Surgical versus Interventional Treatment of Concomitant Aortic Valve Stenosis and Coronary Artery Disease

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Abstract

Background Coronary artery disease (CAD) is frequently diagnosed in patients with aortic valve stenosis. Treatment options include surgical and interventional approaches. We therefore analyzed short-term outcomes of patients undergoing either coronary artery bypass grafting with simultaneous aortic valve replacement (CABG + AVR) or staged percutaneous coronary intervention and transcatheter aortic valve implantation (PCI + TAVI).

Methods From all patients treated since 2017, we retrospectively identified 237 patients undergoing TAVI within 6 months after PCI and 241 patients undergoing combined CABG + AVR surgery. Propensity score matching was performed, resulting in 101 matched pairs.

Results Patients in the CABG + AVR group were younger compared with patients in the PCI + TAVI group (71.9 ± 4.9 vs 81.4 ± 3.6 years; $p < 0.001$). The overall mortality at 30 days before matching was higher after CABG + AVR than after PCI + TAVI (7.8 vs 2.1%; $p = 0.012$). The paired cohort was balanced for both groups regarding demographic variables and the risk profile (age: 77.2 ± 3.7 vs78.5 ± 2.7 years; $p = 0.141$) and EuroSCORE II (6.2 vs 7.6%; $p = 0.297$). At 30 days, mortality was 4.9% in the CABG + AVR group and 1.0% in the PCI + TAVI group ($p = 0.099$). Rethoracotomy was necessary in 7.9% in the CABG + AVR, while conversion to open heart surgery was necessary in 2% in the PCI + TAVI group. The need for new pacemaker was lower after CABG + AVR than after PCI + TAVI (4.1 vs 6.9%; $p = 0.010$). No paravalvular leak (PVL) was noted in the CABG + AVR group, while the incidence of moderate-to-severe PVL after PCI + TAVI was 4.9% ($p = 0.027$).

Conclusion A staged interventional approach comprises a short-term survival advantage compared with combined surgery for management of CAD and aortic stenosis. However, PCI + TAVI show a significantly higher risk of atrioventricular block and PVL. Further long-term trials are warranted.

Keywords
- coronary artery bypass grafts surgery
- CABG
- heart valve surgery
- heart valve
- transapical
- percutaneous (TAVI)
- cardiac catheterization/ intervention (incl. PCI)

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Introduction

The prevalence of a relevant coronary artery disease (CAD) in patients with severe aortic stenosis (AS) varies widely between studies depending on definitions and study design. The German Aortic Valve Registry (GARY), including 140,000 patients who underwent aortic valve replacement (AVR) or transcatheter aortic valve implantation (TAVI) for AS, reported a prevalence of CAD of 24.4 and 62.6%, respectively.[1,2] This finding relates to similar pathogenesis with degenerative and/or arteriosclerotic processes on the basis of similar risk factors.[3] Patients with severe AS and relevant CAD can be treated surgically with simultaneous AVR and coronary artery bypass graft (CABG) (class I; level of evidence: C).[4,5] Nevertheless, a combined surgical procedure is associated with higher perioperative risk compared with an isolated AVR or an isolated CABG due to extended surgical trauma and prolonged operative and ischemia time. The in-hospital mortality was 2.1% after AVR and 4.5% after AVR + CABG for patients undergoing conventional surgery in the GARY registry in 2017.[6] Nonetheless, omission of revascularization during AVR was shown to be the strongest independent predictor of early death in patients with concomitant relevant CAD.[1,7]

A catheter-based approach is an established treatment of severe AS in elderly and high-risk patients, with a massively expanding spectrum. Furthermore, catheter-based approach for complex CAD has shown to be feasible and safe in selected high-risk or inoperable patients.[4,8] A complete interventional approach combining percutaneous coronary intervention (PCI) and TAVI or hybrid procedures could provide an alternative to CABG + AVR. The available evidence allows a European Society of Cardiology/European Association for Cardiothoracic Surgery (ESC/EACTS) recommendation of class IIa for PCI + TAVI.[5]

In our analysis, we compared the early outcome of patients treated surgically with that of patients treated with completely catheter-based approach with severe AS and concomitant CAD. The aim of our work is to highlight the decision-making process and management of these patients by the heart team.

Methods

This is a monocentric observational analysis of consecutive patients with AS and CAD. For the analysis, all patients were identified who were treated for the above two conditions at our hospital since 2017. We included patients who had undergone concomitant CABG + AVR for severe symptomatic AS or combined stenosis and insufficiency and relevant coronary stenosis. For the comparison group, we included all AS + CAD patients who received a staged interventional therapy with PCI + TAVI, with a maximal time interval of 6 months between PCI and TAVI. All included patients were discussed at the weekly interdisciplinary conference at our institution. The clinical condition and comorbidities of each patient were evaluated with appropriate assessment of the operative risk. The most appropriate therapeutic procedure for each patient was consensually chosen by the heart team. An agreement of the ethical committee was exempted due to the retrospective character of this study. Preoperative data on patient demographics, comorbidities, and previous cardiac interventions were extracted out of digital patients records and analyzed. Early patient outcome was examined to identify in-hospital mortality and complications.

We excluded all patients who had one of the following diagnoses as an indication for surgery: aortic valve insufficiency without stenosis, endocarditis of the aortic valve, combined procedures including valve intervention/surgery other than aortic valve (in mitral, tricuspid, or pulmonary position).

The end points were in-hospital mortality, periprocedural new onset of atrioventricular block (AVB) II–III°, paravalvular leak (PVL), myocardial infarction (MI), cerebrovascular stroke, the length of stay in the intensive care unit (ICU), and the total in-hospital stay.

Severe AS was defined according to the current echocardiographic guidelines.[5] CAD was defined according to the current angiographic guidelines.[9] CAD severity was classified into 1-, 2-, and 3-vessel disease (3-VD). The European System for Cardiac Operative Risk Evaluation (EuroSCORE) II was used to assess the operative risk. The corresponding definitions of the Valve Academic Research Consortium (VARC) criteria were applied to define the above-mentioned end points.[10,11] The 30-day mortality included all-cause death during the hospital stay or within 30 days postprocedural. PVL presence and severity was detected with echocardiography and classified after the European Association of Cardiovascular Imaging (EACVI) guideline into "none," "mild," "moderate," and "severe."[11] MI was defined as type 5 MI associated with surgical revascularization, AVR, or TAVI.[12] Cerebrovascular events (CVEs) were considered to be any new-onset neurologic deficit of cerebral origin, assessed by a neurologist, in association with signs of hemorrhage or ischemia on computed tomography/magnetic resonance imaging (CT/MRI) of the brain that occurred during the primary hospital stay.

All CABG and AVR were performed as combined procedures, whereas TAVI were staged within 6 months after PCI. Surgical management was performed under general anesthesia via median sternotomy, with CPB, mild hypothermia, and cardioplegic arrest. In this study, the following conventional prothesis were implanted: Perimount (Carpentier-Edwards Lifesciences Corp., Irvine, California, United States), Magna Ease (Carpentier-Edwards Lifesciences Corp., Irvine, California, United States), and Trifecta (Abbott, Valve with Glide Technology (GT), Allschwil, Switzerland). Rapid deployment prostheses such as Perceval (LivaNova, London, United Kingdom) and INTUITY (Edwards Lifesciences Corp., Irvine, California, United States) were used. Stentless valves were not used in this work. In young patients (<60 years), mechanical valves comprising Carbomedics (LivaNova, Saluggia (VC), Italy) and On-X (Life Technologies, Kennesaw, Georgia, United States) were used.

TAVI procedures were performed in the hybrid operating room in our institution by the interdisciplinary heart team

involving an interventional cardiologist, a cardiac surgeon, and a cardio-anesthetist. Transfemoral (TF), transapical (TA), or transaxillary (TAx) access routes were used in this study. The procedure was usually performed under general anesthesia for TA-TAVI and TAx-TAVI, whereas conscious sedation was usually enough for TF-TAVI. The predefined access route for the TAVI sheath was then prepared accordingly either percutaneously or surgically. Balloon valvuloplasty before, through, and/or after valve delivery was decided according to extension of annulus calcification, prothesis type, and/or a resulting PVL. In this study, balloon-expandable SAPIEN prostheses (SAPIEN; SAPIEN XT, SAPIEN 3, Edwards Lifesciences Corporation, Irvine, California, United States) were used. The following self-expanding prostheses were implanted: Core Valve prostheses (COREVALVE, COREVALVE Evolut R, and COREVALVE Evolut pro, Medtronic, Minneapolis, Minnesota, United States); ACURATE and ACURATE neo (formerly Symetis Inc., Ecublens, Switzerland and now Boston Scientific, Marlborough, Massachusetts, United States); JENAVALVE (JenaValve Technology Inc., Munich, Germany); and LOTUS (Boston Scientific, Marlborough, MA, USA).

Statistical Analysis

All data were statistically analyzed using SPSS Statistics version 27.0 (IBM Corporation, Armonk. New York, United States) and R Statistical Software (V.3.3.2; R Foundation for Statistical Computing, Vienna. Austria). For nominal variables, the absolute number (n) was calculated with percentages. For metric variables, the mean with the respective standard deviation or the median with the 25th and 75th percentiles were calculated for their description, depending on the variable distribution. Group comparisons were performed using the Student's t-test or Wilcoxon–Mann–Whitney test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. Univariate normality assumptions were verified using the Shapiro–Wilk test. The significance level was set at $\alpha = 0.05$ and a p-value < 0.05 was thus considered statistically significant.

Propensity Score Matching

Propensity score matching (PSM) was used to minimize differences in demographic characteristics and potential bias. This was done using logistic regression analysis with inclusion of the following variables: age, gender, body mass index (BMI), body surface area, CAD 3-VD, left main stem involvement, diabetes mellitus, hypertension, previous MI, chronic obstructive pulmonary disease (COPD), calculated creatinine clearance, peripheral vascular disease, atrial fibrillation (AF), left ventricular ejection fraction (<30%), and EuroSCORE II. A one-to-one matching algorithm was performed identifying 101 PS-matched pairs. The logrank test was used to analyze survival rates and graphically presented in Kaplan–Meier curves.

Results

Of all patients treated since 2017 by TAVI, we identified 242 (17.7%) patients who underwent PCI within 6 months (median, 43 days; interquartile range, 1–171 days) before TAVI. After adjusting the exclusion criteria, a total of 237 patients were included in the PCI + TAVI group. In the surgical group, 517 patients underwent CABG + AVR during the same period. After adjustment of the exclusion criteria, 241 patients were included in the CABG + AVR group. All patients received the appropriate revascularization method deemed feasible by the heart team at the time of TAVI or at the time of CABG + AVR, with no further planned coronary interventions.

The median age of patients in the CABG + AVR group was 71.9 years (67.7–77.8) at the time of the operation, while the median age in the PCI + TAVI group was 81.4 (78.7–85.8) years ($p < 0.001$). Also, 23.2% in the CABG + AVR group and 40.9% in the PCI + TAVI group were females. The mean BMI was comparable between the two groups: 28.2 kg/m^2 in CABG +AVR and 26.4 kg/m^2 in PCI + TAVI ($p = 0.100$) (►**Table 1**).

In the CABG + AVR group, 54.3% of patients had 3-VD versus 21.9% in the PCI + TAVI group. 1-VD was noted in 19.9 and 60.7% in the CABG + AVR and PCI + TAVI groups, respectively ($p < 0.001$). Left main stem involvement was documented in 59 (24.4%) versus 34 (14.6%) in the CABG + AVR group versus PCI + TAVI ($p = 0.05$). There were no patients with previous cardiac surgery in the CABG + AVR group. In the PCI + TAVI group, 65 (27.2%) patients had a prior cardiac surgery. Pulmonary vascular disease (PVD), severely impaired left ventricular function, renal insufficiency, AF, and pulmonary hypertension (PHT) were more prevalent in the PCI + TAVI group. The EuroSCORE II was 5.6% (±3.5) in the CABG + AVR group versus 7.9% (±5.4) in the PCI + TAVI group ($p = 0.059$).

All TAVI patients in this analysis were elective, whereas 7 (2.9%) patients underwent emergency and 12 (4.9%) patients underwent urgent surgery for acute coronary syndrome (ACS). Seventeen (7.05%) patients were hemodynamically unstable with high catecholamine requirement due to preoperative cardiogenic shock (►**Table 2**). Of these, three (1.2%) patients were on intra-aortic balloon pump support and three (1.2%) patients were on extracorporeal membrane oxygenation support.

Rethoracotomy for relevant hemorrhage or tamponade was necessary in 16 (6.6%) patients in the CABG + AVR group. In the PCI + TAVI group, thoracotomy was necessary in nine (3.7%) patients ($p < 0.010$). Postoperatively, new AVB requiring a permanent pacemaker therapy was significantly higher after TAVI with 10.5 versus 4.1% after CABG + AVR. A moderate-to-severe PVL was detected in 16 (6.7%) patients after TAVI ($p < 0.001$). No PVL was noted in the CABG + AVR group. Patients stayed a median of 2 days longer in the ICU after surgical management ($p = 0.010$). CVEs were documented in 1.6% after CABG + AVR and 2.9% after TAVI ($p = 0.070$). All-cause mortality was 2.1% after TAVI versus 7.8% after CABG + AVR ($p = 0.012$) (►**Table 3**).

Comparison of Patient Population by PSM

After PSM, 101 matched pairs were identified. The baseline variants were well balanced between groups (►**Table 4**). The prevalence of AF, arterial hypertension, and diabetes mellitus was comparable in both groups. Nonetheless, significantly higher prevalence of PVD, chronic kidney disease, COPD, and

Table 1 Demographics of both CABG + AVR and PCI + TAVI groups before PSM

Preoperative variables	CABG + AVR	PCI + TAVI	*p*-Value
	Unmatched cohort		
	n = 241	*n* = 237	
Age (y)	71.9 (67.7–77.8)*	81.4 (78.7–85.8)	<0.001
Gender (male), *n* (%)	185 (76.8)	140 (59.1)	0.198
BMI (kg/m^2)	28.2 (24.9–30.5)*	26.4 (23.8–28.3)	0.100
BSA (m^2)	1.9 (±0.18)	1.8 (±0.19)	0.101
NYHA, *n* (%)			
I	17 (3.1)	33 (13.8)	0.118
II	25 (10.3)	52 (21.8)	
III	158 (66.0)	99 (41.4)	
IV	41 (17)	53 (22.7)	
CCS (III–IV), *n* (%)	28 (11.6)	2 (0.8)	0.010
Decompensation	22 (9.1)	4 (1.7)	<0.001
CAD (number of vessel disease treated)			
1, *n* (%)	48 (19.9)	144 (60.7)	<0.001
2, *n* (%)	55 (22.8)	30 (12.6)	
3, n (%)	131(54.3)	52 (21.9)	
Left main disease	59 (24.4)	34 (14.6)	0.05
ACS, *n* (%) (unstable AP/STEMI/NSTEMI within 2 wk before index procedure)	19 (7.8)	0	<0.001
Previous PCI (older than 6 mo before index procedure)	37 (15.4)	132 (57.6)	<0.001
PCI/DES, *n* (%) (within 6 mo before index-procedure)	47 (19.5)	237 (100)	<0.001
Previous cardiac surgery, *n* (%)	0	65 (27.2)	<0.001
CABG		29 (12.2)	
AVR		6 (2.5)	
Others		30 (12.6)	
CKD, *n* (%) (creatinine clearance <50 mL/min)	48 (19.9)	41 (17.2)	0.105
Peripheral vascular disease, *n* (%)	22 (9.1)	53 (22.3)	<0.001
COPD, *n* (%)	50 (21.0)	64 (27.0)	0.134
Arterial hypertension, *n* (%)	228 (94.6)	220 (92.8)	0.456
Pulmonary hypertension, *n* (%)	6 (2.5)	149 (62.8)	<0.001
Diabetes mellitus, *n* (%)	95 (39.4)	76 (32.0)	0.105
Atrial fibrillation, *n* (%)	34 (14.1)	103 (43.4)	<0.001
LVEF < 30%, *n* (%)	6 (2.4)	36 (15.1)	<0.001
EuroSCORE II (%)	5.6 (±3.5)	7.9 (±5.4)	0.059

Abbreviations: ACS, acute coronary syndrome; AVR, aortic valve replacement; AP, Angina Pectoris; BMI, body mass index; BSA, body surface area; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CCS, Canadian Cardiovascular Society classification for angina pectoris; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DES, drug-eluting stent; LVEF, left ventricular ejection fraction.; NYHA, New York Heart Association; NSTEMI, Non-ST-elevation myocardil infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; TAVI, transcatheter aortic valve implantation.

Note: Depending on variable distribution, metric variables are calculated either as mean with respective standard deviation (±) or median with 25th and 75th percentiles (*). For nominal variables, the absolute number (*n*) is calculated with percentage (%).

PHT was noticed in the PCI + TAVI group. The mean operative risk assessed with EuroSCORE II was 6.2% (±2.7) versus 7.6% (±5.1) for CABG + AVR versus PCI + TAVI, respectively ($p = 0.279$). Emergency surgery patients were excluded. However, 9 (8.9%) patients underwent CABG + AVR urgently (►**Table 5**).

In the CABG + AVR group, 36 rapid-deployment valves (16 Edwards Intuity and 20 Sorin Perceval), 55 Perimount CE Pericardial prostheses, 4 Magna Ease, 3 Trifecta, 2 Carbomedics, and 1 On-X aortic valve prosthesis were implanted. In the matched TAVI cohort, 74 balloon-expandable valves (65 S3 and 9 Edwards XT) and 27

Table 2 Procedural data of both groups CABG + AVR and PCI + TAVI before PSM

Procedural data	CABG + AVR	PCI + TAVI	*p*-Value
	Unmatched population		
	n = 241	*n* = 237	
Urgency, *n* (%)			
Elective	222 (92.1)	237 (100)	<0.001
Urgent	12 (4.9)	0	
Emergency	7 (2.9)	0	
Perioperative instability, *n* (%) (high vasopressors or assist device)	17 (7.1)	6 (2.5)	0.045
Access route			
Median sternotomy	241 (100)	–	
Transfemoral	–	214 (90.2)	
Transapical	–	20 (8.4)	
Transaxillary	–	3 (1.3)	
Duration (h)	3.8 (3.12–7.2)*	1.1 (1.0–1.3)	<0.001
Valve prothesis size (mm)	23.0 (23–25)*	26.0 (24–27)	<0.001

Abbreviations: AVR, aortic valve replacement; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; TAVI, transcatheter aortic valve implantation.
Note: Metric variables are calculated as median with 25th and 75th percentiles (*). For nominal variables, absolute number (*n*) is calculated with percentage (%). Assist device: intra-aortic balloon pump support and/or extracorporeal membrane oxygenation and/or Impella.

self-expandable prostheses (19 Symetis, 7 Core Valve, and 1 Lotus) were implanted.

The 30-day all-cause mortality was 5 (4.9%) after CABG + AVR and 1 (1.0%) after PCI + TAVI ($p = 0.099$) and after Fischer's exact test ($p = 0.212$). ►**Figs. 1** and **2** show the 30-day survival before and after PSM in Kaplan–Meier curves. Two male patients in the CABG + AVR died of cardiogenic shock, one patient died of hemorrhagic shock, one patient died of sepsis

Table 3 Postoperative outcome of both groups CABG + AVR and PCI + TAVI before PSM

Postoperative variables	CABG + AVR	PCI + TAVI	*p*-Value
	Unmatched population		
	n = 241	*n* = 237	
Rethoracotomy or conversion, *n* (%)	16 (6.6)	9 (3.7)	0.010
Packed RBCs, unit	1.2 (0–4)*	0.74 (0–2)	<0.001
Creatinine (mg/dL)	1.7 (±0.3)	1.3 (±0. 3)	<0.525
CK (U/L)	1112.3 (±205.1)	151.1 (±23.4)	<0.001
CK-MB (U/L)	71.1 (±20.3)	19.0 (±2.3)	<0.001
Troponin (ug/L)	2.11 (±0.7)	0.23 (±0.1)	<0.001
New AVB II–III°, *n* (%)	10 (4.1)	25 (10.5)	<0.010
Wound infection, *n* (%)	14 (5.8)	0 (0)	<0.001
Major peripheral vascular complications, *n* (%)	7 (2.9)	3 (1.3)	0.068
CVEs, *n* (%)	4 (1.6)	7 (2.9)	0.070
PVL II–III, *n* (%)	0	16 (6.7)	<0.001
ICU stay (d)	3 (1–6)*	1 (1–4)	0.010
In-hospital stay (d)	13 (11–17)*	8 (5–23)	0.375
30-d mortality, *n* (%)	19 (7.8)	5 (2.1)	0.012

Abbreviations: AVB, atrioventricular block; AVR, aortic valve replacement; CABG, coronary artery bypass grafting; CK, creatinine kinase; CVE, cerebrovascular event; ICU, intensive care unit; PCI, percutaneous coronary intervention; PVL, paravalvular leak; TAVI, transcatheter aortic valve implantation.
Note: Metric variables are calculated either as mean with respective standard deviation (±) or median with 25th and 75th percentiles (*), depending on variable distribution. For nominal variables, the absolute number (*n*) is calculated with percentage (%).

Table 4 Preoperative data of CABG + AVR and PCI + TAVI after PSM

Preoperative variables	CABG + AVR	PCI + TAVI	*p*-Value
	Matched population		
	n = 101	*n* = 101	
Age (y)	77.2 (74.8–80.2)*	78.5 (74.5–82.0)	0.141
Gender (male), *n* (%)	69 (68.3)	69 (68.3)	1.000
BMI (kg/m^2)	27.1 (23.8–29.4)*	26.7 (24.2–29.7)	0.867
BSA (m^2)	1.9 (±0.18)	1.8 (±0.19)	0.318
NYHA, *n* (%)			
I	2 (2.0)	14 (13.8)	0.295
II	10 (9.9)	22 (21.8)	
III	68 (67.3)	42 (41.4)	
IV	17 (16.8)	23 (22.7)	
CCS (III–IV), *n* (%)	9 (8.9)	7 (6.9)	0.093
Decompensation, *n* (%)	9 (8.9)	11 (10.8)	0.785
CAD (number of vessel disease treated)			
1, *n* (%)	23 (22.8)	48 (47.5)	1.000
2, *n* (%)	35 (34.7)	10 (9.9)	
3, *n* (%)	39 (38.6)	39 (38.6)	
Left main disease, *n* (%)	37 (36.6)	29 (28.7)	0.187
ACS, *n* (%) (unstable AP/STEMI/NSTEMI within 2 wk before the index procedure)	13 (12.8)	0	<0.001
Recent PCI, *n* (%) (within 6 mo before the index procedure)	20 (19.8)	101 (100)	<0.001
Previous cardiac surgery, *n* (%) CABG AVR Other procedures	0	40 (39.6) 40 (100) 0 (0) 11 (27.5)	<0.001
CKD, *n* (%) (creatinine clearance < 50 mL/min)	17 (16.8)	24 (23.8)	<0.040
Peripheral vascular disease, *n* (%)	22 (9.1)	53 (22.3)	<0.001
COPD, *n* (%)	17 (16.8)	30 (29.7)	0.045
Arterial hypertension, *n* (%)	94 (93.1)	95 (94.1)	1.000
Pulmonary hypertension, *n* (%)	1 (0.9)	57 (56.4)	<0.001
Diabetes mellitus, *n* (%)	37 (36.6)	33 (32.7)	0.658
Atrial fibrillation, *n* (%)	28 (27.7)	26 (25.7)	0.874
LVEF < 30%, *n* (%)	4 (3.9)	7 (6.9)	0.537
EuroSCORE II (%)	6.2 (±2.7)	7.6 (±5.1)	0.279

Abbreviations: ACS, acute coronary syndrome; AVR, surgical aortic valve replacement; BMI, body mass index; BSA, body surface area. NYHA, New York Heart Association; CABG, aortocoronary bypass surgery; CCS, Canadian Cardiovascular Society classification for angina pectoris; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; PHT, pulmonary hypertension; TAVI, transcatheter aortic valve implantation; VHF, atrial fibrillation.
Note: Metric variables are calculated either as mean with respective standard deviation (±) or median with 25th and 75th percentiles (*), depending on variable distribution. For nominal variables, the absolute number (*n*) is calculated with percentage (%).

and multiple organ failure, and one female patient died due to massive cerebral ischemia. Four of the five deceased patients in the CABG + AVR were over 80 years old.

Rethoracotomy due to massive bleeding or tamponade was performed in eight (7.9%) cases in the CABG + AVR group. In the PCI + TAVI group, an unplanned sternotomy with CPB was emergently performed in two (2.0%) cases because of pericardial tamponade due to left ventricular perforation and valve dislocation. One patient survived the emergency procedure and could be discharged home.

Cerebral events were comparable in both groups with 2.0% after CABG + AVR and 3.0% after PCI + TAVI ($p = 1.00$). Cardiac biomarkers were significantly higher after CABG + AVR. Postprocedural, new permanent pacemaker

Table 5 Procedural data of both groups CABG + AVR und PCI + TAVI after PSM

Procedural data	CABG + AVR	PCI + TAVI	*p*-Value
	Matched population		
	n = 101	*n* = 101	
Urgency, *n* (%)			
Elective	91 (90.1)	101 (100)	<0.055
Urgent	9 (8.9)	0	
Emergency	0 (0.0)	0	
Access route, *n* (%)			
Median sternotomy	101 (100)	–	
Transfemoral	–	88 (87.1)	
Transapical	–	11 (10.9)	
Transaxillary	–	2 (2.0)	
Duration (h)	3.8 (3.1–4.1)*	1.1 (1.0–1.3)	<0.001
Size of valve prothesis (mm)	23.0 (23–25)*	26.0 (24–27.5)	<0.001
Valve prothesis type, *n* (%)			
Conventional bioprothesis	62 (61.3)	–	
Rapid deployment valves	36 (35.6)	–	
Balloon expandable	–	74 (73.3)	
Self-expandable	–	27 (26.7)	

AVR, surgical aortic valve replacement; CABG, aortocoronary bypass surgery; N/A, not applicable; PCI, percutaneous coronary intervention; TAVI, transcatheter aortic valve implantation.
Note: Metric variables are calculated as median with 25th and 75th percentiles (*). For nominal variables, absolute number (*n*) is calculated with percentage (%).

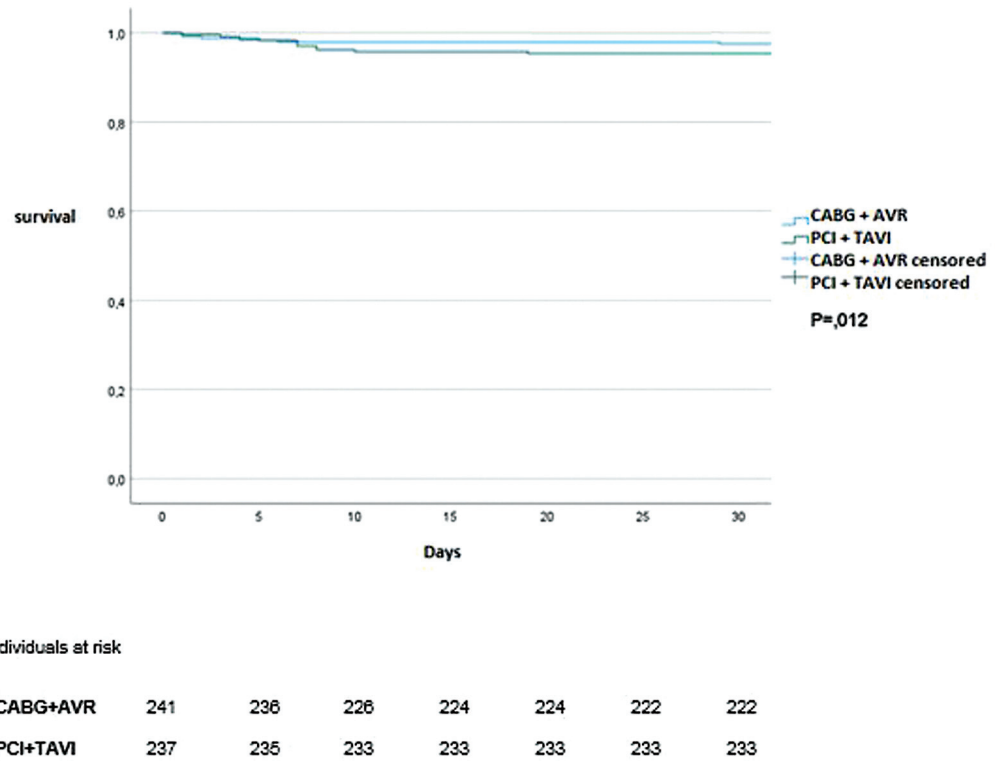

Fig. 1 Kaplan–Meier curve for 30-day survival before matching.

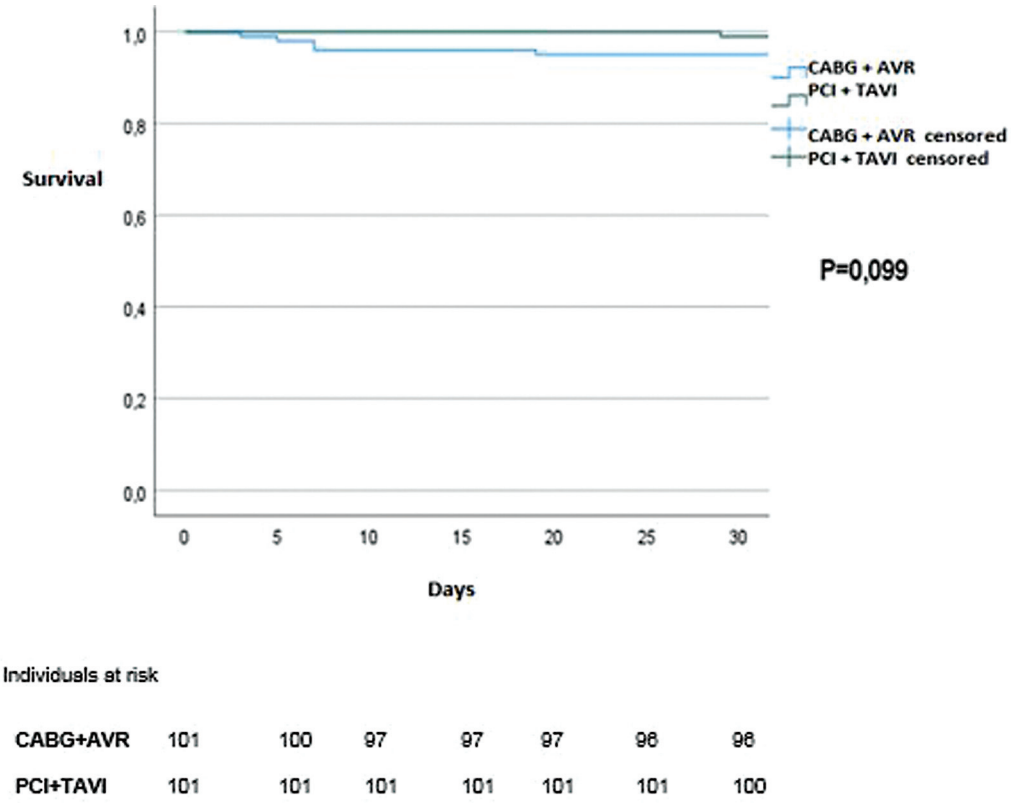

Fig. 2 Kaplan–Meier curve of overall survival after CABG + AVR vs PCI + TAVI after PSM.

implantation was significantly higher after PCI + TAVI with 6.9% than after CABG + AVR with 4.1% ($p = 0.010$). A relevant PVL II–III° was diagnosed in five (4.9%) patients after TAVI ($p < 0.027$). There was no detected PVL after CABG + AVR. Although TAVI patients received significantly larger valves, there was no difference in PPM after matching ($p < 0.872$). Other postoperative complications such as major peripheral vascular complications, periprocedural acute renal failure, and dialysis showed no significant statistical difference between both groups. Complications related to sternotomy including wound dehiscence or mediastinitis were noted in four (3.9%) patients in the CABG + AVR group. The length of ICU stay after PSM was comparable between groups ($p = 0.066$). However, the overall length of hospital stay remained longer after CABG + AVR ($p = 0.001$). Postoperative outcomes after PSM are summarized in ►**Table 6**.

Discussion

Variable treatment options are available for patients presenting with severe AS and relevant CAD, including open surgical, minimally invasive, interventional, and hybrid procedures. Individual operative risk assessment and anatomical conditions guide decision making.[13,14] Combined surgical procedure comprising of AVR + CABG is associated with higher perioperative risk compared with an isolated AVR or an isolated CABG, with an in-hospital mortality of 4.5 versus 2.1% respectively.[6] With the steadily increasing accessibility of catheter-based techniques, a staged interventional approach in terms of PCI and TAVI could minimize the operative/interventional burden.[15] Nonetheless, a meta-analysis of patients who underwent a concomitant PCI + TAVI reported a significantly higher 30-day mortality rate compared with patients who underwent an isolated TAVI.[16] Moreover, the currently available evidence to support a staged interventional treatment strategy relies on two meta-analyses by Kotronias et al and Tarus et al, which were mainly based on retrospective and monocentric studies that reported unadjusted and inconsistent results.[16,17] The SURTAVI trial is the only available randomized controlled trial (RCT) for patients with AS + CAD. The authors reported no difference in the end point outcome after CABG + AVR or PCI + TAVI at 2 years.[18] However, the included patients did not have a complex CAD with a mean SYNTAX score of 8.1 and 8.5 in both groups, respectively. Thus, a generalization for more complex CAD patients is not justifiable. Therefore, the role of the heart team in patient/procedure coupling is pertinent.[5] An individual evaluation for each patient considering underlying anatomical features of the coronaries and the aortic valve annulus as well as other bystander cardiac or systemic conditions is recommended.[5] Moreover, outcome aspects such as completeness of revascularization, durability of the valve prosthesis, and the expected complication spectrum of each procedure have to be taken into consideration in the decision-making process.

In the present work, the PCI + TAVI cohort was significantly older, with higher operative risk and frequent previous cardiac surgery. Similar distribution of demographics and risk profiles for surgically or interventionally treated patients with AS and CAD was reported in numerous

Table 6 Postoperative outcome for CABG + AVR vs PCI + TAVI after PSM

Postoperative variables	CABG + AVR	PCI + TAVI	*p*-Value
	Matched population		
	n = 101	n = 101	
Rethoracotomy or conversion, *n* (%)	8 (7.9)	2 (2.0)	0.035
PRBCs, unit	1.3 (0–4)*	0.72 (0–2)	0.026
Creatinine clearance < 50 mL/min, *n* (%)	42 (41.5)	31 (30.6)	0.084
Dialysis postoperative, *n* (%)	1 (1.0)	3 (3.0)	0.100
CK post-op (U/L) (normal <190 U/L)	977.4 (±96.7)	186.5 (±15.4)	<0.001
CK-MB post-op (U/L) (normal < 25 U/L)	73.7 (±11.2)	21.7 (±7.5)	<0.001
Troponin post-op (ug/L) (normal < 0.014 ug/L)	1.72 (±0.3)	0.25 (±0.2)	<0.001
New AVB II–III°, *n* (%)	4 (4.1)	7 (6.9)	0.010
Wound infections, *n* (%)	4 (4.0)	0 (0.0)	0.021
Major peripheral vascular complications, *n* (%)	1 (1.0)	3 (3.0)	0.100
CVEs, *n* (%)	2 (2.0)	3 (3.0)	1.000
PVL II–III, *n* (%)	0	5 (4.9)	0.027
Moderate PPM (iAVA < 0.85 cm^2/m^2), *n* (%)	31 (31)	30 (29)	1.000
Severe PPM (iAVA < 0.65 cm^2/m^2), *n* (%)	10 (9.9)	9 (8.9)	0.872
ICU stay (d)	3.7 (1–6)*	3.1 (1–4)	0.066
In-hospital stay (d)	14.4 (11–17)*	9.4 (5–23)	<0.001
30-d mortality, *n* (%) (with Fischer's exact test)	5 (4.9)	1 (1.0)	0.099 (0.212)

Abbreviations: AVR: surgical aortic valve replacement. PCI: percutaneous coronary intervention. TAVI: transcatheter aortic valve implantation. CK: creatinine kinase. CVE: cerebrovascular event. PVL: paravalvular leak. AVB: AV block. PPM: patient-prosthesis mismatch. ICU: intensive care unit. Metric variables are calculated either as mean with respective standard deviation (±) or median with 25th and 75th percentiles (*). depending on variable distribution. For nominal variables, the absolute number (n) is calculated with percentage (%). CABG: aortocoronary bypass surgery.

studies.[16,17,19] A prior cardiac surgery per se is not a contraindication to surgical treatment and was not considered as an exclusion criterion in our analysis. Nevertheless, those patients were more likely to undergo TAVI in consensus of the heart team due to the considerably higher operative risk.

We refer the inverse proportion of 1- or 3-VD in both groups before PSM to the heart team decision made by the time of treatment assignment. Obviously, surgical revascularization was more often recommended in cases of 3-VD (54.3%) or left main stem involvement (24.4%). On the contrary, a percutaneous approach was performed more often in less complex CAD, with 60.7% of patients having had 1-VD . This variation was balanced after PSM with 38.6% of patients having had 3-VD in both groups ($p = 1.00$). Left main involvement was adjusted as well, after matching, with 36.6 and 28.7% in the CABG + AVR and PCI + TAVI group, respectively ($p = 0.187$). Further, SYNTAX score–based or functional-based assessment of CAD severity was not conducted in this analysis.

In our analysis, the sequence of PCI and TAVI was discussed individually depending on the patient's clinical condition, severity of CAD, and risk of myocardial ischemia. Available data seem to indicate that PCI is feasible both before and together with TAVI without impact on early survival. However, PCI weeks to months before TAVI is currently the most established strategy with dividing of the interventional burden and easier cannulation of coronary ostia before TAVI. Nevertheless, the ACTIVATION study showed that a routine PCI strategy in patients with obstructive CAD before TAVI is not clinically beneficial.[20] Furthermore, it is associated with higher bleeding rates with dual antiplatelet therapy and a propensity for more frequent acute renal failure.[20] Regardless, a recent study reported technical success in 46 cases of coronary angiography, including 26 PCI, performed immediately after implantation of self-expandable CoreValve Medtronic prostheses within the same operative session without additional procedural complexity.[21]

In our analysis, patients in the CABG + AVR had more frequently ACS preoperatively. As in the PCI + TAVI group, PCI was already performed before the index intervention (TAVI). Most patients had, by definition, no longer ACS at the time of the index intervention, even if ACS was diagnosed at the time of PCI.

In our analysis, 30-day all-cause mortality after PSM was 4.9% in the CABG + AVR group and 1.0% in the PCI + TAVI group ($p = 0.212$) (►**Fig. 2**). Our results are comparable with the national average of 30-day mortality risk after CABG + AVR of 4.5%; however, in the GARY register, patients were younger with a mean age of 73 years.[6] In an analysis from the U.S. National Registry for aortic valve procedures with a mean age of 73 years, the authors reported 5.1% incidence of

in-hospital mortality after CABG + AVR. This incidence increased with age, with 7.4% in patients older than 85 years.[22] On the other hand, the GARY registry showed in 2015 an in-hospital mortality of 2.3% after TF-TAVI and 3.7% after TA-TAVI in a high-risk cohort with an average age of 80 years.[6] A more recent evaluation in 2020 showed a significant reduction in TAVI mortality at average of all access routes of 1.6%.[2] Furthermore, a recent meta-analysis showed an advantage in favor of PCI + TAVI regarding the 30-day mortality incidence with 5.2 versus 7.5% after combined surgical approach, without statistical significance.[16] Nonetheless, the initial advantage of PCI + TAVI group equaled out in the 2-year mortality analysis compared with CABG + AVR. The small number of included studies limited this meta-analysis.

In the CABG + AVR group, 7.9% of patients underwent rethoracotomy due to major hemorrhage or pericardial tamponade with subsequently significant more blood transfusion than in the PCI + TAVI group. A single-center analysis by Baumbach et al showed a comparable incidence of rethoracotomy of 7.8% after CABG + AVR.[3] The incidence of surgical conversion during TAVI procedures was 0.7%, as published in the National German Register.[2,6] Despite the fact that serious complications during PCI or TAVI procedures are rare with an overall incidence of 0.4 to 1.3%, they are associated with a higher mortality of more than 50%.[23] Our experience supports the current ESC/EACTS guideline for valve disease insisting on the presence of a cardiac surgery department "on-site" as a prerequisite for performing TAVI (class I; evidence level: C).[5]

The rate of CVEs at 30 days was comparable between groups in our analysis, with 2% in the CABG + AVR group and 3% in the PCI + TAVI group ($p = 1.00$). In an analysis from the U.S. National Registry in 2015, a CVE incidence of 2.9% was reported after CABG + AVR perioperatively.[22] The risk increased with age, with an incidence of 1.3% in patients younger than70 years and 3.2% in those older than 85 years. The incidence of CVEs after TAVI ranged from 2.7 to 5.5% at 30 days in most TAVI RCTs.[13–15]

In our study, the absolute values of cardiac biomarkers were significantly higher postoperatively in the CABG + AVR group than in the PCI + TAVI. However, after applying the definition of type 5 MI, there was no clear evidence of more frequent MI postoperatively in the CABG + AVR compared with PCI + TAVI.[12] There were no coronary obstructions or repeat revascularization in the matched cohort at 30 days. In a recent multicenter analysis of AS patients with complex CAD (156 pairs after PSM), Alperi et al reported a comparable outcome of major adverse cardiac and cerebrovascular events (MACCE) at 3 years.[19] However, the authors further reported a significantly higher incidence of repeat revascularization in the PCI + TAVI group.

We observed moderate-to-severe PVL in 4.9% of cases in the PCI + TAVI group. No PVL was reported in the matched CABG + AVR cohort. Moderate-to-severe PVL occurs in 0.9% of conventional AVR and in approximately 6.4% of TAVI procedures.[23] Furthermore, the 1-year report of the PERSIST trial showed a similar low incidence of PVL using perceval valves compared with conventional prostheses in AVR.[24] Several studies report that moderate and severe PVL are associated with 2- to 12-fold increase in 1-year mortality.[25] The PARTNER II study reported a significantly higher mortality among patients with moderate or severe PVL (64.8%) than among patients with mild PVL (48.7%) or minor PVL (41.1%) after TAVI with balloon expandable valves.[26] Despite reduction of its incidence over the past decade, PVL still represents one of the major limitations of the TAVI procedure.

Conduction disturbances with subsequent pacemaker dependency is the most procedure-associated complication after both AVR and TAVI with a considerably higher risk after TAVI.[23] Moreover, new pacemaker implantation was independently associated with 1-year mortality after TAVI. Furthermore, the development of a pacemaker dependency postinterventional is associated with longer hospitalization of patients and higher costs as well as a relative reduction in the quality of life.[27] In our analysis, we noted a pacemaker dependency of 4.0% after CABG + AVR and 6.9% after PCI + TAVI at 30 days ($p = 0.010$). Taking into consideration that more than one-third of patients in the CABG + AVR group received a rapid-deployment prosthesis, this may be considered a very good outcome. A retrospective analysis showed a higher risk for AVB postoperatively after using rapid deployment prostheses with 8.8% compared to conventional bioprosthesis with 3.7%, without survival benefit.[28] Furthermore, the 1-year report of the PERSIST trial mentioned a higher incidence of new pacemaker implantation after perceval of 11.1% versus 3.6% compared with conventional bioprothesis.[24] On the other hand, the rate of AVB after TAVI varies between 3.5 and 28.6% for currently available prosthesis models (Sapien 3: 12.4%; Evolut R: 17.5% Acurate neo: 9.9%).[23] The GARY registry showed a rate of AVB across all TAVI prosthesis between 2011 and 2015 of 16.6%.[6] This was significantly higher compared with conventional bioprothesis with 3.5% over the same period. Nevertheless, with establishment of new generations TAVI prothesis and a better recognition of the predictors of AVB, the risk is supposedly going to continue to decrease.

Patients who underwent CABG + AVR stayed longer in hospital with a mean of 14.4 (11–17) versus 9.4 (5–23) days after PCI + TAVI ($p < 0.001$). However, the last refers to the length of stay for TAVI without adding that for the corresponding previously performed PCI. A recent meta-analysis showed a mean length of stay of 12.1 (±6.7) and 8.35 (±5.95) in CABG + AVR and PCI + TAVI, respectively.[17]

Limitations

The present study is limited due to its retrospective design. The collected data originate from an unselected patient collective from a single center. This may have resulted in a referral or selection bias.

Furthermore, the collective size was limited for the evaluation of some relatively rare outcomes such as CVEs or MI. Therefore, a type II statistical error cannot be excluded in this regard. A treatment by means of hybrid approach was excluded in this analysis.

Based on the profound differences of both groups, even matching for COPD and PHT did not result in an equal distribution among treatment groups. This imbalance was finally accepted balancing the number of patients to be analyzed. Post hoc case review of all included individuals did not show a relevant influence of COPD and PHT on the final conclusion.

Conclusion

Our analysis showed a short-term survival advantage in favor of PCI + TAVI compared with CABG + AVR for management of CAD and AS. However, PCI + TAVI provide a significantly higher risk of AVB and PVL. Long-term results including data on revascularization incidence, durability of TAVI prostheses, and impact of PVL on long-term survival are necessary to guide decision making by the heart team.

Authors' Contribution

A.E. contributed to study design, data collection, data analysis, interpretation, and writing of the manuscript. S.G., K.E. and M.A. contributed to data collection and data analysis. P.R. and S.B. contributed to data collection and interpretation. E.K. and T.W. contributed equally to data analysis and interpretation, review, and correction of the manuscript.

Conflict of Interest

None declared.

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