Coronary revascularization after surgical aortic valve replacement

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ABSTRACT

Objective: It remains unclear how often coronary revascularization is necessary after aortic valve interventions, either by surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement. However, these data are relevant for treatment and prosthesis choice. The authors sought to analyze the incidence and characteristics of coronary revascularization after SAVR during follow-up.

Methods: Of 2256 patients undergoing isolated SAVR between 1987 and 2015, 420 patients (mean age 56.9 ± 15.5 years, 66.9% male) were followed at the Erasmus Medical Center. Incidence, predictors, and characteristics of coronary revascularization were analyzed. Cumulative incidence of revascularization was assessed using a competing risk approach.

Results: Mean follow-up after SAVR was 17.2 years (total of 4541 patient-years). A total of 24 patients underwent 28 procedures of revascularization. The cumulative incidence of revascularization after SAVR was 0.5%, 2.2%, 4.1%, and 6.9% at 1, 5, 10, and 20 years, respectively. The linearized rate of revascularization was 6.2 per 1000 patient-years. Percutaneous coronary intervention was the most common revascularization method (64%; N = 18/28). Revascularization before SAVR (N = 36/420; of whom 27 percutaneous coronary intervention) was an independent predictor of revascularization during follow-up (hazard ratio, 6.6; 95% confidence interval, 2.6-17.1; P < .001).

Conclusions: After SAVR, the rate of coronary revascularization was 6.9% (N = 24/420) at 20-year follow-up. Patients were at particular risk if they had undergone previous revascularization before SAVR. These data may furthermore be relevant to the transcatheter aortic valve replacement population. (JTCVS Open 2020;3:91-101)

CENTRAL MESSAGE

In a large SAVR cohort, the rate of coronary revascularization was 6.9% after 20-year follow-up. Previous revascularization was an independent predictor of revascularization after SAVR during follow-up.

PERSPECTIVE

Coronary revascularization rates after SAVR can be used to predict the need for revascularization after TAVR, should TAVR further expand into younger, lower-risk populations. Dedicated studies are required to address the incidence, predictors, and feasibility of revascularization after TAVR.

See Commentaries on pages 102 and 104.

Transcatheter aortic valve replacement (TAVR) is now recommended for patients with severe aortic valve stenosis (AS) at intermediate and high surgical risk, adding more evidence to the already ongoing increase in the number of performed TAVR procedures in North America and Europe. Recent trials that included low-risk patients have reported noninferiority or even superiority of TAVR versus surgical aortic valve replacement (SAVR).
Abbreviations and Acronyms
AS = aortic valve stenosis
CABG = coronary artery bypass grafting
CAD = coronary artery disease
LVEF = left ventricular ejection fraction
PCI = percutaneous coronary intervention
SAVR = surgical aortic valve replacement
TAVR = transcatheter aortic valve replacement

Reports have suggested that access to the coronary arteries may be difficult to establish after TAVR as a result of the positioning of the transcatheter valve.\(^1\) When indication expands toward low-risk patients, who often are younger, the need for coronary revascularization after TAVR may increase. However, due to the advanced age and presence of multiple comorbidities of patients in current TAVR trials and the relatively short-term follow-up available, the incidence of coronary revascularization has been difficult to determine. The probability of coronary revascularization after TAVR may increase in patients with longer life expectancies, with potential implications for procedure and prosthesis choices.

SAVR has been the standard of care for AS over the past 50 years. Therefore, long-term follow-up is available to determine the incidence of coronary revascularization after SAVR in low-risk patients. Since the historical SAVR patient population overlaps with current and future TAVR patient populations, data of revascularization after SAVR can provide insights into determining which surgical or transcatheter prostheses may be more appropriate in specific patients. The aim of this study was to assess the incidence and risk factors of coronary revascularization during long-term follow-up after SAVR.

METHODS
Study Design
This observational, retrospective study consisted of adult (>18 years) patients who underwent isolated SAVR with a mechanical or bioprosthetic valve between 1987 and 2015 at the Erasmus Medical Center (Erasmus MC), Rotterdam, The Netherlands. To ensure that all coronary revascularization procedures during follow-up were captured, only patients followed up at the outpatient clinic of the Erasmus MC were included in this study (Figure 1). Patients undergoing concomitant procedures or with active endocarditis were excluded. Coronary artery disease (CAD) was routinely assessed before SAVR by coronary angiography, and patients with CAD underwent concomitant coronary artery bypass grafting (CABG) according to the recommendations of clinical guidelines in use at the time of surgery and were excluded.

The study was approved by the local institutional review board, and patient-informed consent was waived. All the authors assured for the validity of the data and adherence to the protocol.

Data Collection and Follow-up
Baseline patient and procedural characteristics were collected from electronic medical records. Survival status was obtained through the National Death Registry.

After SAVR, patients returned to their referring cardiologist at Erasmus MC for routine, regular outpatient clinic visits at 3 and 6 months postoperatively and (bi-)annually thereafter. If CAD was diagnosed and revascularization was deemed necessary, patients underwent either percutaneous coronary intervention (PCI) or CABG at the Erasmus MC.

End Points and Definitions
The primary end point was coronary revascularization either by PCI or CABG. SAVR within 24 hours of establishing the indication was classified as urgent, between 24 hours and 3 days as semi-elective, and after 3 days as elective. Left ventricular function was classified as normal if the left ventricular ejection fraction (LVEF) was >50%, as mildly reduced if the LVEF was 40% to 50%, as moderately reduced if the LVEF was 30% to 40%, and as severely reduced if the LVEF was less than 30%, as measured or estimated by a trained echocardiographer.

Statistical Analyses
Discrete variables are presented as numbers, percentages or proportions, and compared with either the \(x^2\) test or the Fisher exact test, where appropriate. Continuous variables are presented as means ± standard deviation or median with the interquartile range if there was evidence of skewed data according to the Kolmogorov–Smirnov test, and compared with either the 2-sample \(t\) test or Wilcoxon rank-sum test, where appropriate.

Probabilities of the occurrence of revascularization and mortality were visualized using cumulative incidence curves with their according 95% confidence intervals. The cumulative incidence based on Kaplan–Meier estimates does not reflect the competing risk of death and the occurrence of revascularization and therefore overestimate the remaining lifetime risk of revascularization when the competing risk is high.\(^1\) To account for this overestimation, competing risk survival analysis was performed by means of nonparametric methods using the cumulative incidence competing risk method.\(^10\) Post-hoc subgroup analyses were performed according to whether revascularization had taken place before the SAVR procedure, age at time of SAVR (aged <65 or ≥65 years), history of hypercholesterolemia, history of diabetes mellitus, indication of SAVR (AS, aortic valve regurgitation, or combined disease), and type of implanted valve (mechanical or bioprosthetic). Competing risk survival analyses in subgroups were compared with the Fine and Gray test.\(^11\) Furthermore, the linearized rate of revascularization was calculated per 1000 patient-years of follow-up.

Predictors of revascularization after SAVR were identified in a Cox proportional hazards model. Significant variables on univariable analyses were included in a multivariable Cox proportional hazards model. Data analyses were performed using SPSS 24.0 (IBM Corp, Armonk, NY) and R software, version 3.4 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS
Baseline and Procedural Characteristics
From 4228 patients who underwent SAVR between 1987 and 2015, 420 patients underwent isolated SAVR and were followed up at the Erasmus MC and were included in this study (Figure 1). The mean age of the patients at the time of SAVR was 56.9 ± 15.5 years, and 66.9% (281/420) were male. The primary indication for SAVR was pure AS in 52.1% (219/420). A total of 8.6% (36/420) had previous revascularization. Mechanical valve prostheses were used in 66.7% (280/420). The rates of survival were 98.3%, 96.4%, 87.4%, 71.8%, 58.6%, and 47.4% at 30 days, and 1, 5, 10, 15, and 20 years of follow-up, respectively (Figure 2). Detailed baseline and procedural
characteristics are provided in Table 1. Patients excluded from our study were older (66.1 ± 11.1 vs 56.9 ± 15.5 years, \( P < .001 \)), had undergone more redo SAVR procedures (16.7% vs 4.3%, \( P < .001 \)), more often underwent SAVR with an urgent indication (4.0% vs 0.4%, \( P < .001 \)), and had less-frequent implantation of mechanical valve prosthesis (66.7% vs 48.0%, \( P < .001 \)) compared with the included patients. Further detailed characteristics of patients excluded from our study are provided in Table 2.

Revascularization After SAVR

The mean follow-up after SAVR was 17.2 years, with a total follow-up accumulating to 4541 patient-years. During follow-up, 24 patients underwent coronary revascularization, with 3 patients requiring a second and 1 patient requiring a third revascularization procedure. In the time-to-first event competing risk analysis with mortality, the rates of revascularization were 0.5%, 0.5%, 2.2%, 4.1%, 5.3%, and 6.9% at 30 days and 1, 5, 10, 15, and 20 years of follow-up, respectively (Figure 2). The mean time to the first revascularization was 8.9 ± 7.4 (range 0-26.9 years). The linearized rate of revascularization was 6.2 per 1000 patient-years.

Characteristics of Revascularization

More patients underwent PCI than CABG, accounting for 64.2% of revascularization procedures (n = 18/28). Three patients (12.5%) needed urgent revascularization due to acute myocardial infarction (treated with PCI in all cases). Single-vessel disease was present in 16 patients (67%) and multivessel disease was present in 8 patients (33%). Four patients had lesions in both the left and right coronary artery. Characteristics of revascularization are displayed in Table 3.

Subgroup Analysis and Predictors of Revascularization After SAVR

The incidence of revascularization at 15 years of follow-up was significantly greater in patients with previous revascularization than in patients without previous revascularization (22.1% vs 3.7%, \( P < .001 \)), respectively. Further, the incidence of revascularization was greater in patients with hypercholesterolemia compared with patients without hypercholesterolemia (14.2% vs 4.1%, \( P = .002 \)), respectively. There were no differences in revascularization rates during follow-up in subgroups according to age (4.9% for patients aged <65 vs 5.9% for patients aged ≥65, \( P = .42 \)), diabetes mellitus (8.8% for patients with a history of diabetes mellitus vs 5.0% for no diabetes mellitus, \( P = .24 \)), primary indication for SAVR (5.6% for AS vs 7.9% for aortic valve regurgitation vs 2.2% for combined disease, \( P = .36 \)), or type of valve used (6.8% for biological vs 4.4% for mechanical, \( P = .16 \)) (Figures 3 and 4).

Factors Associated With Coronary Revascularization During Follow-up

Patients who underwent coronary revascularization during follow-up more often had hypercholesterolemia at baseline (8/24 vs 44/396, \( P = .001 \)) and undergone revascularization before the index procedure (7/24 vs 29/396, \( P = .36 \)) (Figures 3 and 4).
P < .001) than patients that did not undergo revascularization during follow-up (Table 1). In multivariable analyses, the presence of revascularization, hypercholesterolemia, and diabetes mellitus before the index procedure were the only independent predictor of revascularization during follow-up (Table 4).

DISCUSSION

In this cohort of 420 patients who underwent isolated SAVR, 24 (5.7%) patients underwent a total of 28 revascularization procedures. The cumulative incidence of revascularization was 6.9% at 20-year follow-up, with a linearized rate of 6.2 per 1000 patient-years. In the current study, concomitant CABG was generally performed in patients with significant coronary stenosis. The risk of requiring coronary intervention during follow-up after SAVR in patients with no significant coronary stenosis at the time of intervention appears to be low as 6.9% at 20-year follow-up (Figure 5).

The incidence of revascularization was greater than that of the general population. Subgroup analyses showed that patients who had undergone previous revascularization before SAVR and patients with a history of hypercholesterolemia had significantly greater rates of revascularization during follow-up. Clearly patients with already established CAD, but nonsignificant at the time of SAVR, carry a risk of progression of CAD to a severity requiring intervention. Other risk factors of CAD, like hypertension and diabetes, were not associated with revascularization in our multivariable analysis, although this may be the result of a relatively low sample size in our study.

Of the patients who underwent revascularization, 16 patients had single-vessel disease and 8 patients 2-vessel disease. There were no patients with left main or 3-vessel disease. Considering the current guidelines for revascularization, the majority of patients would be referred for PCI on the basis of the complexity of coronary disease. Eight patients with more complex coronary disease underwent CABG during follow-up.

These data are important in the era of expanding indications for TAVR. Recently, 2 randomized controlled trials showed significant benefit of TAVR compared with SAVR in the low-risk population. Revascularization with PCI after TAVR can be associated with multiple technical challenges related to transcatheter heart valve
| TABLE 1. Baseline and procedural characteristics | All patients (n = 420) | No revascularization (n = 396) | Revascularization (n = 24) | P value |
|-----------------------------------------------|------------------------|-------------------------------|---------------------------|---------|
| Age, y                                        | 56.9 ± 15.5 (420)      | 56.8 ± 15.7 (396)             | 58.5 ± 11.6 (24)          | .592    |
| Male sex                                      | 66.9 (281/420)         | 67.2 (266/396)                | 62.5 (15/24)              | .637    |
| Primary indication                            |                        |                               |                           |         |
| AS                                           | 52.1 (219/420)         | 52.3 (207/396)                | 50.0 (12/24)              | .590    |
| AR                                           | 25.5 (107/420)         | 25.5 (101/396)                | 25.0 (6/24)               |         |
| Combined AS + AR                             | 22.4 (94/420)          | 22.2 (88/396)                 | 25.0 (6/24)               | .900    |
| Bicuspid aortic valve                        | 24.0 (101/420)         | 24.0 (95/396)                 | 25.0 (6/24)               |         |
| Previous cardiac operation                   | 28.6 (120/420)         | 28.8 (114/396)                | 25.0 (6/24)               | .690    |
| SAVR                                         | 16.7 (70/420)          | 16.7 (66/396)                 | 16.7 (4/24)               | .990    |
| CABG                                         | 2.6 (11/420)           | 2.3 (9/396)                   | 8.3 (2/24)                | .071    |
| Other                                        | 9.3 (39/420)           | 9.3 (39/396)                  | 0                         | .107    |
| Hypertension                                 | 29.8 (125/420)         | 29.8 (118/396)                | 29.2 (7/24)               | .948    |
| Hypercholesterolemia                         | 12.4 (52/420)          | 11.1 (44/396)                 | 33.3 (8/24)               | .001    |
| Diabetes mellitus                            | 9.3 (39/420)           | 8.8 (35/396)                  | 16.7 (4/24)               | .199    |
| Arterial disease                              | 3.6 (15/420)           | 3.3 (13/396)                  | 8.3 (2/24)                | .195    |
| Periphera                                     | 3.6 (15/420)           | 3.3 (13/396)                  | 8.3 (2/24)                | .195    |
| Carotid                                      | 0.5 (2/420)            | 0.5 (2/396)                   | 0                         | .727    |
| Renal failure                                 | 2.6 (11/420)           | 2.5 (10/420)                  | 4.2 (1/24)                | .625    |
| Previous myocardial infarction               | 4.3 (18/420)           | 4.0 (16/396)                  | 8.3 (2/24)                | .313    |
| Previous revascularization                   | 8.6 (36/420)           | 7.3 (29/396)                  | 29.2 (7/24)               | <.001   |
| Previous PCI                                  | 6.4 (27/420)           | 5.6 (22/396)                  | 20.8 (5/24)               | .003    |
| Previous CABG                                 | 2.6 (11/420)           | 2.3 (9/396)                   | 8.3 (2/24)                | .071    |
| Previous decompensated heart failure         | 16.9 (71/420)          | 16.4 (65/396)                 | 25.0 (6/24)               | .276    |
| Left ventricular function                    |                        |                               |                           | .460    |
| Preserved                                    | 77.6 (287/370)         | 77.6 (273/370)                | 77.8 (14/18)              |         |
| Mildly reduced                               | 7.6 (28/370)           | 8.0 (28/370)                  | 0                         |         |
| Moderately reduced                           | 9.2 (34/370)           | 8.8 (31/370)                  | 16.7 (3/18)               |         |
| Severely reduced                             | 5.7 (21/370)           | 5.7 (20/370)                  | 5.6 (1/18)                |         |
| Atrial fibrillation                          | 13.3 (56/420)          | 13.4 (53/396)                 | 12.5 (3/24)               | .902    |
| Previous neurologic event                    | 10.5 (44/420)          | 11.1 (44/396)                 | 0                         | .084    |
| CVA                                          | 4.8 (20/420)           | 5.1 (20/396)                  | 0                         | .259    |
| TIA                                          | 7.1 (30/420)           | 7.6 (30/396)                  | 0                         | .162    |
| COPD                                         | 8.3 (35/420)           | 8.3 (33/396)                  | 8.3 (2/24)                | >.999   |
| Liver disease                                | 1.4 (64/420)           | 1.5 (6/396)                   | 0                         | .544    |
| History of malignancy                        | 8.1 (34/420)           | 8.1 (32/396)                  | 8.3 (2/24)                | .965    |
| Urgency                                      |                        |                               |                           | .610    |
| Elective                                     | 49.3 (173/351)         | 49.4 (165/334)                | 47.1 (8/17)               |         |
| Semi-elective                                | 46.7 (164/351)         | 46.7 (156/334)                | 47.1 (8/17)               |         |
| Urgent                                       | 4.0 (14/351)           | 3.9 (13/334)                  | 5.9 (1/17)                |         |
| Logistic EuroSCORE                           | 5.7 ± 6.2 (204)        | 5.5 ± 6.1 (193)               | 8.8 ± 7.3 (11)            | .085    |
| Mechanical prosthesis                        | 66.7 (280/420)         | 66.7 (264/396)                | 66.7 (16/24)              | >.999   |
| Year of operation                            |                        |                               |                           | .383    |
| 1987-1994                                    | 24.5 (103/420)         | 23.7 (94/396)                 | 37.5 (9/24)               |         |
| 1995-2001                                    | 23.3 (98/420)          | 24.0 (95/396)                 | 12.5 (3/24)               |         |
| 2002-2008                                    | 26.7 (112/420)         | 26.8 (106/396)                | 25.0 (6/24)               |         |
| 2009-2015                                    | 25.5 (107/420)         | 25.5 (101/396)                | 25.0 (6/24)               |         |

Data are presented as % (n/N) and mean ± standard deviation or median (interquartile range). AS, Aortic valve stenosis; AR, aortic regurgitation; SAVR, surgical aortic valve replacement; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; CVA, cerebrovascular accident; TIA, transient ischemic attack; COPD, chronic obstructive pulmonary disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation.
|                          | Patient followed-up in Erasmus MC | Patient not followed-up in Erasmus MC | P value |
|--------------------------|-----------------------------------|----------------------------------------|---------|
| Age, y                   | 56.9 ± 15.5 (420)                 | 66.1 ± 11.1 (1782)                     | <.001   |
| Male sex                 | 66.9 (281/420)                    | 57.4 (1023/1782)                       | <.001   |
| Primary indication       |                                   |                                        |         |
| AS                       | 52.1 (219/420)                    | 69.8 (1243/1782)                       | <.001   |
| AR                       | 25.5 (107/420)                    | 12.7 (226/1782)                        | <.001   |
| Combined AS + AR         | 22.4 (94/420)                     | 17.3 (308/1782)                        | .015    |
| Bicuspid aortic valve    | 24.0 (101/420)                    | 19.2 (343/1782)                        | .027    |
| Previous cardiac operation |                                   |                                        |         |
| SAVR                     | 28.6 (120/420)                    | 8.6 (154/1782)                         | <.001   |
| CABG                     | 16.7 (70/420)                     | 4.3 (76/1782)                          | <.001   |
| Other                    | 2.6 (11/420)                      | 3.7 (66/1782)                          | .276    |
| Hypertension             | 29.8 (125/420)                    | 34.3 (612/1782)                        | .073    |
| Hypercholesterolemia     | 12.4 (52/420)                     | 14.8 (264/1782)                        | .201    |
| Diabetes mellitus        | 9.3 (39/420)                      | 12.2 (218/1782)                        | .091    |
| Arterial disease         | 3.6 (15/420)                      | 2.6 (47/1782)                          | .298    |
| Peripheral               | 3.6 (15/420)                      | 2.4 (42/1782)                          | .159    |
| Carotid                  | 0.5 (2/420)                       | 0.3 (5/1782)                           | .522    |
| Renal failure            | 2.6 (11/420)                      | 2.3 (33/1782)                          | .312    |
| Previous myocardial infarction | 4.3 (18/420)                     | 5.6 (99/1782)                          | .297    |
| Previous revascularization |                                   |                                        |         |
| Previous PCI             | 8.6 (36/420)                      | 7.8 (139/1782)                         | .599    |
| Previous CABG            | 6.4 (27/420)                      | 5.1 (90/1782)                          | .257    |
| Previous decompensated heart failure | 2.6 (11/420)                     | 3.7 (66/1782)                          | .276    |
| Left ventricular function |                                   |                                        |         |
| Preserved                | 77.6 (287/370)                    | 82.5 (1348/1633)                       | .026    |
| Mildly reduced           | 7.6 (28/370)                      | 6.3 (103/1633)                         | .376    |
| Moderately reduced       | 9.2 (34/370)                      | 8.3 (136/1633)                         | .592    |
| Severely reduced         | 5.7 (21/370)                      | 2.8 (46/1633)                          | .006    |
| Atrial fibrillation      | 13.3 (56/420)                     | 13.5 (241/1782)                        | .918    |
| Previous neurologic event |                                   |                                        |         |
| CVA                      | 10.5 (44/420)                     | 8.0 (142/1782)                         | .096    |
| TIA                      | 4.8 (20/420)                      | 3.5 (62/1782)                          | .212    |
| COPD                     | 7.1 (30/420)                      | 5.1 (91/1782)                          | .099    |
| Liver disease            | 1.4 (6/420)                       | 0.2 (4/1782)                           | .001    |
| History of malignancy    | 8.1 (34/420)                      | 6.1 (109/1782)                         | .139    |
| Urgency                  |                                   |                                        |         |
| Elective                 | 49.3 (173/351)                    | 62.0 (975/1573)                        | <.001   |
| Semi-elective            | 46.7 (164/351)                    | 37.6 (591/1573)                        | .001    |
| Urgent                   | 4.0 (14/351)                      | 0.4 (7/1573)                           | <.001   |
| Logistic EuroSCORE       | 5.7 ± 6.2 (204)                   | 5.8 ± 5.8 (970)                        | .740    |
| Mechanical prosthesis    | 66.7 (280/420)                    | 48.0 (855/1782)                        | <.001   |
| Year of operation        |                                   |                                        |         |
| 1987-1994                | 24.5 (103/420)                    | 16.3 (290/1782)                        | <.001   |
| 1995-2001                | 23.3 (98/420)                     | 25.4 (452/1782)                        | .387    |
| 2002-2008                | 26.7 (112/420)                    | 28.2 (502/1782)                        | .536    |
| 2009-2015                | 25.5 (107/420)                    | 30.2 (538/1782)                        | .056    |

Data are presented as % (n/N) and mean ± standard deviation or median (interquartile range). AS, Aortic valve stenosis; AR, aortic regurgitation; SAVR, surgical aortic valve replacement; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; CVA, cerebrovascular accident; TIA, transient ischemic attack; COPD, chronic obstructive pulmonary disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation.
### TABLE 3. Characteristics of revascularization after SA VR

| Patient # | Date of SAVR | Previous revascularization before SAVR | Subsequent revascularization(s) |
|-----------|--------------|----------------------------------------|-------------------------------|
| #1        | June 25, 1987 | June 1, 1995 Elective OM, IM PCI | September 11, 1995 PCI |
| #2        | August 12, 1987 | December 20, 2007 Elective OM, PD CABG SVG-OM-PD | |
| #3        | May 18, 1988 | June 24, 2003 Elective LAD CABG SVG-LAD | |
| #4        | June 3, 1988 | November 21, 2003 Elective RCA PCI | |
| #5        | September 1, 1988 | August 4, 2015 Elective LAD, LCx PCI | |
| #6        | March 21, 1989 | November 4, 1994 Elective RCA PCI | January 29, 2001, and September 12, 2001 CABG and CABG |
| #7        | July 25, 1990 | March 29, 1993 Elective LAD CABG LIMA-LAD | |
| #8        | October 7, 1993 | September 27, 2004 Elective LAD PCI | August 27, 2012 PCI |
| #9        | November 9, 1993 | March 10, 2015 Elective LAD, RCA PCI | |
| #10       | July 1, 1998 | August 3, 2012 Elective CABG SVG-RCA | |
| #11       | August 7, 1998 | June 30, 2015 Urgent LAD, RCA PCI | |
| #12       | June 2, 2001 | July 4, 2014 Elective LAD CABG LIMA-LAD | |
| #13       | November 28, 2002 | September 3, 2009 Elective LAD, IM, OM CABG SVG-IM-OM LIMA-LAD | |
| #14       | January 31, 2003 | December 6, 2005 Elective RCA PCI | October 30, 2002 PCI |
| #15       | December 20, 2004 | October 26, 2010 Elective OM PCI | |
| #16       | June 28, 2006 | May 2, 2014 Urgent SVG PCI | May 2, 2000 CABG |
| #17       | October 31, 2008 | December 7, 2012 Elective RCA PCI | January 19, 2004 PCI |
| #18       | November 4, 2008 | August 27, 2012 Elective RCA PCI | September 27, 2004 PCI |
| #19       | May 13, 2009 | December 31, 2015 Elective LAD, LCx PCI | May 20, 2003 PCI |
| #20       | December 2, 2011 | January 9, 2013 Elective OM PCI | November 4, 2011 PCI |
| #21       | April 27, 2012 | February 5, 2015 Urgent LAD PCI | July 17, 1997 CABG |
| #22       | October 5, 2012 | March 11, 2015 Elective LAD CABG LIMA-LAD | (Continued) |
## TABLE 3. Continued

| Patient | Date of SAVR | Date of SA VR | Urgency | Lesion | Modality | Details | Date | Modality | Details | Date | Modality |
|---------|--------------|---------------|---------|--------|----------|---------|------|----------|---------|------|----------|
| #23    | May 2, 2013  | May 2, 2013   | Elective | PD     | CABG     | SVG-PD  |      |          |         |      |          |
| #24    | October 18, 2013 | October 24, 2013 | Elective | LCx    | PCI      |         |      |          |         |      |          |

SAVR, Surgical aortic valve replacement; OM, obtuse marginal artery; IM, intermediate artery; PCI, percutaneous coronary intervention; PD, posterior descending artery; SVG, saphenous vein graft; LAD, left anterior descending artery; RCA, right coronary artery; LCx, left circumflex artery; CABG, coronary artery bypass grafting; LIMA, left internal mammary artery.

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![Graph A](image1.png)

**A**

Numbers at risk
- Previous revascularization: 36
- No previous revascularization: 384

Cumulative incidence (%) for revascularization after SAVR in various patient subgroups.

Follow-up (years)
- 0
- 1
- 5
- 10
- 15

Cumulative incidence (%) vs Follow-up (years)
- Previous revascularization: 5.9%
- No previous revascularization: 4.9%

**B**

Numbers at risk
- Age ≥ 65: 152
- Age < 65: 268

Cumulative incidence (%) for revascularization after SAVR in various patient subgroups.

Follow-up (years)
- 0
- 1
- 5
- 10
- 15

Cumulative incidence (%) vs Follow-up (years)
- Age ≥ 65: 14.2%
- Age < 65: 4.1%

**C**

Numbers at risk
- Hypercholesterolemia: 52
- No hypercholesterolemia: 368

Cumulative incidence (%) for revascularization after SAVR in various patient subgroups.

Follow-up (years)
- 0
- 1
- 5
- 10
- 15

Cumulative incidence (%) vs Follow-up (years)
- Hypercholesterolemia: 22.1%
- No hypercholesterolemia: 3.7%

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**FIGURE 3.** Revascularization after SAVR in various patient subgroups. Competing risk cumulative incidences of revascularization after SAVR in subgroups according to the following: (A) with and without previous revascularization. Blue line shows patients with no history of revascularization. Red line shows patients with a history of revascularization. (B) Age at SAVR younger or older than 65 years. Blue line shows patients aged 65 or older. Red line shows patients aged younger than 65 years. (C) With and without a history of hypercholesterolemia. Blue line shows patients with history of hypercholesterolemia. Red line shows patients without a history of hypercholesterolemia.
platform, coronary access, with potential consequences of (1) damaging the prosthetic heart valve, (2) dissecting the coronary artery, (3) acute kidney injury related to increased contrast usage, and (4) an unsuccessful procedure. Because CAD is present in 40% to 75% of patients undergoing TAVR, algorithms on obtaining coronary access have already been developed from experiences during concomitant or staged TAVR and PCI procedures. The presence of CAD in the younger population undergoing TAVR is not well known, as studies mostly consist of elderly patients. Therefore, this study is the first to systematically assess the long-term rate of revascularization after aortic valve intervention in low-risk patients without CAD. Although our population consists exclusively of

![Graph](image-url)
isolated SAVR procedures, it provides evidence on rates of revascularization that may be extrapolated to an overall TAVR population of low- to high-risk patients. Yet, literature also suggests that a proportion of patients might benefit from revascularization in the setting of acute coronary syndrome post-TAVR, and therefore greater incidences of revascularization could be expected in patients who initially would have been treated with medical

### TABLE 4. Predictors of revascularization after SAVR

| Characteristics                      | Univariable HR (95% CI); P value | Multivariable HR (95% CI); P value |
|--------------------------------------|----------------------------------|---------------------------------|
| Age                                  | 1.0 (1.0-1.1); P = .16           |                                 |
| Sex (female)                         | 1.5 (0.6-3.4); P = .55           |                                 |
| Indication AS                        | 1.1 (0.5-2.5); P = .79           |                                 |
| Indication AR                        | 1.1 (0.4-2.7); P = .90           |                                 |
| Indication AS + AR                   | 0.8 (0.3-2.1); P = .68           |                                 |
| Hypertension                         | 1.2 (0.5-2.9); P = .68           |                                 |
| Hypercholesterolemia                 | 5.0 (2.1-11.7); P < .001         | 3.4 (1.3-8.6); P = .010         |
| Diabetes mellitus                    | 3.2 (1.1-9.7); P = .037          | 2.1 (0.7-6.5); P = .214         |
| Arterial disease                     | 3.7 (0.9-15.9); P = .08          |                                 |
| Renal failure                        | 3.9 (0.5-29.1); P = .19          |                                 |
| Previous MI                          | 2.7 (0.6-11.7); P = .17          |                                 |
| Previous revascularization           | 8.2 (3.3-20.2); P < .001         | 6.6 (2.6-17.1); P < .001        |
| Decompensated heart failure         | 1.8 (0.7-4.6); P = .20           |                                 |
| LVEF <50%                            | 1.2 (0.4-3.6); P = .76           |                                 |
| Atrial fibrillation                  | 1.0 (0.3-3.4); P = .97           |                                 |
| Previous stroke or TIA               | 0.0 (0.0-18.5); P = .31          |                                 |
| COPD                                 | 1.7 (0.4-7.3); P = .49           |                                 |
| Urgent SAVR vs non-urgent            | 1.6 (0.2-12.2); P = .64          |                                 |
| Log EuroSCORE                        | 1.1 (1.0-1.1); P = .078          |                                 |
| Mechanical prosthesis                | 0.5 (0.2-1.3); P = .18           |                                 |

HR, Hazard ratio; CI, confidence interval; AS, aortic valve stenosis; AR, aortic regurgitation; MI, myocardial infarction; LVEF, left ventricular ejection fraction; TIA, transient ischemic attack; COPD, chronic obstructive pulmonary disease; SAVR, surgical aortic valve replacement; EuroSCORE, European System for Cardiac Operative Risk Evaluation.
therapy, when TAVR will expand toward the younger population. Of note, the mean age of our population was 57 years old as opposed to the current TAVR population with an advanced age, but a subgroup analysis according to age showed that the long-term rate of revascularization was comparable in patients younger or older or equal to 65 years. Expanding indication to lower-risk patients may have consequences for valve choice, given the younger age, and considering that coronary access is more challenging with a supra-annular TAVR than an intra-annular TAVR.7

Limitations
This is a retrospective study that has inherent shortcomings related to data collection, changes in definitions of comorbidities, and patients being lost to follow-up. However, we included only patients who were followed after SAVR at our own outpatient clinic to minimize this risk. The multivariable analyses to identify predictors of revascularization may have been underpowered due to the small number of patients that needed a revascularization procedure and the unavailability of all known risk factors for coronary artery disease. Furthermore, although the decision was made not to include patients undergoing SAVR with concomitant CABG in this cohort, we did not have any information on the presence and degree of nonsignificant CAD that may increase the risk of coronary revascularization during follow-up as a result of progression of disease. CONCLUSIONS

In this retrospective analysis of patients who underwent isolated SAVR, the rate of requiring coronary revascularization at 20-year follow-up was relatively low. However, the rate was greater in patients who had undergone previous revascularization at the time of SAVR. These data provide some insights into requirements for coronary revascularization that may be relevant for the TAVR population. Future, larger studies are required on surgical and transcatheter cohorts to provide more insights into which patients are at particular risk of requiring coronary revascularization after aortic valve intervention.

Conflict of Interest Statement
Dr van Mieghem has received institutional research grant support from Boston Scientific, Medtronic, and Abbott and is an advisor to Medtronic and Boston Scientific. Dr Head is an employee of Medtronic, plc. Prof Kappetein is also an employee of Medtronic, plc. All other authors reported no conflicts of interest.

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