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Comparison of a Complete Percutaneous versus Surgical Approach to Aortic Valve Replacement and Revascularization in Patients at Intermediate Surgical Risk: Results from the Randomized SURTAVI Trial

Running Title: *Søndergaard et al.; Transcatheter vs Surgical AVR and Revascularization*

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Abstract

Background: For patients with severe aortic stenosis (AS) and coronary artery disease (CAD), the completely percutaneous approach to aortic valve replacement and revascularization has not been compared to the standard surgical approach.
Methods: The prospective SURTAVI trial enrolled intermediate-risk patients with severe AS from 87 centers in the United States, Canada, and Europe between June 2012 and June 2016. Complex coronary artery disease with SYNTAX score >22 was an exclusion criterion. Patients were stratified according to need for revascularization and then randomized to treatment with transcatheter aortic valve replacement (TAVR) or surgical aortic valve replacement (SAVR). Patients assigned to revascularization in the TAVR group underwent percutaneous coronary intervention (PCI), while those in the SAVR group had coronary artery bypass grafting (CABG). The primary endpoint was the rate of all-cause mortality or disabling stroke at two years.
Results: Of 1,660 subjects with attempted aortic valve implants, 332 (20%) were assigned to revascularization. They had a higher STS risk score for mortality (4.8±1.7% vs 4.4±1.5%; p<0.01) and were more likely to be male (65.1% vs 54.2%; p<0.01) than the 1,328 patients not assigned to revascularization. After randomization to treatment, there were 169 TAVR and PCI patients, 163 SAVR and CABG patients, 695 TAVR patients, and 633 SAVR patients. No significant difference in the rate of the primary endpoint was found between TAVR and PCI and SAVR and CABG (16.0%; 95% CI 11.1 – 22.9 vs. 14.0%; 95% CI 9.2 – 21.1; p=0.62), or between TAVR and SAVR (11.9%; 95% CI 9.5 – 14.7 vs. 12.3%; 95% CI 9.8 – 15.4; p=0.76).
Conclusions: For patients at intermediate surgical risk with severe AS and non-complex CAD (SYNTAX score ≤ 22), a complete percutaneous approach of TAVR and PCI is a reasonable alternative to SAVR and CABG.
Clinical Trial Registration: URL: www.clinicaltrials.gov Unique Identifier: NCT01586910

Key Words: Aortic valve stenosis; coronary artery disease; TAVR; SAVR; revascularization

Non-Standard Abbreviations and Acronyms
AS = aortic stenosis
CABG = coronary artery bypass graft
CAD = coronary artery disease
mITT = modified intent to treat
PCI = percutaneous coronary intervention
SAVR = surgical aortic valve replacement
TAVR = transcatheter aortic valve replacement
VARC = Valvular academic research consortium

Clinical Perspective

What is new?

- This sub-analysis from SURTAVI was the first to compare outcomes of TAVR and PCI to SAVR and CABG for intermediate risk patients with severe aortic stenosis and non-complex coronary artery disease within the context of a randomized clinical trial.
- We provide clinical evidence that TAVR and PCI produces similar outcomes to SAVR and CABG in this patient population.

What are the clinical implications?

- As physicians design a treatment strategy for severe AS patients presenting with coronary artery disease, the completely percutaneous approach of TAVR and PCI may be a good alternative to open surgery.

Introduction

Transcatheter aortic valve replacement (TAVR) has during the last decade matured as a treatment option for patients with symptomatic severe aortic stenosis (AS). Compared to surgical aortic valve replacement (SAVR), TAVR has been proven to be non-inferior with regards to mortality and disabling stroke in five randomized trials which studied patients across the spectrum of risk[1–5]. Most of these trials excluded patients requiring revascularization, but significant coronary artery disease (CAD) is a typical comorbidity in severe AS patients[6]. Registry data confirms that for patients undergoing TAVR in real-world practice, approximately half present with CAD, and over 20% have a history of coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI)[7–9].

For patients that require both aortic valve replacement and revascularization, the guideline-recommended treatment is SAVR and CABG[10,11]. However, because of the favorable outcomes following isolated TAVR, a fully percutaneous approach consisting of TAVR and PCI has become an attractive alternative. Currently there are no randomized studies which compare these treatments and demonstrate that the percutaneous approach is non-inferior to the surgical approach. As TAVR expands to patients for which surgery is a lower-risk treatment option, the management strategy for patients needing aortic valve replacement and revascularization should be based on robust clinical evidence.

The SURTAVI trial stratified intermediate surgical risk patients with severe AS according to need for revascularization and then randomized the patients to treatment with TAVR or SAVR. Patients with complex lesions including multi-vessel coronary artery disease with a SYNTAX score >22 were excluded from the trial. The present analysis compared the safety and efficacy outcomes of TAVR and PCI to SAVR and CABG through two years of

follow-up. In addition, for patients having undergone percutaneous treatment, the outcomes of staged procedures (where PCI was performed separately in the days prior to TAVR) were compared to those of concomitant TAVR and PCI.

Methods

The data, analytic methods, and study materials are owned by the sponsor and will not be made available to other researchers for purposes of reproducing the results or replicating the procedure,

Patients

The prospective SURTAVI trial (NCT01586910, www.clinicaltrials.gov) enrolled 1,746 intermediate-risk patients with severe AS from 87 centers in the United States, Canada, and Europe between June 19, 2012 and June 30, 2016. The design, endpoint definitions, and primary endpoint results using a Bayesian analysis have been previously reported[4]. Severe AS was defined as an aortic valve area ≤1.0 cm^2 or aortic valve index <0.6 cm^2/m^2 and either a mean aortic valve gradient >40 mm Hg or a peak aortic valve velocity >4.0 meters per second, at rest or during a dobutamine stress test[4]. Patients were classified as intermediate risk if they had an estimated risk of 30-day mortality between 3% and 15% per heart team discussion, based on the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) and other factors including comorbidity, frailty, or disability. The STS-PROM scores were calculated for AVR/CABG among the patients needing revascularization. The trial complied with the Declaration of Helsinki, all local ethics committees approved the research protocol and written informed consent was obtained from all patients.

Screening and patient flow

Candidates underwent systematic screening tests including risk, frailty, and disability

assessment, multi-slice computed tomography to determine anatomic suitability for TAVR, two-dimensional transthoracic echocardiography to confirm the diagnosis of severe AS, and coronary angiography to diagnose CAD. Those with multivessel coronary artery disease having a SYNTAX score >22 and / or an unprotected left coronary artery were not considered for the trial. Local multidisciplinary Heart Teams comprised of at least one interventional cardiologist and one cardiac surgeon identified eligible patients and considered revascularization for those demonstrating at least 70% stenosis in at least one major coronary artery. They were then presented to the SURTAVI screening committee for the final enrollment decision. Patients were stratified by center and the need for revascularization, and then were randomized one to one to treatment with either TAVR or SAVR. Revascularization for patients assigned to SAVR was accomplished through concomitant CABG. The revascularization strategy for TAVR patients was decided by the local Heart Team. Concomitant PCI was encouraged, however if it was anticipated to require extra time or significantly more contrast media, a staged approach with PCI occurring at least seven days prior to TAVR was allowed. The selection of bare metal or drug eluting stent was at the discretion of the operator, as was the post-procedure antithrombotic medication regimen.

Endpoints

The primary endpoint for this analysis was the rate of all-cause mortality or disabling stroke at two years. Other important clinical outcomes at two years, including the individual components of the primary endpoint, all strokes, life-threatening or disabling bleeding, myocardial infarction, and atrial fibrillation were compared for percutaneous and surgical approaches using the modified intention-to-treat (mITT) population, which includes patients who had undergone randomization and an attempted procedure. Comparisons between procedure-related outcomes

for staged and concomitant TAVR + PCI were made using the as-treated population. Events were adjudicated by an independent clinical events committee using Valvular Academic Research Consortium-2 (VARC-2) criteria or other standardized definitions described in the trial protocol[4,12]. All patients were seen by a neurologist or trained stroke specialist, and neurologic events were adjudicated by a neurologist on the clinical events committee.

Statistical analysis

Categorical variables were compared using the chi squared or Fisher's exact test, where appropriate. Continuous variables were presented as mean ± standard deviation and compared using the Student's *t* test or Wilcoxon Rank-Sum test, where appropriate. Ordinal variables were compared using the Mantel-Haenszel test. Kaplan-Meier estimates were used to construct the all-cause mortality or disabling stroke curves for the time-to-event analysis and comparisons between groups were done using the log-rank test. Event rates for non-fatal endpoints were estimated using the cumulative incidence function with death as the competing risk. The cumulative incidence functions were compared between groups using Gray's test. All testing used a 2-sided alpha level of 0.05. Statistical analyses were performed with the use of SAS software, version 9.4 (SAS Institute, Cary, NC).

Role of the funding source

The SURTAVI trial was funded by Medtronic (Mounds View, MN, USA). The trial executive committee designed the protocol in conjunction with the funder. The funder was responsible for selection of clinical sites, in collaboration with the executive committee, as well as collection, monitoring and analysis of the data. The manuscript was written by the lead author with substantial contributions from the executive committee and co-authors. The authors had unrestricted access to the data and take full responsibility for its integrity and the data analysis.

Results

The SURTAVI trial enrolled 1,746 intermediate-risk patients with severe AS from 87 centers in the United States, Canada, and Europe between June 2012 and June 2016. Of these enrolled patients, 1,660 were randomized and had an attempted aortic valve replacement procedure, thereby forming the mITT population (**Figure 1**). Revascularization was assigned to 332 patients, whereas 1,328 patients were not assigned revascularization. Operators changed the assigned treatment for 109 patients (6.6% of the total population) based on clinical judgment at the time of the scheduled procedure. These changes were captured as protocol deviations. A planned revascularization was cancelled in 68 patients, whereas revascularization was added to the procedure for 40 patients. A single patient was converted from SAVR to TAVR. As a result, the as-treated revascularization cohort had 304 patients, with 128 patients in the TAVR and PCI group and 176 patients in the SAVR and CABG group. The as-treated no revascularization cohort had 1,356 patients, with 737 patients in the TAVR group and 619 patients in the SAVR group.

Patients in the mITT population who were assigned to revascularization were more often male, had a higher mean STS score, a higher mean SYNTAX score, and more often reported angina at baseline relative to patients not requiring revascularization (**Table 1**). There were no differences in history of myocardial infarction or PCI between groups, however patients with prior CABG were less likely to have been assigned to revascularization. Coronary artery disease was ubiquitous in patients assigned to revascularization, and present in 54.7% of those not assigned to revascularization.

The pattern of CAD based on angiography was similar between TAVR and PCI and SAVR and CABG patients (**Table 2**). Most patients had multivessel disease involving territories

of the left anterior descending artery and the right coronary artery, with at least one of the lesions being more than 70% stenosed. Chronic total occlusions occurred in approximately 13% of patients in each group.

Procedural details for patients assigned to revascularization are reported in **Table 3**. Most patients had one-vessel revascularization. Those undergoing TAVR and PCI on average received 1.6±1.1 stents, the majority of which were drug eluting. The SAVR and CABG patients most often received saphenous vein grafts. Complete revascularization was achieved in 44.4% of TAVR and PCI patients and 51.5% of SAVR and CABG patients (p=0.19). Relative to SAVR and CABG, the TAVR and PCI procedure required less time, less intensive care, and resulted in shorter hospitalization. It also led to significantly more major vascular complications, as well as a higher need for new permanent pacemakers. The SAVR and CABG procedure led to a significantly higher rate of acute kidney injury and atrial fibrillation. Other early safety outcomes including all-cause mortality and stroke were similar between groups (**Table 4**).

Patients assigned to revascularization had a higher rate of all-cause mortality at 30 days and 2 years compared to those that did not (30 days: 3.9% vs. 1.4%; p<0.01; 2 years: 14.5% vs. 10.2%; p=0.02). The rate of disabling stroke was similar between groups at both time points (30 days: revascularization 1.8% vs. no revascularization 1.7%; 0.92; 2 years: revascularization 3.5% vs. no revascularization 2.9%; p=0.64). When these groups were analyzed according to percutaneous or surgical treatment modality, there was no significant difference in the rate of the primary endpoint between TAVR and PCI and SAVR and CABG (16.0% vs. 14.0%; p=0.62) (**Figure 2A**), or between TAVR and SAVR (11.9% vs. 12.3%; p=0.76) (**Figure 2B**). Other 2-year outcomes are summarized in **Table 5**. New-onset atrial fibrillation was more frequent in

patients treated surgically while the requirement for a new permanent pacemaker was higher in patients treated percutaneously.

Of the 128 patients that underwent TAVR and PCI, 76 (59.4%) were treated through a staged approach, while 52 (40.6%) were treated concomitantly. The median duration between PCI and TAVR in the 76 patients with a stage procedure was 6 days. The baseline characteristics were balanced between the groups except for angina, which was more commonly reported in patients treated through the staged approach (38.2 vs. 17.3%; p<0.01) (**Table 6**). The staged and concomitant strategies both resulted in a mean index hospital stay of 7±5 days, and similar duration of index intensive care unit stay (53±54 vs. 52±33 hours; p=0.91). More contrast media was used in patients having a staged procedure, and they also experienced significantly more acute kidney injury compared to patients treated concomitantly (11.8 vs. 2.0%; p=0.04). Other 30-day clinical outcomes were similar between the two treatment strategies (**Table 7**).

Discussion

The main findings of this pre-specified subgroup analysis of the SURTAVI trial can be summarized as follows: 1) intermediate-risk patients with severe, symptomatic AS have a different baseline clinical profile than patients with severe AS and non-complex CAD needing revascularization; 2) significantly higher rates of 30-day and 2-year all-cause mortality in patients assigned to revascularization may be reflective of these baseline differences; 3) for patients that were assigned to revascularization and aortic valve replacement, a fully percutaneous approach of TAVR and PCI produced similar safety and efficacy outcomes as the gold-standard SAVR and CABG; 4) concomitant TAVR and PCI had fewer complications and

more procedural efficiency relative to a staged approach where TAVR and PCI were separated by several days.

We demonstrated that patients with severe AS and CAD at intermediate risk for surgery who underwent both aortic valve replacement and revascularization had an overall worse prognosis than patients with severe AS and no need for revascularization. This finding is expected, given early reports from surgical series[13,14] and more recent reports from TAVR studies which have identified CAD as a predictor of mortality[15,16]. The German Aortic Valve Registry (GARY), an all-comers registry in which 85 German centers participate, recently showed that the rate of in-hospital mortality for 26,618 patients undergoing isolated SAVR between 2011 and 2015 was 1.7%[17]. The rate was significantly higher at 3.3% within a cohort of 16,158 patients undergoing SAVR and CABG during that same time-frame. As in SURTAVI, there were significant differences in baseline characteristics between the groups, including higher risk scores and more markers of atherosclerotic disease in the SAVR and CABG group. The GARY report also showed higher rates of sepsis, a higher requirement for blood transfusions, and longer hospital stay in the SAVR and CABG group which all point to more procedural complexity relative to isolated SAVR. Likewise, it is reasonable to assume that TAVR and PCI has higher inherent risk relative to TAVR alone. Isolated PCI has worse outcomes in certain elderly patients, such as those with poor renal function, reduced left ventricular function, peripheral arterial disease, or prior stroke[18–20]. In addition, coronary stenosis with anatomically difficult PCI targets is more prone to unsuccessful outcome, including restenosis or stent thrombosis[21]. On the other hand, revascularization status may not affect clinical endpoints in elderly TAVR patients[22]. Therefore, it is unclear whether differences in outcome between TAVR patients with and without CAD are attributable to the more atherosclerotic burden *per se*

or to inadequate revascularization. In an Israeli study of more than 1,200 patients, those with severe CAD had increased mortality post-TAVR over a 1.9-year follow-up period when compared to those with less-than-severe coronary atherosclerosis[23]. This is in accordance with these present data.

Current guidelines recommend surgical aortic valve replacement and concomitant CABG for patients with symptomatic, severe aortic stenosis and significant coronary artery disease[10,11]. This gold-standard treatment is associated with excellent outcomes, especially for patients at lower surgical risk. The report from GARY stratified the SAVR and CABG cohort according to risk, and for the 4,044 patients in the intermediate category, the in-hospital rate of mortality was 5·4%, disabling stroke was 2.4%, and need for new pacemaker or ICD was 4.6%[17]. This serves as a real-world benchmark by which the SURTAVI data can be compared. In the as-treated SAVR and CABG patient population, the 30-day mortality rate was 2.3%, disabling stroke was 2.3%, and need for new pacemaker was 6.3%, all in line with or slightly better than the GARY results. Of note, in both surgical and catheter-based cohorts of SURTAVI complete revascularization was achieved in approximately half of the patients. Incomplete revascularization did not impact outcome in a contemporary cohort elderly TAVR patients[22]. Whether this also holds for younger patients at lower risk and with longer life expectancy is unsettled. Our trial was conducted with rigorous inclusion and exclusion criteria, in a smaller number of patients with non-complex CAD, and in highly experienced centers, all of which could have contributed to the better outcomes. These data set a very high standard for the randomized comparator of TAVR and PCI. Other groups have demonstrated similar outcomes between these percutaneous and surgical strategies through propensity-matched analyses[24], but SURTAVI is the first trial to compare SAVR and CABG to TAVR and PCI within a randomized

trial and show that the two strategies result in similar rates of all-cause mortality or disabling stroke at two years.

There is no clear consensus as to whether PCI and TAVR should be performed concomitantly or through a staged approach. We showed that the staged approach resulted in a higher overall contrast load and significantly more acute kidney injury relative to a concomitant procedure. Importantly, patients were not randomized to staged or concomitant treatment, but instead the decision was left to the operators. Though there were no differences in baseline characteristics between the two groups except for angina, there could be unmeasured confounders upon which operators based their decisions, thus biasing the results. Randomized studies are needed to provide confirmation that the concomitant strategy leads to better outcomes.

Our study has limitations. First, the diagnosis of bystander CAD was based on angiography. Non-invasive or invasive ischemia tests were not performed. Therefore, the true burden of ischemia may be overestimated. Second, SYNTAX score was low, and the data therefore do not allow for extrapolation of outcomes to patients with more advanced CAD. Third, SURTAVI was not designed to show whether revascularization should be performed in patients with severe AS and non-complex CAD, as there was no control group of patients eligible for revascularization in which this procedure was deliberately not performed. SURTAVI was instead designed to test whether a percutaneous treatment strategy is safe and effective for these patients. Lastly, repeat revascularizations performed at an institution separate from the original clinical site are not captured thus we cannot provide an accurate rate of post-procedure revascularizations.

In conclusion, the present sub-study of the SURTAVI trial showed that for patients at intermediate surgical risk with severe AS and moderate CAD (SYNTAX score ≤ 22), a complete percutaneous approach of TAVR and percutaneous coronary intervention is a reasonable alternative to SAVR and coronary artery bypass grafting.

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Table 1. Baseline characteristics of the modified intention-to-treat population

Characteristic Mean ± SD (N) or % (n/N)	**Assigned to Revascularization (N=332)**	**Not Assigned to Revascularization (N=1328)**	**P**
Age (years)	79.5 ± 5.9 (332)	79.9 ± 6.2 (1328)	0.33
Male	65.1% (216/332)	54.2% (720/1328)	<0.01
STS-PROM (%)	4.8 ± 1.7 (332)	4.4 ± 1.5 (1328)	<0.01
New York Heart Association class			0.97
I	0.0% (0/332)	0.0% (0/1328)	
II	39.2% (130/332)	41.2% (547/1328)	
III	57.2% (190/332)	52.2% (693/1328)	
IV	3.6% (12/332)	6.6% (88/1328)	
Meters walked in 6 minutes	268.0 ± 120.4 (297)	254.6 ± 115.8 (1195)	0.08
Diabetes	35.8% (119/332)	34.1% (453/1328)	0.55
Renal dysfunction			0.76
None / mild	55.4% (184/332)	53.8% (715/1328)	
Moderate	41.3% (137/332)	44.2% (587/1328)	
Severe	3.3% (11/332)	2.0% (26/1328)	
Coronary artery disease	97.9% (325/332)	54.7% (727/1328)	<0.01
SYNTAX score	8.3 ± 5.6 (332)	2.7 ± 4.7 (1328)	<0.01
Number of diseased vessels			<0.01
0	2.4% (8/332)	49.5% (658/1328)	
1	39.5% (131/332)	18.4% (244/1328)	
2	35.5% (118/332)	12.6% (167/1328)	
3	17.2% (57/332)	14.4% (191/1328)	
>3	5.4% (18/332)	5.1% (68/1328)	
Subjects with at least one lesion >70% stenosed	67.5% (224/332)	22.0% (292/1328)	<0.01
Cerebrovascular disease	21.4% (71/332)	15.8% (210/1328)	0.02
Prior stroke	9.3% (31/332)	6.3% (83/1328)	0.05
Peripheral vascular disease	31.3% (104/332)	30.1% (400/1328)	0.67
Prior CABG	9.6% (32/332)	18.1% (241/1328)	<0.01
Prior PCI	18.7% (62/332)	21.9% (291/1328)	0.20
Prior myocardial infarction	16.6% (55/332)	13.6% (181/1328)	0.17
Angina	29.5% (98/332)	13.3% (176/1328)	<0.01
Congestive heart failure	97.3% (323/332)	95.6% (1270/1328)	0.17
Chronic lung/obstructive pulmonary disease	31.3% (104/332)	35.3% (468/1326)	0.17
History of arrhythmia	29.2% (97/332)	32.2% (428/1328)	0.29

SD: standard deviation; STS-PROM: Society of Thoracic Surgeons predicted risk of mortality; SYNTAX: SYNergy between PCI with TAXus and cardiac surgery trial; CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention

Table 2. Coronary artery anatomical characteristics for the modified intention-to-treat patients assigned to revascularization

Characteristic Mean ± SD or % (N)	**TAVR + PCI (N=169)**	**SAVR + CABG (N=163)**	**P**
SYNTAX score	8.1 ± 5.6 (169)	8.5 ± 5.6 (163)	0.45
Number of diseased vessels			0.35
0	3.0% (5/169)	1.8% (3/163)	
1	39.1% (66/169)	39.9% (65/163)	
2	39.6% (67/169)	31.3% (51/163)	
3	13.6% (23/169)	20.9% (34/163	
>3	4.7% (8/169)	6.1% (10/163)	
Subjects with at least one lesion >70% stenosed	67.5% (114/169)	67.5% (110/163)	>0.99
Chronic total occlusions*	13.6% (23/169)	12.3% (20/163)	0.72
Lesion location			
Left main	4.1% (7/169)	7.4% (12/163)	0.21
Left anterior descending	67.5% (114/169)	64.4% (105/163)	0.56
Left circumflex	40.8% (69/169)	44.2% (72/163)	0.54
Right coronary artery	54.4% (92/169)	63.8% (104/163)	0.08
Multivessel disease†	60.4% (102/169)	62.6% (102/163)	0.68

SD: standard deviation; TAVR: transcatheter aortic valve replacement; PCI: percutaneous coronary intervention; SAVR: surgical aortic valve replacement; CABG: coronary artery bypass grafting; SYNTAX: SYNergy between PCI with TAXus and cardiac surgery trial

*Defined as 100% stenosis; †Defined as any patient with stenosis in 2 or more locations

Table 3. Procedural outcomes for the modified intention-to-treat patients assigned to revascularization

Characteristic Mean ± SD or % (N)	**TAVR + PCI (N=169)**	**SAVR + CABG (N=163)**	**P**
Procedure time (minutes)	54.6 ± 34.3 (169)	239.7 ± 74.3 (163)	< 0.01
Length of hospital stay (days)	6.8 ± 5.4 (169)	10.4 ± 8.6 (163)	< 0.01
Time in intensive care (hours)	49.9 ± 43.4 (169)	75.9 ± 87.7 (163)	<0.01
Number of vessels treated			
0	0.8% (1/126)	0.0% (0/138)	
1	67.5% (85/126)	61.6% (85/138)	
2	23.0% (29/126)	29.7% (41/138)	
3	8.7% (11/126)	6.5% (9/138)	
>3	0.0% (0/126)	2.2% (3/138)	
Mean number	1.4 ± 0.7 (126)	1.5 ± 0.7 (138)	0.24
Complete revascularization	44.4% (75/169)	51.5% (84/163)	0.19
Number of stents placed	1.6 ± 1.1 (126)		
Type of stent			
Bare metal	4.8% (6/126)	NA	
Drug eluting	92.1% (116/126)	NA	
Type of graft			
LIMA	NA	48.6% (67/138)	
SVG	NA	72.5% (100/138)	
Other	NA	4.3% (6/138)	
Treated lesion location			
Left main	3.2% (4/126)	0.7% (1/138)	0.20
Left anterior descending	53.2% (67/126)	56.5% (78/138)	0.59
Left circumflex	28.6% (36/126)	33.3% (46/138)	0.40
Right coronary artery	42.9% (54/126)	47.1% (65/138)	0.49

SD: standard deviation; TAVR: transcatheter aortic valve replacement; PCI: percutaneous coronary intervention; SAVR: surgical aortic valve replacement; CABG: coronary artery bypass grafting

Table 4. Clinical outcomes at 30 days for the modified intention-to-treat patients assigned to revascularization

	TAVR + PCI (N=169)		**SAVR + CABG (N=163)**		**P**
	Events (n)	Cumulative KM Estimates (%)	Events (n)	Cumulative KM Estimates (%)	
All-cause mortality or disabling stroke	10	5.3%	9	4.9%	0.87
All-cause mortality	7	4.1%	6	3.7%	0.84
Stroke	6	3.6%	7	4.3%	0.72
Disabling stroke	3	1.8%	3	1.9%	0.97
Myocardial infarction	1	0.6%	3	1.9%	0.30
Life-threatening or disabling bleeding	12	7.1%	13	8.0%	0.75
Major bleeding	12	7.1%	4	2.5%	0.05
Major vascular complications	19	9.5%	1	0.6	<0.01
Acute kidney injury	12	7.1%	31	19.1%	<0.01
Stage 1	8	4.8%	20	12.3%	0.01
Stage 2	1	0.6%	5	3.1%	0.09
Stage 3	3	1.8%	6	3.7%	0.29
Pacemaker implant	38	22.7	9	5.6	<0.01
Atrial fibrillation	20	11.3%	72	41.3%	<0.01

KM: Kaplan-Meier; TAVR: transcatheter aortic valve replacement; SAVR: surgical aortic valve replacement; CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention

Table 5. Clinical outcomes at 2 years for the modified intention-to-treat population

	Assigned to Revascularization					Not Assigned to Revascularization				
	TAVR + PCI N=169		SAVR + CABG N=163			TAVR N=695		SAVR N=633		
	Events (n)	Event Rate Estimates (95% CI)	Events (n)	Event Rate Estimates (95% CI)	*P*	Events (n)	Event Rate Estimates (95% CI)	Events (n)	Event Rate Estimates (95% CI)	*P*
All-cause mortality or disabling stroke*	31	16.0% (11.1-22.9)	28	14.0% (9.2-21.1)	0.62	87	11.9% (9.5-14.7)	84	12.3% (9.8-15.4)	0.76
All-cause mortality*	25	14.9% (10.1-21.6)	22	14.1% (9.3-21.2)	0.85	73	10.7% (8.5-13.5)	58	9.6% (7.3-12.4)	0.51
Disabling stroke	6	3.6% (1.5-7.2)	6	3.1% (1.2-6.8)	0.83	14	1.9% (1.1-3.1)	26	4.0% (2.7-5.8)	0.02
All stroke	14	7.7% (4.3-12.4)	13	7.6% (4.1-12.5)	0.96	38	5.4% (3.9-7.2)	55	8.5% (6.5-10.9)	0.02
Life-threatening or disabling bleeding	19	9.5% (5.7-14.5)	20	11.8% (7.4-17.4)	0.50	61	8.0% (6.1-10.1)	47	7.3% (5.5-9.6)	0.69
Major bleeding	22	11.8% (7.5-17.2)	13	6.4% (3.3-11.0)	0.08	88	11.4% (9.2-14.0)	59	8.8% (6.7-11.2)	0.09
Myocardial infarction	6	3.6% (1.5-7.2)	4	2.5% (0.8-5.9)	0.60	16	2.3% (1.4-3.7)	12	2.0% (1.1-3.3)	0.64
Aortic valve re-intervention	6	2.4% (0.8-5.6)	1	0.6% (0.1-3.2)	0.20	16	2.3% (1.4-3.7)	3	0.5% (0.1-1.3)	<0.01
Aortic valve hospitalization	24	6.5% (3.5-11.0)	28	10.2% (6.1-15.5)	0.25	136	13.7% (11.3-16.4)	73	8.9% (6.8-11.3)	<0.01
Permanent pacemaker implant	46	28.9% (22.0-36.2)	13	8.9% (5.0-14.2)	<0.01	218	34.5% (30.8-38.3)	59	10.0% (7.7-12.6)	<0.01
Atrial fibrillation	42	18.4% (12.9-24.6)	84	43.0% (35.3-50.4)	<0.01	183	22.1% (19.1-25.3)	340	47.4% (43.5-51.3)	<0.01

*Percentages are Kaplan-Meier estimates and *P* values were calculated from log-rank tests in the intention-to-treat population. The remaining rows report cumulative incidence function estimates and P values from Grey's tests.

CI: confidence interval; TAVR: transcatheter aortic valve replacement; PCI: percutaneous coronary intervention; SAVR: surgical aortic valve replacement; CABG: coronary artery bypass grafting

Table 6. Baseline and procedural characteristics of the as-treated TAVR + PCI population

Characteristic Mean ± SD or % (N)	**Staged** **(N=76)**	**Concomitant** **(N=52)**	**P**
Age (years)	79.5 ± 5.7 (76)	80.7 ± 4.9 (52)	0.23
Male	59.2% (45/76)	71.2% (37/52)	0.17
STS-PROM (%)	4.8 ± 1.5 (76)	5.1 ± 1.8 (52)	0.28
SYNTAX score	8.8 ± 5.7 (76)	7.8 ± 5.3 (52)	0.31
Renal dysfunction			0·83
None / mild	60.5% (46/76)	57.7% (30/52)	
Moderate	35.5% (27/76)	40.4% (21/52)	
Severe	3.9% (3/76)	1.9% (1/52)	
Cerebrovascular disease	22.4% (17/76)	15.4% (8/52)	0.33
Peripheral vascular disease	30.3% (23/76)	36.5% (19/52)	0.46
Prior CABG	10.5% (8/76)	7.7% (4/52)	0.76
Prior PCI	15.8% (12/76)	21.2% (11/52)	0.44
Prior myocardial infarction	13.2% (10/76)	17.3% (9/52)	0.52
Angina	38.2% (29/76)	17.3% (9/52)	0.01
Congestive heart failure	96.1% (73/76)	98.1% (51/52)	0.65
History of arrhythmia	28.9% (22/76)	26.9% (14/52)	0.80
Number of vessels treated			
0	0.0% (0/76)	1.9% (1/52)	
1	64.5% (49/76)	73.1% (38/52)	
2	26.3% (20/76)	17.3% (9/52)	
3	9.2% (7/76)	7.7% (4/52)	
>3	0.0% (0/76)	0.0% (0/52)	
Mean number	1.4 ± 0.7 (76)	1.3 ± 0.6 (52)	0.24
Complete revascularization	56.6% (43/76)	51.9% (27/52)	0.60
Number of stents placed	1.7 ± 1.2 (76)	1.5 ± 0.9 (52)	0.22
Type of stent			
Bare metal	3.9% (3/76)	5.8% (3/52)	0.69
Drug eluting	92.1% (70/76)	92.3% (48/52)	>0.99
Treated lesion location			
Left main	3.9% (3/76)	3.8% (2/52)	>0.99
Left anterior descending	50.0% (38/76)	55.8% (29/52)	0.52
Left circumflex	36.8% (28/76)	15.4% (8/52)	0.01
Right coronary artery	42.1% (32/76)	44.2% (23/52)	0.81
Contrast used (cc)	308.1 ± 161.0 (70)	217.2 ± 104.6 (51)	<0.01

SD: standard deviation; STS-PROM: Society of Thoracic Surgeons predicted risk of mortality; SYNTAX: SYNergy between PCI with TAXus and cardiac surgery trial; CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention

Table 7. Clinical outcomes at 30 days for the as-treated TAVR + PCI population

	Staged TAVR + PCI (N=76)		**Concomitant TAVR + PCI (N=52)**		**P**
	Events (n)	Cumulative KM Estimates (%)	Events (n)	Cumulative KM Estimates (%)	
All-cause mortality or disabling stroke	6	7.9%	3	3.8%	0.35
All-cause mortality	4	5.3%	2	3.8%	0.71
Stroke	2	2.6%	2	3.8%	0.71
Disabling stroke	2	2.6%	1	1.9%	0.80
Myocardial infarction	0	0.0%	1	1.9%	0.23
Life-threatening or disabling bleeding	5	6.6%	4	7.7%	0.82
Major bleeding	5	6.6%	4	7.7%	0.81
Major vascular complications	11	10.5%	4	7.7%	0.58
Acute kidney injury	9	11.8%	1	2.0%	0.04
Stage 1	6	7.9%	1	2.0%	0.15
Stage 2	1	1.3%	0	0.0%	0.41
Stage 3	2	2.6%	0	0.0%	0.24

KM: Kaplan-Meier; TAVR: transcatheter aortic valve replacement; PCI: percutaneous coronary intervention

Figure Legends

Figure 1. Randomization and patient flow

Figure 2. Cumulative incidence of all-cause mortality or disabling stroke at 2 years for A) patients assigned to revascularization and B) patients not assigned to revascularization in the modified intention-to-treat population