



# Coronary artery disease, revascularization, and clinical outcomes in transcatheter aortic valve replacement: Real-world results from the East Denmark Heart Registry

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## Abstract

Transcatheter aortic valve replacement (TAVR) has become an established therapeutic option for patients with symptomatic, severe aortic stenosis. The optimal treatment strategy for concomitant coronary artery disease (CAD) has not been tested prospectively in a randomized clinical trial. This study aimed to describe the degree of CAD, revascularization strategies, and long-term clinical outcomes in a large-scale all-comers TAVR-population. Nine hundred and forty-four consecutive patients underwent TAVR. Obstructive CAD was reported in 224 patients (23.7%)—of these, 150 (66.9%) presented with one-vessel disease (1-VD), 51 (22.8%) with 2-VD, and 23 (10.3%) with 3-VD. Two-thirds underwent coronary revascularization before TAVR; half of those patients with 1-VD and only one-third of those with multivessel disease were completely revascularized. In general, borderline stenoses (50%–70%) were more frequently revascularized in proximal coronary segments than in more distal segments. Long-term survival rates by Kaplan–Meier analysis of the total TAVR population at 5 and 9 years were 64.7% and 54.1%, respectively. A diagnostic coronary angiography was performed in 16.5% of patients within 5 years after TAVR; only 4.8% underwent consequent percutaneous coronary intervention (PCI). There was no difference in survival and need for revascularization post-TAVR between those patients with or without obstructive CAD  $\pm$  revascularization. Neither was there a survival difference between those with or without previous CABG and/or chronic total occlusion(s). In conclusion, CAD is prevalent in TAVR patients and pre-TAVR coronary revascularization is typically focused on treating proximal and high-grade stenosis. A selective pre-TAVR PCI strategy results in favorable clinical outcomes with very low rates of post-TAVR coronary revascularization.

## KEYWORDS

clinical outcome, coronary artery disease, percutaneous coronary intervention, transcatheter aortic valve replacement

**Abbreviations:** ACC, American College of Cardiology; AS, aortic stenosis; ASA, acetylsalicylic acid; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CAD, coronary artery disease; CAG, coronary angiography; CTO, chronic total occlusion; FFR, fractional flow reserve; MSCT, multislice computed tomography; RCT, randomized controlled trial; RV, revascularization; STS, Society of Thoracic Surgeons; PCI, percutaneous coronary intervention; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement; THV, transcatheter heart valve; VD, vessel disease.

## 1 | INTRODUCTION

Transcatheter aortic valve replacement (TAVR) has become an established therapeutic option for patients with symptomatic, severe aortic stenosis (AS) who are ineligible or at higher risk for conventional cardiac surgery [1–4]. In recent years, TAVR is also being increasingly used to treat patients with a lower risk profile; this practice is supported by results from the NOTION, PARTNER-II, and SURTAVI

trials indicating that TAVR is a viable option for patients at lower surgical risk [5–7].

The optimal treatment strategy for concomitant coronary artery disease (CAD) has not been tested prospectively in a randomized clinical trial. Patients with “untreated clinically significant CAD requiring revascularization” have typically been excluded from the large randomized TAVR trials. TAVR has not been studied in patients with significant CAD without prior percutaneous coronary intervention (PCI) [8–12]. During SAVR, coronary artery bypass grafting (CABG) and aortic valve replacement are performed simultaneously. In 1,308 consecutive patients with significant CAD undergoing SAVR with or without CABG, the 5- and 8-year mortality rates were lower in patients undergoing revascularization at the time of SAVR [13]. Current American and European guidelines do not make specific recommendations for coronary revascularization before TAVR [13]. Nevertheless, it is a standard practice in most countries to perform a diagnostic coronary angiography (CAG) and PCI for significant CAD at least few weeks before TAVR.

The aim of this retrospective study was to describe the degree and management of CAD, procedure-related safety, and long-term clinical outcomes—both mortality and need for revascularization—in a large-scale TAVR population, consisting mainly of patients at intermediate surgical risk.

## 2 | METHODS

### 2.1 | Study population

Between November 2007 and July 2016, 944 consecutive patients with severe symptomatic AS underwent TAVR at The Heart Center, Rigshospitalet, Copenhagen, Denmark. The indication for TAVR is made at a Heart Team meeting. All referring hospitals from Eastern Denmark (2.8 million inhabitants) dial-in on a daily video conference call centralized at Rigshospitalet, Copenhagen, and discuss their potential cases for AVR with a senior cardiac surgeon, interventional cardiologist and noninvasive imaging specialist. An informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

### 2.2 | TAVR procedure

All TAVR procedures were performed as previously described [2]. Transfemoral vascular access was the preferred route of access; other access routes utilized were the subclavian, transapical and direct aortic approach. Prosthetic valve size selection was based on echocardiographic (until 2013) and multislice computed tomography (MSCT) measurements of the aortic valve annulus. All patients received a combination of clopidogrel (75 mg daily) and acetylsalicylic acid (ASA, 75 mg daily) for three months post-procedural, followed by ASA lifelong. In case of indication for oral anticoagulant therapy, anticoagulation was combined with clopidogrel for 3 months; thereafter, anticoagulant therapy was continued lifelong.

### 2.3 | CAG and PCI procedure

All patients underwent a diagnostic CAG in order to identify obstructive CAD within 3 months before the TAVR procedure. The decision to

TABLE 1 Baseline characteristics

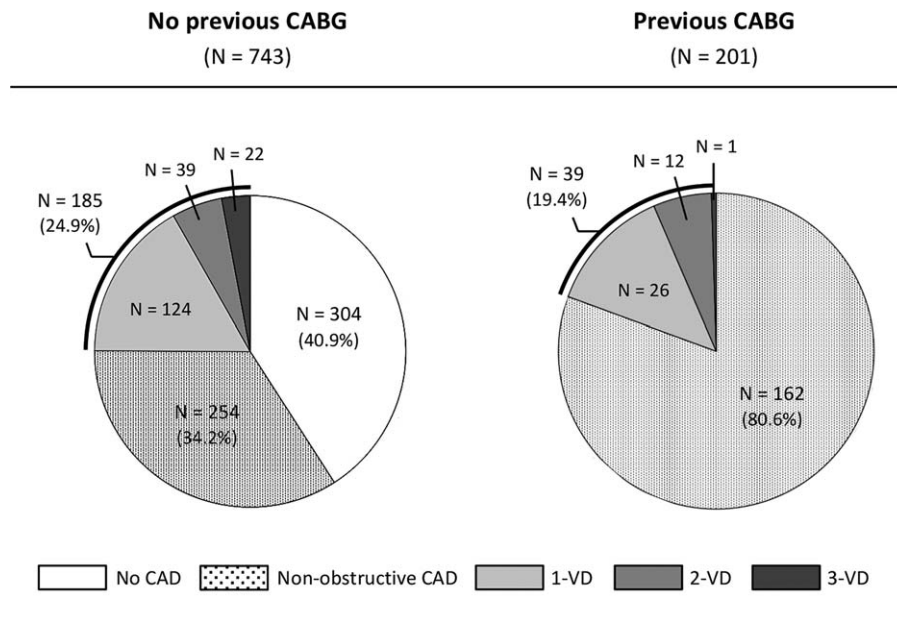
|  | Total TAVR, N = 944 |
|--|---------------------|
| <b>Patient characteristics</b>           |                     |
| Male                                     | 538 (57%)           |
| Age, years                               | 80 ± 7              |
| Arterial hypertension                    | 593 (63%)           |
| Hyperlipidemia                           | 440 (47%)           |
| Diabetes mellitus                        | 179 (19%)           |
| Body mass index (kg/m <sup>2</sup> )     | 27 ± 6              |
| Coronary artery disease                  | 640 (67.8%)         |
| Previous myocardial infarction           | 85 (9%)             |
| Previous PCI                             | 219 (23%)           |
| Previous CABG                            | 201 (21%)           |
| Peripheral vascular disease              | 121 (13%)           |
| Atrial fibrillation, history             | 283 (30%)           |
| Cerebrovascular accident, history        | 123 (13%)           |
| Chronic renal failure (eGFR < 30 mL/min) | 101 (11%)           |
| COPD, moderate or severe                 | 146 (15%)           |
| EuroSCORE, Log                           | 13.9 ± 9.1          |
| STS score                                | 4.4 ± 2.8           |
| <b>Echocardiographic assessment</b>      |                     |
| LVEF < 35%                               | 125 (13%)           |
| Peak velocity, m/s                       | 4.2 ± 0.8           |
| Mean aortic valve gradient, mmHg         | 43 ± 14             |
| Aortic valve area, cm <sup>2</sup>       | 0.7 ± 0.2           |
| Aortic regurgitation ≥ grade 2           | 53 (6%)             |
| Angina pectoris                          | 302 (32%)           |
| NYHA III-IV                              | 813 (86%)           |
| <b>Procedural characteristics</b>        |                     |
| Access                                   |                     |
| Transfemoral                             | 884 (93.6%)         |
| Transsubclavian                          | 47 (5.0%)           |
| Transapical                              | 12 (1.3%)           |
| Direct aortic                            | 1 (0.1%)            |
| Transcatheter aortic valve               |                     |
| CoreValve                                | 594 (62.9%)         |
| Portico                                  | 139 (14.7%)         |
| Lotus                                    | 73 (7.7%)           |
| Sapien-3                                 | 71 (7.5%)           |
| Evolut R                                 | 35 (3.7%)           |
| Symetis                                  | 22 (2.3%)           |
| Centera                                  | 10 (1.1%)           |
| TAVR-valve-in-valve                      | 23 (2.4%)           |

Abbreviations: CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STS, society of thoracic surgeons; TAVR, transcatheter aortic valve replacement.

opt for conservative medical treatment or proceed with PCI in case of obstructive CAD was left to the treating physician's discretion. Angiographic stenoses of 50% or more in proximal coronary segments are systematically described and could be considered for PCI based on angiography alone or based on additional fractional flow reserve (FFR) measurement. Drug-eluting stents were used unless contraindicated.

### 2.4 | Data sources and definitions

All cardiac interventions including CAG, PCI and TAVR are registered in the East Denmark Heart Registry; registration is linked to reimbursement. All data are reported using standardized electronic data entry and are self-adjudicated by the sites. Mortality data are obtained from



**FIGURE 1** Degree of CAD in all-comers TAVR population. Schematic diagrams showing the distribution of different degrees of CAD in TAVR patients with or without previous CABG. CABG, coronary artery bypass graft surgery; CAD, coronary artery disease; VD, vessel disease

the Danish Centralized Civil Registry using the civil person registration number. Follow-up data including CAG, PCI, and mortality rates were 99% complete, based on data from the Heart Registry and the Danish Centralized Civil Registry. Follow-up started from the date of the TAVR procedure and ended on the first coming date of death, emigration, or end of the study (July 31, 2016).

Consistent with standard definitions of flow-limiting stenoses, non-obstructive CAD was defined as a coronary artery stenosis 20% or greater but <50% in the left main coronary artery, or a stenosis 20% or greater but <70% in any other epicardial coronary artery, as recorded by the clinician in the catheterization report. Obstructive CAD was defined as any stenosis 50% or greater in the left main coronary artery, 70% or greater in any other coronary artery, or both. No apparent CAD was defined as all coronary stenoses <20% or luminal irregularities [14–16]. The extent of the CAD is defined as one-vessel, two-vessel, or three-vessel disease. In case of previous coronary artery bypass graft (CABG) surgery, the extent of CAD is defined by the amount of myocardial areas with insufficient coronary blood supply.

Acute kidney injury  $\geq$  stage 2 was defined as a creatinine increase >50% as compared to baseline value. Procedure-related myocardial infarction was defined as a clinical overt myocardial infarction described as such in the electronic patient record; systematic measurements of troponin T and/or CK-MB values post-TAVR are not available.

## 2.5 | Statistical analysis

Categorical variables are reported as absolute values and percentages. Continuous variables are expressed as mean  $\pm$  SD. Categorical variables were compared using Chi-square or Fisher exact tests, as appropriate. The Kaplan–Meier survival plots were constructed from the date

of the TAVR procedure up to a maximum of 9 years of follow-up and statistical comparison was made using the log-rank test. All tests were two-sided, and  $P$  values <0.05 were considered to indicate statistical significance. All analyses were conducted using SPSS statistical software version 20.0 (IBM, Armonk, New York).

## 3 | RESULTS

### 3.1 | Study population

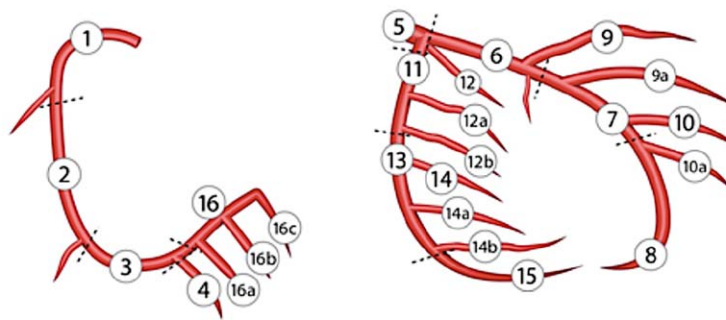
Nine hundred and forty-four consecutive patients with symptomatic, severe AS underwent TAVR during the study period. Table 1 summarizes the baseline characteristics. The mean age of the total study population was  $80 \pm 7$  years and 57% were male. Nonobstructive and

**TABLE 2** Degree of revascularization in different TAVR groups with obstructive CAD

|                         | Coronary revascularization | Complete coronary revascularization |
|-------------------------|----------------------------|-------------------------------------|
| <b>No previous CABG</b> |                            |                                     |
| 1-VD                    | 73/124 (59%)               | 64/124 (52%)                        |
| 2-VD                    | 27/39 (69%)                | 14/39 (36%)                         |
| 3-VD                    | 17/22 (77%)                | 7/22 (32%)                          |
| <b>Previous CABG</b>    |                            |                                     |
| 1-VD                    | 17/26 (65%)                | 13/26 (50%)                         |
| 2-VD                    | 10/12 (83%)                | 5/12 (42%)                          |
| 3-VD                    | 1/1 (100%)                 | 0/1 (0%)                            |
| <b>All patients</b>     |                            |                                     |
| 1-VD                    | 90/150 (60%)               | 77/150 (51%)                        |
| 2-VD                    | 37/51 (73%)                | 19/51 (37%)                         |
| 3-VD                    | 18/23 (78%)                | 7/23 (30%)                          |
|                         | <b>145/224 (65%)</b>       | <b>103/224 (46%)</b>                |

| Segment | Stenosis grade (%) |     |      |     |      |     |     |     |     |      |
|---------|--------------------|-----|------|-----|------|-----|-----|-----|-----|------|
|         | 60%                | 65% | 70%  | 75% | 80%  | 85% | 90% | 95% | 99% | 100% |
| 1       | -                  | 2/2 | 4/5  | 3/4 | 3/3  | 2/3 | 8/9 | 2/3 | 1/2 | 0/15 |
| 2       | 2/2                | 1/1 | 2/2  | 1/1 | 8/10 | 1/2 | 3/5 | 2/2 | 4/5 | 1/4  |
| 3       | 1/3                | 0/2 | 4/4  | 1/1 | 1/1  | 1/1 | 2/2 | 1/1 | -   | 2/3  |
| 4       | -                  | -   | 0/5  | 1/3 | 2/3  | 2/3 | 1/2 | -   | 0/1 | 0/3  |
| 5       | 0/2                | 1/1 | 5/5  | 1/1 | 1/1  | -   | -   | -   | -   | -    |
| 6       | 2/4                | 2/3 | 7/11 | 2/2 | 4/4  | 1/1 | 5/5 | 2/2 | 1/1 | 0/1  |
| 7       | 1/5                | 0/2 | 6/11 | 1/2 | 9/12 | 6/6 | 3/3 | -   | 3/3 | 1/4  |
| 8       | -                  | -   | 1/7  | 0/3 | 0/3  | -   | 1/3 | -   | -   | 0/3  |
| 9       | -                  | -   | 0/8  | 1/4 | 2/7  | 1/4 | 5/8 | 1/2 | 0/1 | 0/3  |
| 10      | -                  | -   | -    | -   | 0/4  | -   | 0/1 | -   | 0/1 | -    |
| 11      | 0/2                | 1/3 | 5/7  | 7/7 | 1/1  | 1/2 | 5/6 | -   | -   | 0/1  |
| 12      | 0/2                | -   | 2/7  | 1/3 | 1/5  | -   | 3/6 | 2/3 | -   | 1/5  |
| 13      | -                  | 0/1 | 3/7  | 1/1 | 1/2  | -   | 2/3 | -   | 0/1 | 0/1  |
| 14      | -                  | -   | 1/2  | 0/1 | 0/3  | 1/2 | 1/4 | -   | -   | -    |
| 15      | -                  | -   | 0/2  | -   | 0/2  | 0/1 | 1/2 | -   | -   | 0/2  |
| 16      | -                  | -   | 0/2  | 1/2 | 0/1  | -   | 0/2 | -   | -   | -    |

More than 50% of these lesions revascularised by PCI before TAVR



**FIGURE 2** Degree of revascularization for the different coronary segments and stenosis grades. Comprehensive overview indicating the number of lesions that were revascularized by means of PCI per coronary segment and stenosis grade—as evaluated for those patients without previous CABG. The numerator indicates the number of lesions that were treated by PCI; the denominator indicates the total number of these lesions as recorded by the clinician in the catheterization report. Dark grey indicates that more than half of these specific lesions were treated by PCI before TAVR [Color figure can be viewed at wileyonlinelibrary.com]

obstructive CAD was prevalent in a large portion of patients ( $n = 640$ , 68%). The calculated STS mortality risk score and logistic EuroSCORE were  $4.4\% \pm 2.8\%$  and  $13.9\% \pm 9.1\%$ , respectively. Based on the Society of Thoracic Surgeons (STS) risk score, 12% of patients could be categorized as high-risk ( $STS \geq 8\%$ ), 63% as intermediate-risk ( $STS 4\%–8\%$ ), and 25% as low-risk patients ( $STS \leq 4\%$ ).

The majority of TAVR procedures were performed by transfemoral route (93.6%). Self-expanding transcatheter heart valves (THV) were implanted in 84.8%, mechanically expandable THV in 7.7%, and balloon-expandable THV in 7.5% of all patients.

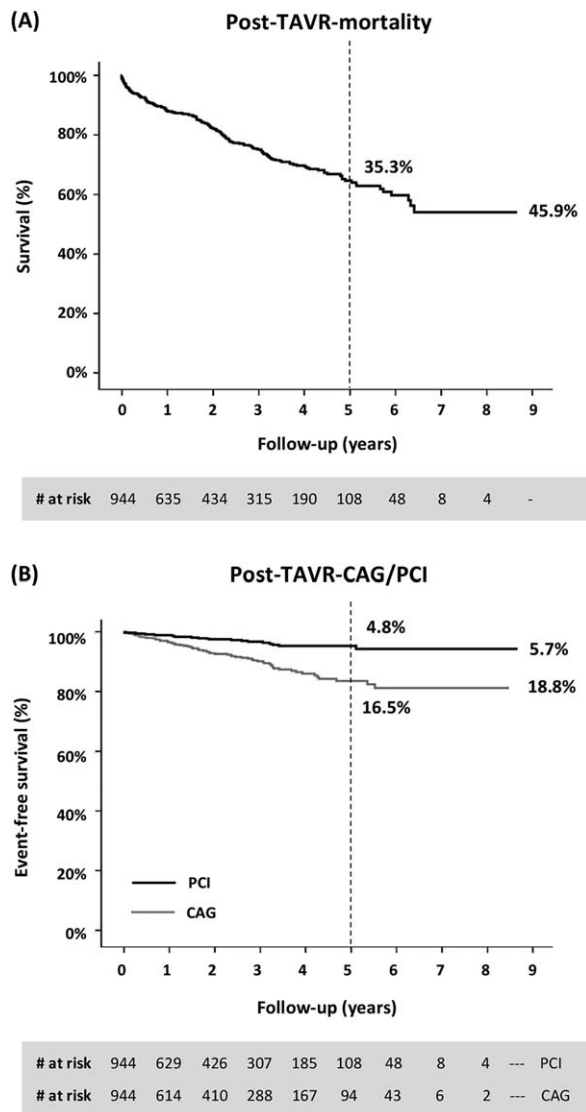
### 3.2 | Coronary status and management before TAVR

Absence of any degree of CAD was noted in 304 patients (32.2%), whereas nonobstructive CAD was reported in 416 patients (44%). Obstructive CAD was reported in 224 out of 944 patients (23.7%), with a similar prevalence rate in those with or without previous CABG

(19.4% vs 24.9%, NS). Of these patients with obstructive CAD, 150 (66.9%) had functional one-vessel disease, 51 (22.8%) two-vessel disease, and 23 (10.3%) three-vessel disease (Figure 1).

FFR was used in 71 patients with borderline stenoses, resulting in a reclassification of obstructive CAD into nonobstructive CAD in 45 out of 944 patients (4.8%).

From those patients with obstructive CAD, 145/224 (65%) underwent coronary revascularization before TAVR (Table 2). From those patients with one-vessel disease (both with or without previous CABG), 90 out of 150 patients (60%) underwent coronary revascularization. Of these, 77 patients underwent complete coronary revascularization; whereas 13 others still had remaining significant lesions after PCI, mainly on (minor) side branches. From those patients with multi-vessel disease, only 26 out of 74 (35.1%) were completely revascularized (Table 2). In general, coronary artery stenoses of 50%–70% were more frequently revascularized in proximal coronary segments (segments 1, 2, 5–7, 11;  $n = 41/68$ , 60%) than in more distal segments (3–4, 8–10,



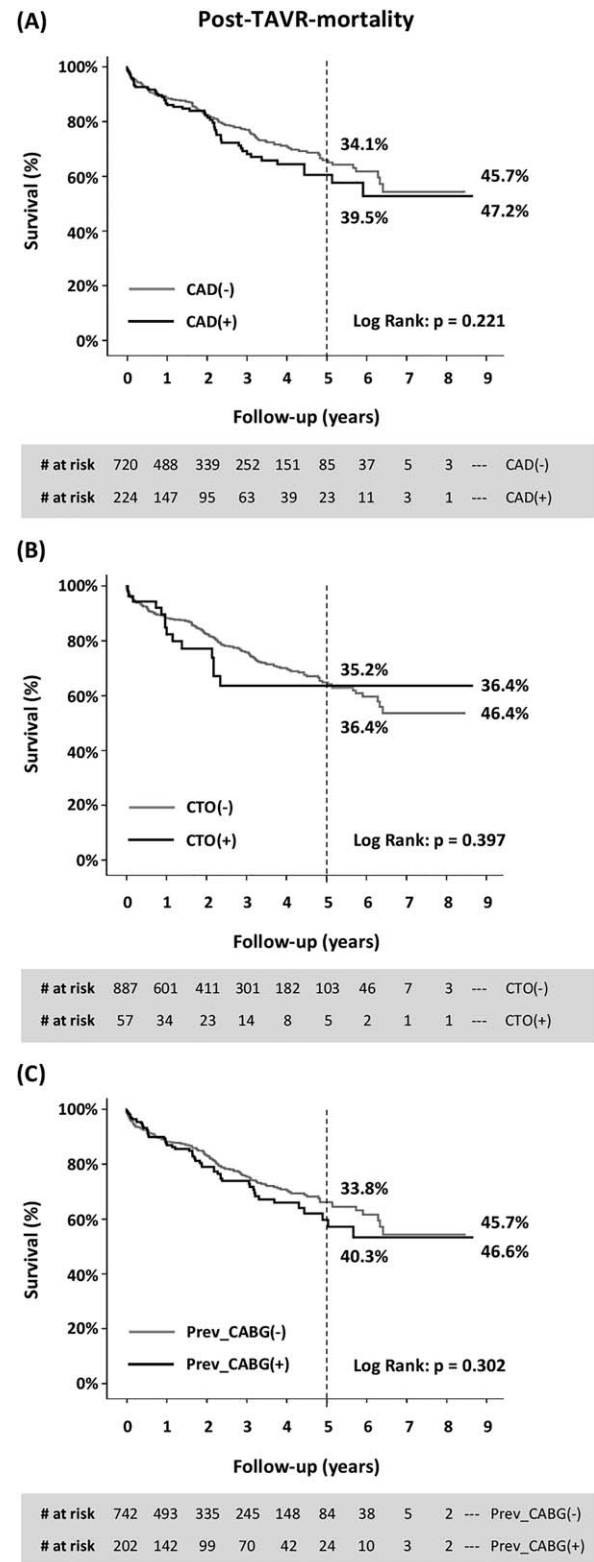
**FIGURE 3** Clinical outcomes in the total TAVR population. Kaplan-Meier curves showing the (A) overall survival for the total TAVR population and (B) cumulative rates of diagnostic coronary angiography (CAG, grey line) and percutaneous coronary intervention (PCI, black line) for the total TAVR population up to 9 years after TAVR

12–16;  $n = 12/52$ , 23%;  $P < 0.001$ ). The most distal coronary segments (8, 10, 14–16) were seldom revascularized ( $n = 7/50$ , 14%) (Figure 2).

Acute kidney injury  $\geq$  stage 2 was noted in 6 out of 145 patients (4.1%) that underwent PCI before TAVR versus in 12 out of 799 patients (1.5%) that underwent diagnostic CAG only ( $P = 0.071$ ). None of the patients needed dialysis following CAG/PCI.

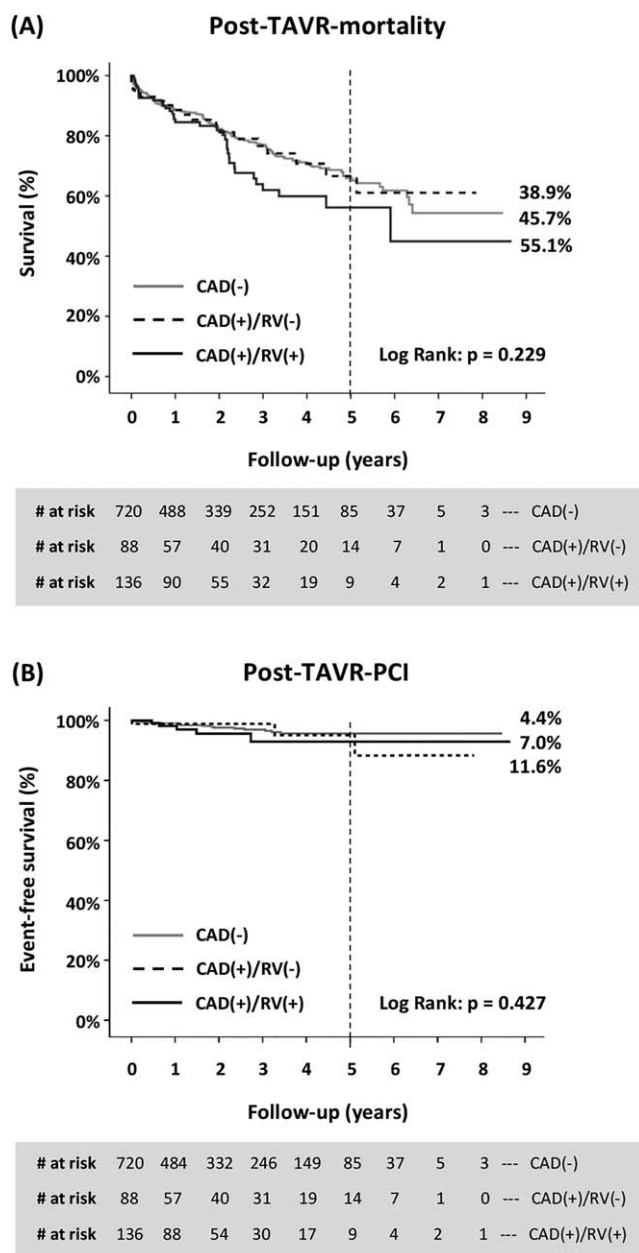
### 3.3 | Clinical outcomes

Long-term survival rates of the total TAVR population at 5 and 9 years of follow-up were 64.7% and 54.1%, respectively (Figure 3A). Based on Kaplan-Meier analysis, the rate of diagnostic CAG at 5-year follow-up was 16.5%; of these, only 4.8% underwent PCI of one or more coronary lesions (Figure 3B). Acute need for coronary revascularization during or immediately after TAVR was reported in only three patients



**FIGURE 4** Survival analysis for different TAVR subgroups. Kaplan-Meier curves showing the overall survival for the TAVR population, dichotomized based on (A) the presence or absence of coronary artery disease (CAD (+)/(-)); (B) the presence or absence of a chronic total occlusion (CTO(+)/(-)); and (C) the presence or absence of previous coronary artery bypass graft surgery (Prev\_CABG(+)/(-)). TAVR, transcatheter aortic valve replacement





**FIGURE 5** Clinical outcomes in different TAVR subgroups. Kaplan-Meier curves showing the (A) overall survival and (B) cumulative rates of percutaneous coronary intervention (PCI) following TAVR, as analyzed for those patients with or without obstructive coronary artery disease (CAD (+)/(-)) and with or without pre-TAVR revascularization (RV(+)/(-)). TAVR, transcatheter aortic valve replacement

(0.3%). A clinical overt post-TAVR myocardial infarction was reported in 5 patients (0.5%); these infarctions were not related to previous coronary stenoses but mechanical obstruction of the coronary ostia by the transcatheter heart valve.

Concerning long-term survival in different TAVR subgroups, there was no difference demonstrated between those patients with or without obstructive CAD (CAD(+) vs CAD(-)), with or without chronic total occlusion(s) (CTO(+) vs CTO(-)), and with or without previous CABG (CABG(+) vs CABG(-)); log-rank:  $P > 0.05$ ; Figure 4). Finally,

there was no difference shown in long-term survival between those patients without obstructive CAD (CAD(-)), those with obstructive CAD and no revascularization (CAD(+)/RV(-)), and those with obstructive CAD and revascularization (CAD(+)/RV(+)) (log rank:  $P = 0.229$ ; Figure 5A, Supporting Information, Table 1).

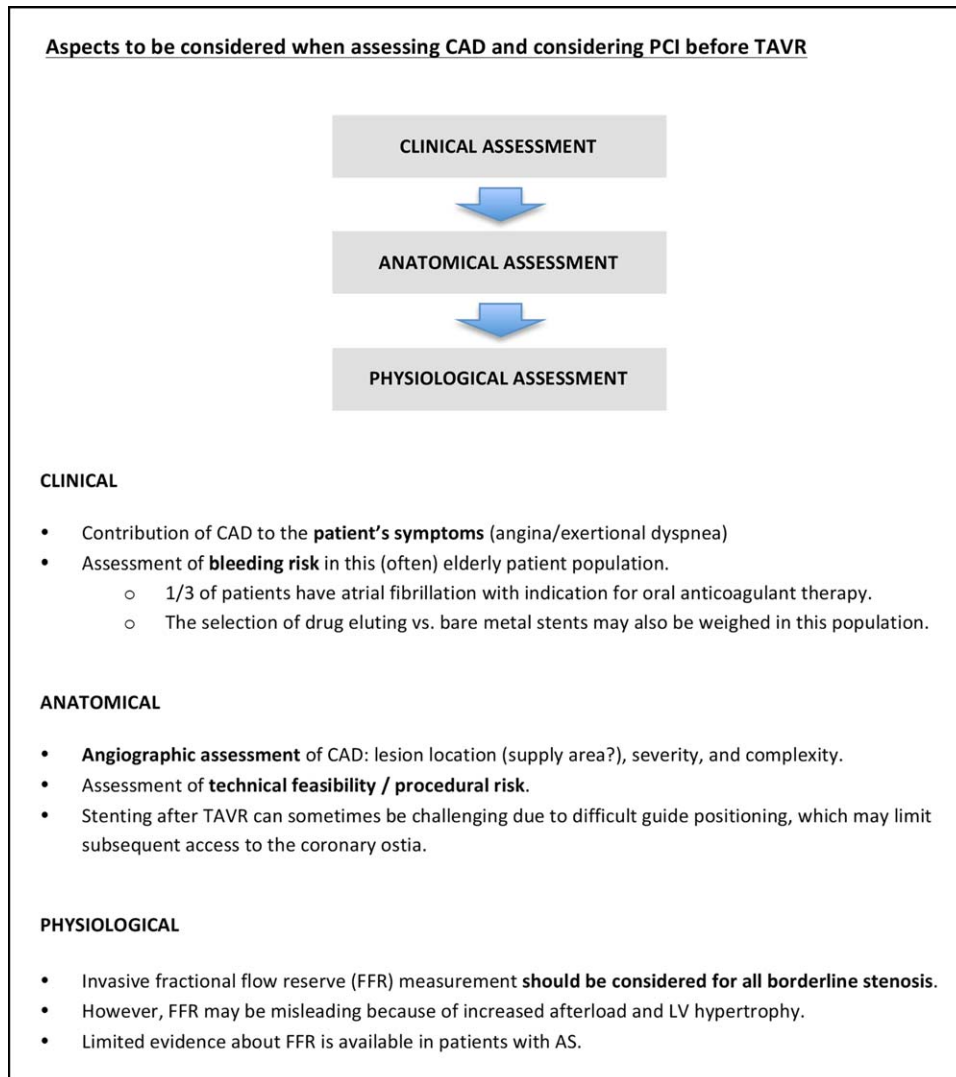
In accordance, there was no difference in the need for revascularization following TAVR between the same three TAVR groups as mentioned above (log rank:  $P = 0.427$ ; Figure 5B). In those patients without obstructive CAD ( $n = 720$ ), 17 new lesions were revascularized within 5 years after TAVR. In those with obstructive CAD and no revascularization ( $n = 88$ ), 2 lesions needed PCI within 5 years after TAVR (only one obstructive lesion that was left untreated before TAVR and one new lesion). In those patients with obstructive CAD and revascularization before TAVR ( $n = 136$ ), 5 lesions needed revascularization within 5 years after TAVR (two lesions that had been revascularized before TAVR needing redo-PCI and three new lesions).

## 4 | DISCUSSION

CAD is common in patients undergoing TAVR and coronary revascularization before TAVR has typically been focused on treating proximal and high-grade stenoses [1,17]. The unique aspect of this study is that it reports on the therapeutic management of CAD in a large-scale, all-comers TAVR population with mainly an intermediate risk profile, including long-term clinical outcomes.

As known from experience with SAVR and considering the high age of TAVR patients, it is not surprising that CAD is prevalent in TAVR populations. The prevalence rates reported in literature can, however, vary depending on the definition used for CAD: obstructive vs nonobstructive CAD, angiographic vs FFR evaluation, only prior revascularization. In our TAVR population, 68% of patients presented with some degree of CAD, which is in line with the CAD rates reported in the large RCTs (60%–75%; Supporting Information, Table 2) [4,11,18–21]. When trying to identify patients that potentially will benefit from coronary revascularization before TAVR, it is more important to detect those patients with obstructive CAD; of these, we identified 224 patients (24%) in our total TAVR population. In a previous study by Khawaja et al. (2015), obstructive CAD was reported in 34% of all 271 TAVR patients [22]. A possible explanation for the lower rate of obstructive CAD in this study may be the lower risk profile of the TAVR population in this study as compared to the TAVR population in Khawaja's study (mean STS risk score 4.4% vs 6.2%, respectively). Moreover, FFR was used in 71 patients with borderline stenoses, resulting in a reclassification into "nonobstructive CAD" in 45 of our patients (4.8%). Finally, the fact that patients with concomitant CAD are still more often referred to SAVR may also be part of the explanation; 38% of all SAVR patients had concomitant CABG at our center during the same study period.

Long-term survival in our all-comers TAVR population was not significantly different between patients with or without obstructive CAD and with or without previous CABG (Figure 4); this is in alignment with previous reports. A meta-analysis analyzing the results of seven observational studies reported that CAD did not affect medium-term TAVR outcomes; at pooled analysis of multivariate approach, diagnosis of CAD did not



**FIGURE 6** Summary figure: considerations on PCI before TAVR [Color figure can be viewed at wileyonlinelibrary.com]

increase risk of death (odds ratio 1.0) at a median follow-up of 452 days [12]. Also prior CABG has previously been reported not to affect medium-term TAVR outcomes [23]. In addition, this study indicates as a first that presence of a CTO does not seem to affect long-term survival following TAVR; however, this result has to be confirmed in future, larger studies and can most likely not be generalized to all types of CTOs.

The role of CAG and PCI in TAVR candidates is still a topic of debate. One of the reasons to treat significant CAD before TAVR is to reduce the risk of myocardial ischemia during the TAVR procedure, especially in cases where rapid pacing is required. Another important consideration may be the difficulty to access the coronary arteries after the TAVR procedure.

Current professional society recommendations have been silent on this specific issue. In accordance with American/European guidelines recommending treatment of significant CAD by concomitant CABG in patients undergoing SAVR, it is a standard practice in most countries to perform CAG and PCI for significant CAD at least few weeks before TAVR [24–26]. In this context, it is also important to know that all prior RCTs that led to TAVR approval required revascularization of all major

coronary arteries with significant stenoses  $\geq 30$  days before TAVR. However, the optimal strategy for treating concomitant CAD when planning TAVR has not been tested prospectively in a RCT. In the 2017 Expert Consensus Decision Pathway from the American College of Cardiology (ACC), it is stated that “*Until more definitive randomized data are available, the Heart Valve Team should decide whether to revascularize before TAVR on a case-by-case basis using the individual patient's anatomic, clinical, and physiological characteristics*” [13].

When assessing patients with a combined severe AS and obstructive CAD, multiple aspects should be considered before considering PCI (Figure 6). Typically, coronary revascularization before TAVR has been focused on treating proximal and high-grade stenoses. In addition, performing PCI on a CTO in the absence of ischemia or symptoms is not advocated [13,27]. The results in this study confirm this approach in daily clinical practice (Figure 2). In general, two-third of all patients with obstructive CAD were revascularized, and 30%–50% of all patients had complete coronary revascularization (Table 2).

Prior data published by Van Mieghem et al. support the proposition that complete revascularization is not a prerequisite for TAVR;

complete versus incomplete revascularization had no effect on one-year survival rates [28]. To the best of our knowledge, this study is the first to show that there is no relationship between minor residual CAD and procedural risk of the TAVR procedure, need for revascularization after TAVR, and long-term mortality. Given these results, it could be speculated that many TAVR patients with concomitant CAD may not need coronary treatment and that CAD in patients undergoing TAVR is just an innocent by-stander. It is, however, important to keep in mind that this study is not a randomized trial and that a selective PCI strategy was applied in this real-life TAVR population. Therefore, it would be wrong to conclude that there is no need for pre-TAVR coronary revascularization based on the data presented in this study.

Remarkably, only one-third of all patients coming back for a diagnostic CAG after TAVR also ended up with a therapeutic PCI. At 5 years post-TAVR, ~17% of patients had returned for a CAG with PCI performed in only 5% of all patients. One explanation for this rather low rate of PCI at re-CAG is that only 2/3 of all patients undergoing a post-TAVR CAG were referred because of angina-like symptoms; the other one-third of patients were referred because of heart failure symptoms. Taken all together, the need for coronary revascularization post-TAVR has been very low in this all-comers TAVR population.

Future randomized trials, such as the ongoing ACTIVATION trial and upcoming NOTION 3 trial, are needed and may provide more evidence on the optimal management of CAD in TAVR patients.

For the time being, most data seem to support PCI of proximal stenosis in major epicardial vessels before TAVR. However, the decision to revascularize or not should be taken on a case-by-case basis using the individual patient's clinical, anatomical, and physiological characteristics [13].

Importantly, this study has some important limitations that have to be pointed out. The main limitations of this study include its retrospective, nonrandomized, single-center design, and the relatively small sample size with more than 5 years of follow-up. Moreover, the survival comparison between the different groups with or without obstructive CAD undergoing coronary revascularization or not is complicated by a difference in baseline characteristics between these groups and the fact that the decision to perform PCI was uncontrolled and depending on multiple unspecified factors. On the other hand, the unique contribution of this study can be found in the fact that this study describes as a first the management of CAD and long-term clinical outcomes in an all-comers TAVR population, consisting mainly of lower risk patients. In addition, the Danish registry systems make that follow-up data describing CAG, PCI, and mortality are 99% complete.

## 5 | CONCLUSIONS

CAD is prevalent in patients undergoing TAVR and coronary revascularization before TAVR is typically focused on treating proximal and high-grade stenosis. The data reported in this study further support that a selective pre-TAVR PCI strategy results in favorable clinical outcomes with very low rates of post-TAVR coronary revascularization. Future prospective RCTs with long-term follow-up will have to confirm these findings.

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## SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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