoing Transcatheter Aortic Valve Implantation With Coronary Artery Disease
TAVI	transcatheter aortic valve implantation

Coronary artery disease (CAD) often coexists with degenerative aortic stenosis (AS), with over 50% of patients with AS undergoing surgical or transcatheter aortic valve implantations (TAVIs) also having CAD.[1–5] In surgical cases, coronary artery bypass grafting is typically performed alongside valve replacement.[6,7] However, for patients with TAVI, the optimal CAD management strategy remains unclear. Severe CAD correlates with higher mortality after TAVI, although performing percutaneous coronary intervention (PCI) in these patients can be challenging.[6–8]

Available retrospective data have reported conflicting results regarding the optimal approach to managing CAD in patients with TAVI.[5,8–13] Two recent randomized clinical trials have significantly added to the current knowledge. On one hand, the ACTIVATION trial demonstrated that a routine revascularization strategy did not significantly reduce adverse outcomes after TAVI.[12] On the other hand, the NOTION-3 trial demonstrated that, when guided by fractional flow reserve (FFR) assessment or an angiographic coronary artery diameter stenosis of at least 90%, PCI was associated with a lower risk of the composite outcome of death from any cause, myocardial infarction (MI), or urgent revascularization compared with conservative management, at 2 years after TAVI.[13] Both trials excluded patients with CAD involving the left main.

Despite recent randomized evidence from the ACTIVATION and NOTION-3 trials, current recommendations remain imprecise and are largely supported by limited evidence, highlighting the persistent uncertainty regarding the optimal management of CAD in patients undergoing TAVI.[14]

In this context, the extent of jeopardized myocardium might constitute a possible modulator of CAD impact, but data in this field are lacking. Thus, we performed the present analysis from the multicenter REVASC-TAVI registry (Management of Myocardial Revascularization in Patients Undergoing TAVI With CAD) to investigate the clinical impact of the residual extent of myocardium at risk due to CAD in an all-comer TAVI population.

METHODS

The data that support the findings of this study are available from Prof Marco Barbanti (mbarbanti83@gmail.com) upon reasonable request.

Data Source

Data for this analysis were obtained from the REVASC-TAVI data set. The REVASC-TAVI registry is an investigator-initiated study of patients with severe AS undergoing TAVI and found to have significant, untreated CAD at the time of pre-TAVI workup. The latter was defined as the presence of visual angiographic stenosis ≥70% (≥50% if protected left main or vein graft), instantaneous wave-free ratio value ≤0.89, FFR value ≤0.80, in ≥1 coronary arteries of at least 2.5 mm in diameter, not revascularized by patent coronary stents or bypass grafts, found at the coronary angiography performed during the pre-TAVI workup or left main minimal lumen area<6 mm^2 at intravascular ultrasound assessment. The registry involves 30 centers across Europe, North America, South America, and Japan, with each center contributing patient-level data through a specialized case report form. The detailed protocols and methodology of the REVASC-TAVI registry have been previously published.[11] Data on baseline demographics, clinical and echocardiographic features, medications, coronary angiography, PCI and TAVI procedural details and adverse events that occurred during the follow-up were collected into a dedicated case report form. The extension of coronary revascularization and the use of physiological assessment to guide the revascularization were selected at the operator's discretion. The registry protocol received approval from the institutional ethics committee at each participating center. All patients involved in this study provided informed consent for the procedure.

Study Population and Definitions

For the purpose of this analysis, patients who received planned PCI (before, during, or within 30 days after TAVI), with available follow-up and assessment of the extent of myocardial revascularization, were included. Those managed conservatively without any PCI were not part of this cohort. Jeopardized myocardium evaluated by the British Cardiovascular Intervention Society Jeopardy Score (BCIS-JS),[15] was part of the original data set of the registry. PCI before TAVI was defined as PCI procedures planned and performed after the indication for TAVI and before the index TAVI procedure (PCI for acute coronary syndromes was excluded by definition). Concomitant PCI was defined as planned PCI procedures performed concomitantly during the index TAVI (either before or after transcatheter aortic valve deployment). PCI after TAVI was defined as PCI procedures planned and performed intentionally after TAVI in a different setting. Planned PCI included PCI performed either before TAVI, concomitantly or intentionally staged after TAVI. Unplanned PCI was defined as PCI procedures performed due to recurrent angina and acute coronary syndrome after TAVI.

For each patient with concomitant CAD, the jeopardized myocardium after planned PCI, was graded using the BCIS-JS.[15] Briefly, the BCIS-JS quantifies the extent of myocardium at risk due to CAD. It assigns points to significant coronary stenoses (≥70% for major vessels and ≥50% for left main). The scoring prioritizes the major branch supplying the largest myocardial territory and accounts for anatomic variations. The final BCIS-JS ranges from 0 to 12, reflecting the myocardial area at risk from ischemia. A cutoff value of 4 for residual BCIS-JS (rBCIS-JS) has been validated in a different setting[10] and was selected for the present study. Accordingly, the study population was stratified into 2 groups according to the rBCIS-JS: patients with extensive residual myocardial at risk (rBCIS-JS >4 group) and patients without extensive residual myocardial at risk (rBCIS-JS ≤4 group; Figure 1).

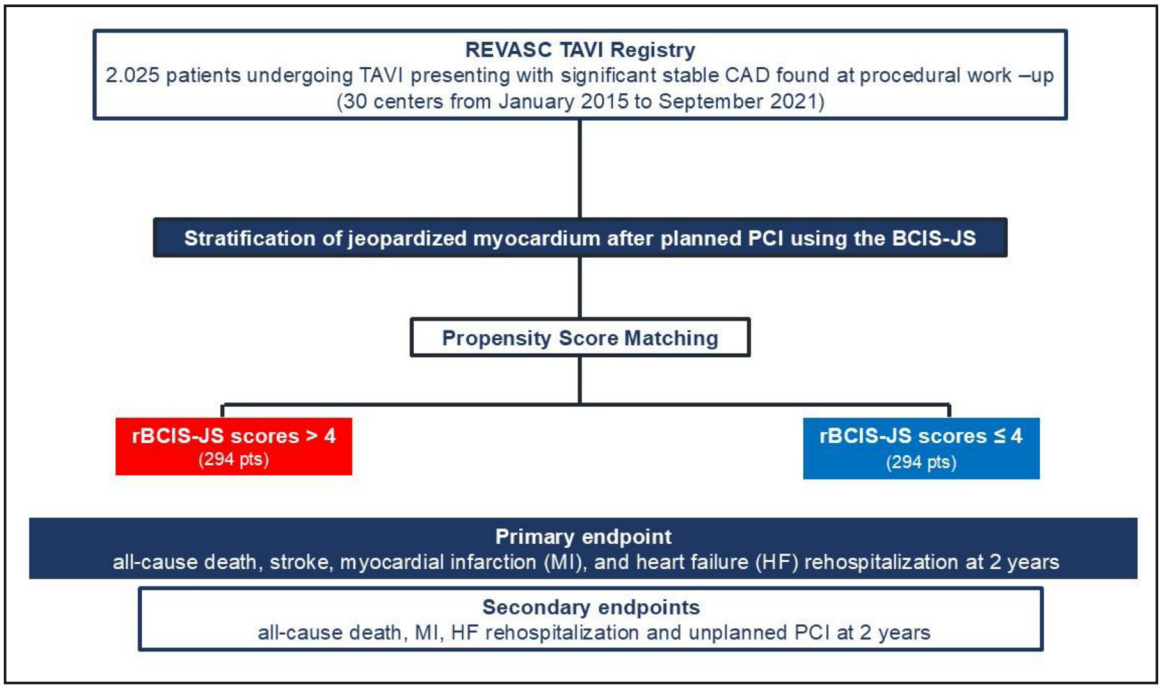

Figure 1. Study flowchart.
The figure shows study design. BCIS-JS indicates British Cardiovascular Intervention Society Jeopardy Score; CAD, coronary artery disease; HF, heart failure; MI, myocardial infarction; PCI, percutaneous coronary intervention; rBCIS-JS, residual British Cardiovascular Intervention Society Jeopardy Score; REVASC-TAVI, Management of Myocardial Revascularization in Patients Undergoing Transcatheter Aortic Valve Implantation With Coronary Artery Disease; and TAVI, transcatheter aortic valve implantation.

Study End Points

The primary outcome was a composite end point including all-cause death, stroke, MI, and heart failure (HF) rehospitalization at 2 years. Secondary outcomes included MI, HF rehospitalization, and unplanned PCI at 2 years. All outcomes were defined according to the Valve Academic Research Consortium-2 definitions,[16] as enrollment started before the publication of the Valve Academic Research Consortium-3 criteria. Clinical events defined according to Valve Academic Research Consortium-2 criteria were adjudicated locally by investigators at each center; no central event committee was used.

Statistical Analysis

Categorical variables are reported as counts and percentages. Continuous variables are reported as medians and interquartile ranges. Continuous variables were compared with the *t* test or Mann-Whitney *U* test, and categorical variables were compared with the χ^2 statistics, Fisher exact, or McNemar tests.

To account for baseline differences and selection bias, adjustment with propensity score matching (PSM) was used. Variables for the propensity score model were selected a priori based on clinical relevance and previous literature, adopting a nonparsimonious approach that included demographic, clinical, echocardiographic, and procedural characteristics potentially associated with outcomes in patients undergoing TAVI with concomitant CAD. Given the large sample size and number of events, the inclusion of multiple covariates was not expected to result in overfitting, as confirmed by standardized mean differences <10% after matching.

Variables included in the PSM were sex, age, body mass index, diabetes, hypertension, peripheral artery disease, chronic obstructive pulmonary disease, renal failure (defined as estimated glomerular filtration rate <30 mL/min), prior coronary artery bypass grafting, prior PCI, prior MI, prior stroke, prior pacemaker implantation, New York Heart Association classification, Canadian Cardiovascular Society classification, prior surgical aortic valve replacement, atrial fibrillation, Society of Thoracic Surgeons mortality score, left ventricular ejection fraction, aortic mean gradient, and aortic valve area (Figure S1). One-to-one PSM with the nearest neighbor method, with a caliper width of 0.1 of the SD of propensity score logit was used (Figure S1). A caliper of 0.10 was used for PS adjustment to achieve closer matching and minimize residual bias.

Time-to-event curves for the outcomes of interest were estimated using the Kaplan-Meier method. For secondary nonfatal end points, death represents a competing risk. As competing-risk methods were not applied, Kaplan-Meier

Table 1. Baseline Characteristics of the Matched Population

	Overall (N=588)	rBCIS ≤4 (n=294)	rBCIS >4 (n=294)	SMD
Female, n (%)	236 (40.1)	124 (42.2)	112 (38.1)	0.083
Age, y; median (IQR)	83.0 (78.0–86.0)	83.0 (79.0–6.0)	83.0 (78.0–86.0)	0.027
BMI, median (IQR)	26.3 (23.8–30.0)	26.1 (23.8–10.0)	26.6 (23.9–30.0)	0.048
Hypertension, n (%)	493 (83.8)	248 (84.4)	245 (83.3)	0.028
Diabetes, n (%)	198 (33.7)	98 (33.3)	100 (34.0)	0.083
PAD, n (%)	123 (20.9)	61 (20.7)	62 (21.1)	0.083
COPD, n (%)	91 (15.5)	43 (14.6)	48 (16.3)	0.094
eGFR, mL/min; median (IQR)	55.1 (42.0–62.9)	55.1 (40.7–62.0)	55.1 (42.8–63.0)	0.063
Prior CABG, n (%)	126 (21.4)	64 (21.8)	62 (21.1)	0.085
Prior PCI, n (%)	248 (42.2)	126 (42.9)	122 (41.5)	0.028
Prior MI, n (%)	162 (27.6)	84 (28.6)	78 (26.5)	0.097
Prior stroke, n (%)	31 (5.3)	17 (5.8)	14 (4.8)	0.075
Prior pacemaker, n (%)	67 (11.4)	33 (11.2)	34 (11.6)	0.083
Prior SAVR, n (%)	12 (2.0)	7 (2.4)	5 (1.7)	0.055
Bicuspid aortic valve, n (%)	15 (2.6)	8 (2.7)	7 (2.4)	0.025
CCS >1, n (%)	150 (29.8)	72 (29.0)	78 (30.5)	0.031
NYHA >2, n (%)	376 (63.9)	189 (64.3)	187 (63.6)	0.014
AF, n (%)	157 (26.7)	80 (27.2)	77 (26.2)	0.073
STS mortality score, %; median (IQR)	5.0 (3.0–6.1)	5.0 (3.1–6.1)	5.0 (3.0–6.1)	0.019
LVEF, %, median (IQR)	55.0 (41.0–60.0)	53.6 (41.0–60.0)	55.0 (43.0–60.0)	0.043
LVEF <40%, n (%)	118 (20.1)	58 (19.7)	60 (20.4)	0.017
Echo mean gradient, mm Hg; median (IQR)	44.0 (35.0–51.0)	44.0 (34.3–51.0)	44.0 (36.0–51.8)	0.004
Echo AVA, cm^2; median (IQR)	0.70 (0.60–0.80)	0.70 (0.60–0.80)	0.70 (0.60–0.80)	0.099
Echo sPAP, mm Hg; median (IQR)	41.8 (38.0–44.0)	41.8 (38.0–43.0)	41.8 (38.0–44.8)	0.047

AF indicates atrial fibrillation; AVA, aortic valve area; BMI, body mass index; CABG, coronary artery bypass graft; CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; PAD, peripheric artery disease; PCI, percutaneous coronary intervention; rBCIS, residual British Cardiovascular Intervention Society; SAVR, surgical aortic valve replacement; SMD, standardized mean difference; sPAP, systolic pulmonary artery pressure; and STS, Society of Thoracic Surgeon.

estimates may overestimate the cumulative incidence of these events. Multivariable Cox-regression analysis was performed for investigating factors independently associated with the study outcome. Available clinical characteristics and the quantification of the residual myocardium at risk (by rBCIS-JS) were taken into account. Results were reported as hazard ratios (HRs) with 95% CIs. The proportional hazards assumption was assessed using Schoenfeld residuals, and no significant violations were observed.

All statistical tests were performed 2-tailed, and $P<0.05$ was considered as the threshold for statistical significance. All statistical analyses were performed with R software, version 3.6.3 (R Foundation for Statistical Computing).

RESULTS

The REVASC-TAVI registry enrolled 2404 patients with significant, stable CAD who underwent TAVI between January 2015 and September 2021. After excluding 377 patients due to a lack of follow-up data or extent of myocardial revascularization information, 2025 patients constituted the prematching cohort. No imputation of missing values was performed. Descriptive analyses indicated that excluded patients were comparable to included ones in terms of age and sex, and missingness appeared largely random across centers. Among patients considered for the present analysis, 408 (20.1%) received a conservative treatment for CAD. The baseline demographic and clinical characteristics of these patients are detailed in Table S1.

Baseline Characteristics of the Matched Cohorts

After adjustment for baseline confounders through the PSM method, 294 patient pairs with rBCIS-JS scores

Table 2. Characteristics of CAD of the Matched Population

	Overall (N=588)	rBCIS ≤4 (n=294)	rBCIS >4 (n=294)	*P* value
CAD characteristics				
Diseased vessels, n (%)				
1	230 (39.1)	169 (57.5)	61 (20.7)	<0.001
2	174 (29.6)	84 (28.6)	90 (30.6)	
≥3	184 (31.3)	41 (13.9)	143 (48.6)	
RCA dominance, n (%)	465 (80.7)	240 (84.5)	225 (77.1)	
Coronary segment involved				
LM, n (%)	89 (15.1)	42 (14.3)	47 (16.0)	0.026
LDA, n (%)	439 (74.7)	167 (56.8)	272 (92.5)	<0.001
Proximal LAD, n (%)	241 (41.0)	55 (18.7)	186 (63.3)	<0.001
Mid LAD, n (%)	238 (40.5)	107 (36.4)	131 (44.6)	0.053
Distal LAD, n (%)	52 (8.8)	29 (9.9)	23 (7.8)	0.468
Diagonal, n (%)	102 (17.3)	30 (10.2)	72 (24.5)	<0.001
LCx, n (%)	279 (47.4)	102 (34.7)	177 (60.2)	<0.001
Proximal LCx, n (%)	134 (22.8)	48 (16.3)	86 (29.3)	<0.001
Mid LCx, n (%)	70 (11.9)	29 (9.9)	41 (13.9)	0.161
Distal LCx/PDA, n (%)	36 (6.1)	18 (6.1)	18 (6.1)	1.000
OM, n (%)	123 (20.9)	38 (12.9)	85 (28.9)	<0.001
RCA, n (%)	326 (55.4)	134 (45.6)	192 (65.3)	<0.001
Proximal RCA, n (%)	186 (31.6)	81 (27.6)	105 (35.7)	0.041
Mid RCA, n (%)	151 (25.7)	61 (20.7)	90 (30.6)	0.008
Distal RCA/PL/PDA, n (%)	95 (16.2)	41 (13.9)	54 (18.4)	0.179
Venous or arterial graft, n (%)	48 (8.2)	23 (7.8)	25 (8.5)	0.880
Calcific disease, n (%)	142 (26.8)	64 (24.0)	78 (29.7)	0.880
Bifurcation, n (%)	126 (25.0)	67 (26.9)	59 (23.1)	0.355
Syntax score, %; median (IQR)	10.0 (6.0–16.0)	8.0 (5.0–14.0)	13.0 (8.0–19.0)	<0.001
Multivessel CAD, n (%)	358 (60.9)	125 (42.5)	233 (79.3)	<0.001
Proximal CAD, n (%)	422 (71.8)	163 (55.4)	259 (88.1)	<0.001
LM/Proximal LAD CAD, n (%)	283 (48.1)	72 (24.5)	211 (71.8)	<0.001

CAD indicates coronary artery disease; IQR, interquartile range; LAD, left anterior descending; LCx, left circumflex artery; LDA, left descending artery; LM, left main; OM, obtuse marginal; PDA, posterior descending artery; PL, posterolateral; rBCIS, residual British Cardiovascular Intervention Society; and RCA, right coronary artery.

≤4 or greater were successfully matched. All standardized mean differences for the baseline confounders considered in the PSM were below 10%. Baseline characteristics of the PSM cohorts of patients are reported in Table 1. The median age was 83.0 years, and the average of Society of Thoracic Surgeons mortality risk was 5.0%. The incidences of angina, evaluated as Canadian Cardiovascular Society >1 (30.5% versus 29.0%), and reduced left ventricular ejection fraction (<40%; 20.4% versus 19.7%) were higher in patients with more myocardium jeopardized (rBCIS-JS > 4). Instead, New York Heart Association class >2 was more frequent in patients with rBCIS-JS ≤4 (64.3% versus 63.6%).

CAD Characteristics of the Matched Cohorts

CAD characteristics of the PSM cohorts of patients are reported in Table 2. In patients with rBCIS-JS >4, the incidence of multivessel disease (79.3% versus 42.5%, *P*<0.001), the involvement of proximal coronary segments (88.1% versus 55.4%, *P*<0.001), and the left main-proximal and left anterior descending disease (71.8% versus 24.5%, *P*<0.001) were more frequent.

TAVI Procedures Characteristics of the Matched Cohorts

TAVI procedures were predominantly performed through a trans-femoral approach (n=545, 93.5%) and under local anesthesia (n=472, 80.8%). The most commonly used TAVI devices were the balloon-expandable Edwards SAPIEN 3/Ultra (Edwards LifeSciences, Irvine, CA; n=222, 37.8%) and the self-expanding Evolut R/PRO/PRO+ (Medtronic, Inc, Marlborough, MA; n=216, 36.8%). Further details of the TAVI procedures after adjustment are reported in Table 3.

Outcomes of the Matched Cohorts

At 2-year follow-up, the incidence of the primary end point was higher in patients with higher rBCIS-JS (37.5% versus 23.0%, *P*=0.035; Figure 2). No statistically significant differences were found in terms of all-cause death (22.2% versus 15.4%, *P*=0.12), unplanned PCI (4.1% versus 2.8%, *P*=0.2), and HF rehospitalization (10.4% versus 6.8% for, *P*=0.2) for patients with rBCIS-JS >4 or ≤4, respectively (Figure 3). Instead, the incidence of MI was more frequent in patients with higher rBCIS-JS (8.2% versus 2.6%, *P*=0.01; Figure 3). The incidence of

Table 3. Characteristics of TAVI Procedures of the Matched Population

	Overall (N=588)	rBCIS ≤4 (n=294)	rBCIS >4 (n=294)	*P* value
Vascular access, n (%)				0.618
Trans-femoral	545 (93.5)	270 (92.2)	275 (94.8)	
Trans-apical	14 (2.4)	8 (2.7)	6 (2.1)	
Trans-subclavian	18 (3.1)	10 (3.4)	8 (2.8)	
SAT protection, n (%)	29 (5.4)	14 (5.3)	15 (5.5)	1.000
Prosthesis type, n (%)				0.660
SAPIEN 3/3 Ultra	222 (37.8)	115 (39.1)	107 (36.5)	
SAPIEN XT	7 (1.2)	3 (1.0)	4 (1.4)	
Evolut R/PRO/PRO+	216 (36.8)	108 (36.7)	108 (36.9)	
CoreValve	23 (3.9)	12 (4.1)	11 (3.8)	
Portico	35 (6.0)	18 (6.1)	17 (5.8)	
Lotus	15 (2.6)	4 (1.4)	11 (3.8)	
Acurate NEO/NEO 2	54 (9.2)	29 (9.9)	25 (8.5)	
Allegra	4 (0.7)	1 (0.3)	3 (1.0)	
Others	11 (1.9)	4 (1.4)	7 (2.4)	
Device success, n (%)	518 (95.4)	256 (92.8)	262 (98.1)	0.005
Anesthesia, n (%)				0.307
Local	472 (80.8)	241 (82.3)	231 (79.4)	
General	104 (17.8)	50 (17.1)	54 (18.6)	
Postdilatation, n (%)	108 (19.5)	48 (17.7)	60 (21.3)	0.342
Need second TAVI, n (%)	8 (1.4)	4 (1.4)	4 (1.4)	1.000
Contrast, mL; median (IQR)	157.5 (100.8–230.0)	160.0 (110.0–230.0)	150.0 (100.0–220.0)	0.461

IQR indicates interquartile range; rBCIS, residual British Cardiovascular Intervention Society; SAT, supra-aortic trunks protection; and TAVI, transcatheter aortic valve implantation.

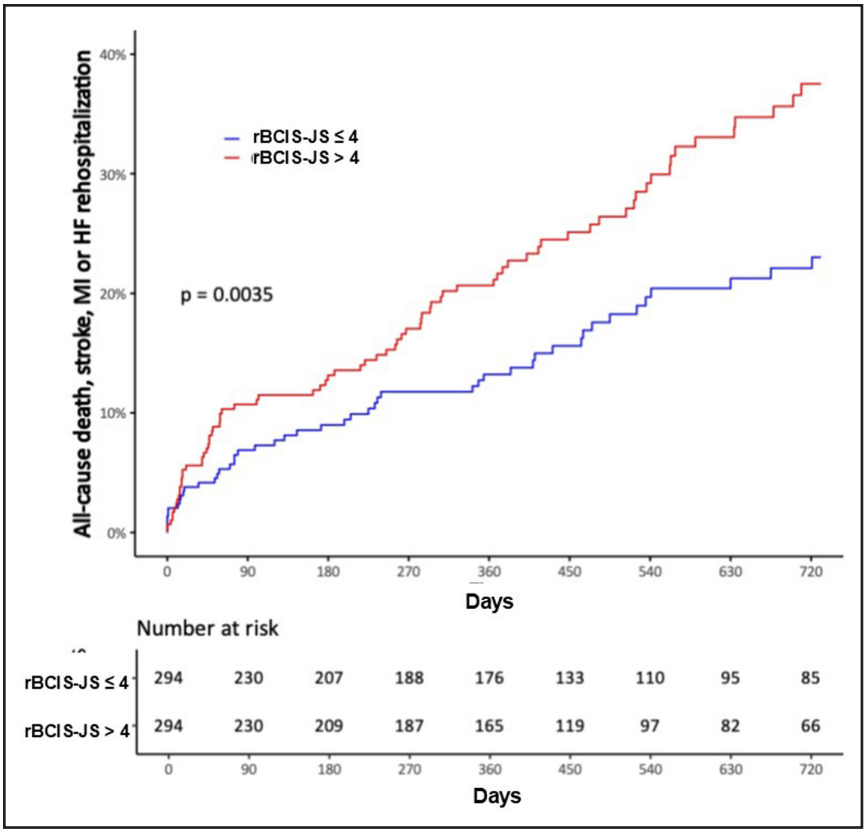

Figure 2. Incidence of primary outcomes.
The figure shows the cumulative incidence of primary outcome (all-cause death, stroke, myocardial infarction [MI], and heart failure [HF] rehospitalization) in matched population stratified according to jeopardized myocardium after planned percutaneous coronary intervention (PCI) using the residual British Cardiovascular Intervention Society Jeopardy Score (rBCIS-JS).

in-hospital adverse events (death, cardiovascular death, MI, minor bleeding and major bleeding) was similar between the 2 matched groups (Table 4). In particular, the incidence of MI did not differ in the in-hospital outcome, suggesting that the difference observed at 2 years is attributable to new MI rather than periprocedural MI.

Predictors of the Primary End Point in the Overall Study Population

At multivariable Cox-regression analysis, rBCIS-JS >4 (HR, 1.43 [95% CI, 1.11–1.84]; *P*=0.005), estimated glomerular filtration rate (mL/min; HR, 0.99 [95% CI, 0.98–0.99]; *P*<0.001), atrial fibrillation (HR, 1.46 [95% CI, 1.18–1.81]; *P*<0.001), and Society of Thoracic Surgeons mortality risk score >4% (HR, 1.39 [95% CI, 1.09–1.76]; *P*=0.007) were independently associated with the 2-year primary composite end point (Table 5).

DISCUSSION

The optimal strategy for managing concomitant CAD in patients with severe AS who are candidates for TAVI remains debated.[3–14] In this analysis of the international REVASC-TAVI registry, we observed that the residual extent of myocardium at risk significantly impacts clinical outcomes in patients with concomitant CAD undergoing TAVI. Specifically, coronary revascularization planning (including PCI performed before, during, and up to 30 days after TAVI) that results in a small amount of residual jeopardized myocardium (rBCIS-JS ≤4) improves prognosis after TAVI by reducing the incidence of the composite end point of all-cause mortality, stroke, MI, and HF rehospitalization at 2 years.

In the trials that led to the approval of TAVI, revascularization of significant coronary stenosis within 30 days before the procedure was mandatory.[17,18] As a result, the safety of performing TAVI without prior revascularization was not explored in these studies. Despite recent evidence from randomized trials such as ACTIVATION and NOTION-3, recommendations regarding coronary revascularization in TAVI candidates remain relatively vague. The 2025 ESC/EACTS Valvular Heart Disease Guidelines provide a Class IIa recommendation for PCI in patients with ≥90% coronary stenosis in vessels ≥2.5 mm, and a Class IIb recommendation for ≥70% stenosis in proximal segments. These weak levels of evidence underscore that the optimal management of concomitant CAD in patients undergoing TAVI remains uncertain and requires further clarification in future studies. However, performing PCI in patients with AS can be challenging due to the perceived high procedural risk.[19] Therefore, careful patient selection and strategic coronary revascularization planning are essential to achieve favorable PCI outcomes in this population.[20–24] Notably, in addition to clinical factors, the extent of myocardium at risk and the choice of target lesions significantly influence PCI effectiveness.[10–25] Previous studies have demonstrated

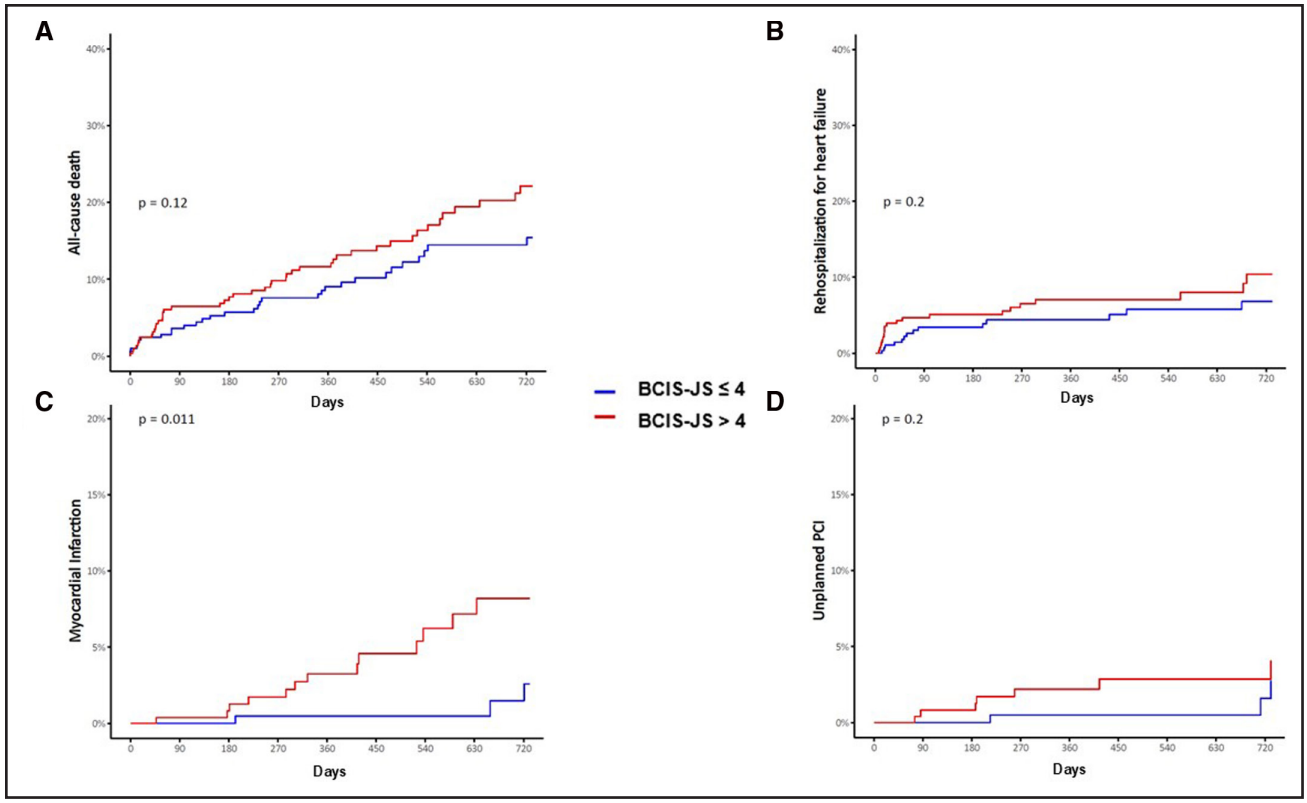

Figure 3. Incidence of secondary outcomes.
The figure shows the cumulative incidence of all-cause death (**A**), heart failure rehospitalization (**B**), myocardial infarction (**C**), and unplanned percutaneous coronary intervention (PCI; **D**) in matched population stratified according to jeopardized myocardium after planned PCI using the British Cardiovascular Intervention Society Jeopardy Score (BCIS-JS).

that CAD severity, as measured by the Syntax Score, and residual incomplete revascularization, as evaluated by the residual Syntax Score, significantly impact mortality after TAVI.[25] In the present study, we evaluated the extent of myocardium at risk using the BCIS-JS because, unlike other angiographic scoring systems that focus on lesion-specific characteristics (such as the Syntax Score), the BCIS-JS provides a simple classification of CAD based on the myocardial territory at risk. Similarly, our findings demonstrated that minimizing the myocardium jeopardized by CAD in patients with TAVI improves clinical outcomes at the 2-year follow-up. A previous smaller study[10] also showed that a BCIS-JS of ≤4 before TAVI was linked to better clinical outcomes in patients with coexisting CAD and severe AS, similar to patients without concomitant CAD. All together, these evidences strongly suggest that, while not all coronary stenoses require revascularization for clinical benefit, a minimalistic approach to revascularization may be insufficient. In this regard, the evaluation of the extent of residual myocardium left unrevascularized emerges as a pivotal factor to be evaluated in the individual patient with concomitant CAD and AS. Interestingly, the REVASC-TAVI study indicated that complete myocardial revascularization, achieved either staged or concomitant with TAVI, was comparable to incomplete revascularization strategies in reducing the risk of all-cause mortality, stroke, MI, and rehospitalization for HF at 2 years.[11] Similarly, the ACTIVATION trial showed that a routine revascularization strategy did not result in a clinical benefit for TAVI patients affected by CAD compared with a conservative management strategy.[13]

Recently, the NOTION-3 trial compared conservative management with routine PCI revascularization in patients with stable CAD and severe symptomatic aortic stenosis. The PCI approach, guided by FFR or significant coronary artery stenosis, showed a lower risk of adverse events, including death, MI, or urgent revascularization, over a 2-year follow-up period.[14] Unlike the ACTIVATION trial, which defined CAD anatomically as a stenosis ≥70%, the NOTION-3 trial defined CAD using FFR or an angiographic stenosis ≥90%, thereby identifying the actual myocardial area at risk. Recently, the FAITAVI trial, presented at EuroPCR 2025, demonstrated that a physiology-guided PCI strategy using FFR in patients with intermediate coronary lesions undergoing TAVI was associated with improved outcomes compared with an angiography-guided approach. Therefore, both the extent of myocardium at risk and functional assessment of coronary lesions should play a central role in guiding revascularization decisions, rather than relying solely on angiographic criteria.

The occurrence of unplanned PCI after TAVI was low in patients without CAD at the time of the procedure

Table 4. In-Hospital Outcomes of the Matched Population

	Overall (N=588)	rBCIS ≤4 (n=294)	rBCIS >4 (n=294)	*P* value
Death, n (%)	14 (2.4)	5 (1.7)	9 (3.1)	0.418
Cardiovascular death, n (%)	6 (1.0)	3 (1.1)	3 (1.0)	1.000
Disabling stroke, n (%)	4 (0.7)	2 (0.7)	2 (0.7)	1.000
No disabling stroke, n (%)	11 (2.0)	6 (2.2)	5 (1.7)	0.766
MI, n (%)	4 (0.7)	1 (0.3)	3 (1.0)	0.624
PPI, n (%)	63 (11.9)	36 (13.4)	27 (10.3)	0.284
Newonset LBBB, n (%)	82 (15.4)	38 (14.1)	44 (16.7)	0.472
Newonset AF, n (%)	20 (3.9)	9 (3.5)	11 (4.4)	0.653
Minor bleeding, n (%)	44 (7.5)	19 (6.6)	25 (8.5)	0.434
Major bleeding, n (%)	39 (6.7)	16 (5.5)	23 (7.8)	0.320
Life-threatening bleeding, n (%)	12 (2.1)	5 (1.7)	7 (2.4)	0.772
Major vascular complication, n (%)	37 (6.3)	16 (5.5)	21 (7.2)	0.498
Minor vascular complication, n (%)	46 (7.9)	25 (8.6)	21 (7.2)	0.542
Acute kidney injury grade, n (%)				0.066
1	50 (8.7)	20 (7.0)	30 (10.3)	
2	14 (2.4)	3 (1.0)	11 (3.8)	
3	9 (1.6)	4 (1.4)	5 (1.7)	
Mean gradient discharge, mm Hg; median (IQR)	8.00 (6.00–11.00)	8.00 (5.00–11.00)	8.00 (6.00–11.00)	0.452
PVR grade, n (%)				0.130
None/trace	256 (47.5)	127 (46.7)	129 (48.3)	
Mild	249 (46.2)	133 (48.9)	116 (43.4)	
Moderate	31 (5.8)	12 (4.4)	19 (7.1)	
Severe	3 (0.6)	0 (0.0)	3 (1.1)	
Length of stay, d; median (IQR)	4.67 (2.00–7.00)	5.00 (2.00–7.00)	4.00 (2.00–7.00)	0.439

AF indicates atrial fibrillation; IQR, interquartile range; LBBB, left bundle branch block; MI, myocardial infarction; PPI, permanent pacemaker implantation; PVR, paravalvular regurgitation; and rBCIS, residual British Cardiovascular Intervention Society.

Table 5. Multivariable Cox-Regression Analysis of Factors Associated With the Study Composite End Point at 2 Years

Variable	HR (95% CI)	*P* value
rBCIS >4	1.43 (1.11–1.84)	0.005
Female sex	0.85 (0.68–1.04)	0.12
Age, y	1.01 (0.99–1.02)	0.56
Diabetes	1.20 (0.97–1.47)	0.09
PAD	0.85 (0.65–1.11)	0.22
COPD	1.25 (0.97–1.62)	0.08
eGFR, mL/min	0.99 (0.98–0.99)	<0.001
Prior CABG	0.89 (0.63–1.26)	0.50
Prior PCI	1.06 (0.86–1.31)	0.59
Prior myocardial infarction	1.03 (0.80–1.34)	0.80
Prior stroke	1.37 (1.00–1.88)	0.05
Prior pacemaker	0.78 (0.55–1.12)	0.17
CCS >1	1.17 (0.91–1.50)	0.23
NYHA >2	1.04 (0.84–1.29)	0.73
AF	1.46 (1.18–1.81)	<0.001
LVEF <40%	1.20 (0.92–1.57)	0.17
STS PROM >4%	1.39 (1.09–1.76)	0.007

AF indicates atrial fibrillation; CABG, coronary artery bypass graft; CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; HR, hazard ratio; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PAD, peripheric artery disease; PCI, percutaneous coronary intervention; rBCIS, residual British Cardiovascular Intervention Society; and STS PROM, Society of Thoracic Surgeons Predicted Risk of Mortality.

but increased over time in patients with coexisting CAD, especially those with multivessel disease, driven mainly by acute coronary syndromes.[26] Consistent with this, our study found an increased incidence of MI in patients with higher residual jeopardized myocardium.

In the decision-making process regarding coronary revascularization in patients with aortic stenosis and concomitant CAD, many factors should be considered, such as the extent of myocardium at risk and the clinical presentation. Our study demonstrated that minimizing the myocardium jeopardized by CAD in patients with TAVI should be prioritized to improve patient outcomes. Previous studies have demonstrated that clinical presentation with acute coronary syndrome was significantly associated with an increased incidence of cardiovascular death.[27] Therefore, a Heart Team approach can lead the revascularization planning, reinforcing the importance of individualized decision-making rather than a one-size-fits-all strategy. This aligns with emerging evidence emphasizing that the extent of myocardium at risk, rather than the mere presence of coronary stenosis, should drive revascularization decisions.

Limitations

This observational study lacked independent event adjudication and core laboratory imaging analysis, which may have introduced variability in event assessment across centers. Although PSM helped align baseline characteristics between the groups, the nonrandomized design implies that some unmeasured confounders may still have influenced the results. Furthermore, although PSM reduced the sample size potentially limiting statistical precision, this approach ensured excellent covariate balance and minimized confounding. In addition, the inclusion of patients with both preexisting and newly diagnosed CAD may have introduced further bias. Patients with incomplete data were excluded a priori, which may have introduced selection bias, although their demographic profile was comparable to that of the included population. CAD was defined by mixed criteria

(visual angiography, FFR, instantaneous wave-free ratio, or intravascular ultrasound) across centers. Functional or imaging assessment was infrequent (7.5% and 5.5% of cases, respectively), so most lesions were identified angiographically. Despite this datum reflected guidelines recommendations during study period, this heterogeneity may have led to misclassification of CAD severity. Due to the limited number of cases assessed by physiology or intravascular imaging, sensitivity analyses stratified by diagnostic modality were not feasible. It should also be acknowledged that both angiographic assessment based on a ≥70% diameter stenosis cutoff and the functional evaluation in patients with severe aortic stenosis may overestimate the functional significance of coronary lesions. Decision to perform coronary revascularization and the choice of physiological assessment (instantaneous wave-free ratio or FFR) were left to the operator's discretion, introducing potential selection bias and heterogeneity in management. While this real-world, operator-driven approach reflects contemporary clinical practice, it may have influenced the observed outcomes and should be interpreted accordingly. In contrast, the recent NOTION-3 and FAITAVI trials demonstrated the prognostic benefit of physiology-guided coronary revascularization, underscoring the need for more standardized approaches in future studies. We acknowledge that the definitions of planned, staged, and concomitant PCI were based on clinical intent and may therefore be somewhat subjective. Although prespecified criteria were applied for consistency, some overlap between planned staged and unplanned procedures cannot be completely excluded. The rBCIS-JS reflects the extent of myocardium at risk but does not incorporate information on the angiographic severity or plaque burden of individual lesions, which have been shown to influence outcomes, as highlighted by the NOTION-3 trial. Although the rBCIS-JS is a continuous variable, in the present study we applied the established >4 threshold, as previously validated, to allow consistency and comparability with prior research. Future analyses considering the rBCIS-JS as a continuous measure might provide additional insights into the graded relationship between residual myocardial risk and outcomes. Given the nonrandomized, observational design of this study, our findings should be considered hypothesis-generating and warrant confirmation in prospective, randomized trials.

Conclusions

The management of concomitant CAD leading to small residual jeopardized myocardium (rBCIS-JS ≤4) improved prognosis in patients with TAVI by reducing the incidence of MI at 2-year follow-up. Minimizing the myocardium jeopardized by CAD in patients with TAVI should be pursued to improve patient outcomes. Prospective, randomized trials with longer follow-up are needed to corroborate the results of the present analysis.

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Supplemental Material

Table S1
Figure S1

REFERENCES

1. Otto CM, Burwash IG, Legget ME, Munt BI, Fujioka M, Healy NL, Kraft KD, Miyake-Hull CY, Schwaegler RG. Prospective study of asymptomatic valvular aortic stenosis: clinical, echocardiographic, and exercise predictors of outcome. *Circulation*. 1997;95:2262–2270. doi: 10.1161/01.cir.95.9.2262
2. Rapp AH, Hillis LD, Lange RA, Cigarroa JE. Prevalence of coronary artery disease in patients with aortic stenosis with and without angina pectoris. *Am J Cardiol*. 2001;87:1216–7; A7. doi: 10.1016/s0002-9149(01)01501-6
3. Beckmann A, Hamm C, Figulla HR, Cremer J, Kuck KH, Lange R, Zahn R, Sack S, Schuler GC, Walther T, et al; GARY Executive Board. The German Aortic Valve Registry (GARY): a nationwide registry for patients undergoing invasive therapy for severe aortic valve stenosis. *Thorac Cardiovasc Surg*. 2012;60:319–325. doi: 10.1055/s-0032-1323155
4. Eltchaninoff H, Prat A, Gilard M, Leguerrier A, Blanchard D, Fournial G, Iung B, Donzeau-Gouge P, Tribouilloy C, Debrux JL, et al; FRANCE Registry Investigators. Transcatheter aortic valve implantation: early results of the FRANCE (French Aortic National CoreValve and Edwards) registry. *Eur Heart J*. 2011;32:191–197. doi: 10.1093/eurheartj/ehq261
5. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, et al; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med*. 2011;364:2187–2198. doi: 10.1056/NEJMoa1103510
6. Malmberg M, Gunn J, Sipilä J, Pikkarainen E, Rautava P, Kytö V. Comparison of long-term outcomes of patients having surgical aortic valve replacement with versus without simultaneous coronary artery bypass grafting. *Am J Cardiol*. 2020;125:964–969. doi: 10.1016/j.amjcard.2019.12.015
7. Barbanti M, Buccheri S, Capodanno D, D'Errigo P, Ranucci M, Rosato S, Santoro G, Fusco D, Tamburino C, Biancari F, et al; OBSERVANT Research Group. Transcatheter or surgical treatment of severe aortic stenosis and coronary artery disease: a comparative analysis from the Italian OBSERVANT study. *Int J Cardiol*. 2018;270:102–106. doi: 10.1016/j.ijcard.2018.06.011
8. Witberg G, Zusman O, Codner P, Assali A, Kornowski R. Impact of coronary artery revascularization completeness on outcomes of patients with coronary artery disease undergoing transcatheter aortic valve replacement: a meta-analysis of studies using the residual SYNTAX score (synergy between PCI with Taxus and cardiac surgery). *Circ Cardiovasc Interv*. 2018;11:e006000. doi: 10.1161/CIRCINTERVENTIONS.117.006000
9. Aurigemma C, Giannico MB, Burzotta F, Romagnoli E, Cangemi S, Bianchini F, Bruno P, Leone AM, Gaspardone A, Crea F, et al. Clinical impact of the extent of jeopardized myocardium in patients undergoing transcatheter aortic valve intervention. *Rev Esp Cardiol (Engl Ed)*. 2023;76:157–164. doi: 10.1016/j.rec.2022.05.020
10. Costa G, Pilgrim T, Amat Santos IJ, De Backer O, Kim WK, Barbosa Ribeiro H, Saia F, Bunc M, Tchetche D, Garot P, et al; REVASC-TAVI Registry. Management of myocardial revascularization in patients with stable coronary artery disease undergoing transcatheter aortic valve implantation. *Circ Cardiovasc Interv*. 2022;15:e012417. doi: 10.1161/CIRCINTERVENTIONS.122.012417
11. Aurigemma C, Massussi M, Fraccaro C, Adamo M, D'Errigo P, Rosato S, Seccareccia F, Santoro G, Baiocchi M, Barbanti M, et al; OBSERVANT II Research Group. Impact of chronic coronary artery disease and revascularization strategy in patients with severe aortic stenosis who underwent transcatheter aortic valve implantation. *Am J Cardiol*. 2023;206:14–22. doi: 10.1016/j.amjcard.2023.08.045
12. Patterson T, Clayton T, Dodd M, Khawaja Z, Morice MC, Wilson K, Kim WK, Meneveau N, Hambrecht R, Byrne J, et al; ACTIVATION Trial Investigators. ACTIVATION (Percutaneous Coronary Intervention Prior to Transcatheter Aortic Valve Implantation): a randomized clinical trial. *JACC Cardiovasc Interv*. 2021;14:1965–1974. doi: 10.1016/j.jcin.2021.06.041
13. Lønborg J, Jabbari R, Sabbah M, Veien KT, Niemelä M, Freeman P, Linder R, Ioanes D, Terkelsen CJ, Kajander OA, et al; NOTION-3 Study Group. PCI in patients undergoing transcatheter aortic-valve implantation. *N Engl J Med*. 2024;391:2189–2200. doi: 10.1056/nejmoa2401513
14. Praz F, Borger MA, Lanz J, Marin-Cuartas M, Abreu A, Adamo M, Ajmone Marsan N, Barili F, Bonaros N, Cosyns B, et al; ESC/EACTS Scientific Document Group. 2025 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J*. 2025;46:4635–4736. doi: 10.1093/eurheartj/ehaf194
15. De Silva K, Morton G, Sicard P, Chong E, Indermuehle A, Clapp B, Thomas M, Redwood S, Perera D. Prognostic utility of BCIS myocardial jeopardy score for classification of coronary disease burden and completeness of revascularization. *Am J Cardiol*. 2013;111:172–177. doi: 10.1016/j.amjcard.2012.09.012
16. Kappetein AP, Head SJ, Généreux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, et al; Valve Academic Research Consortium-2. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *J Thorac Cardiovasc Surg*. 2013;145:6–23. doi: 10.1016/j.jtcvs.2012.09.002
17. Kodali SK, Williams MR, Smith CR, Svensson LG, Webb JG, Makkar RR, Fontana GP, Dewey TM, Thourani VH, Pichard AD, et al; PARTNER Trial Investigators. Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N Engl J Med*. 2012;366:1686–1695. doi: 10.1056/NEJMoa1200384
18. Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, Gleason TG, Buchbinder M, Hermiller J Jr, Kleiman NS, et al; U.S. CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med*. 2014;370:1790–1798. doi: 10.1056/NEJMoa1400590
19. Paradis JM, Fried J, Nazif T, Kirtane A, Harjai K, Khalique O, Grubb K, George I, Hahn R, Williams M, et al. Aortic stenosis and coronary artery disease: what do we know? What don't we know? A comprehensive review of the literature with proposed treatment algorithms. *Eur Heart J*. 2014;35:2069–2082. doi: 10.1093/eurheartj/ehu247
20. Goel SS, Agarwal S, Tuzcu EM, Ellis SG, Svensson LG, Zaman T, Bajaj N, Joseph L, Patel NS, Aksoy O, et al. Percutaneous coronary intervention in patients with severe aortic stenosis. Implication for transcatheter aortic valve replacement. *Circulation*. 2012;125:1005–1013. doi: 10.1161/CIRCULATIONAHA.111.039180
21. Gasparetto V, Fraccaro C, Tarantini G, Buja P, D'Onofrio A, Yzeiraj E, Pittarello D, Isabella G, Gerosa G, Iliceto S, et al. Safety and effectiveness of a selective strategy for coronary artery revascularization before transcatheter aortic valve implantation. *Catheter Cardiovasc Interv*. 2013;81:376–383. doi: 10.1002/ccd.24434
22. Abdel-Wahab M, Mostafa AE, Geist V, Stöcker B, Gordian K, Merten C, Richardt D, Toelg R, Richardt G. Comparison of outcomes in patients having isolated transcatheter aortic valve implantation versus combined with preprocedural percutaneous coronary intervention. *Am J Cardiol*. 2012;109:581–586. doi: 10.1016/j.amjcard.2011.09.053
23. Wendt D, Kahlert P, Lenze T, Neuhäuser M, Price V, Konorza T, Erbel R, Jakob H, Thielmann M. Management of high-risk patients with aortic stenosis and coronary artery disease. *Ann Thorac Surg*. 2013;95:599–605. doi: 10.1016/j.athoracsur.2012.07.075
24. Chakravarty T, Sharma R, Abramowitz Y, Kapadia S, Latib A, Jilaihawi H, Poddar KL, Giustino G, Ribeiro HB, Tchetche D, et al. Outcomes in patients with transcatheter aortic valve replacement and left main stenting: the TAVR-LM registry. *J Am Coll Cardiol*. 2016;67:951–960. doi: 10.1016/j.jacc.2015.10.103
25. D'Ascenzo F, Verardi R, Visconti M, Conrotto F, Scacciatella P, Dziewierz A, Stefanini GG, Paradis JM, Omedè P, Kodali S, et al. Independent impact of extent of coronary artery disease and percutaneous revascularisation on 30-day and one-year mortality after TAVI: a meta-analysis of adjusted observational results. *EuroIntervention*. 2018;14:e1169–e1177. doi: 10.4244/EIJ-D-18-00098
26. Okuno T, Demirel C, Tomii D, Heg D, Häner J, Siontis GCM, Lanz J, Räber L, Strotecky S, Fürholz M, et al. Long-term risk of unplanned percutaneous coronary intervention after transcatheter aortic valve replacement. *EuroIntervention*. 2022;18:797–803. doi: 10.4244/EIJ-D-22-00342
27. Saia F, Palmerini T, Compagnone M, Battistini P, Moretti C, Taglieri N, Marcelli C, Bruno AG, Ghetti G, Corsini A, et al. Coronary artery disease and reasonably incomplete coronary revascularization in high-risk patients undergoing transcatheter aortic valve implantation. *Catheter Cardiovasc Interv*. 2020;95:19–27. doi: 10.1002/ccd.28211