Valvular Heart Disease

One-Year Outcomes of Cohort 1 in the Edwards SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry

The European Registry of Transcatheter Aortic Valve Implantation Using the Edwards SAPIEN Valve

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Background—Transcatheter aortic valve implantation was developed to provide a therapeutic option for patients considered to be ineligible for, and to mitigate mortality and morbidity associated with, high-risk surgical aortic valve replacement.

Methods and Results—The Edwards SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry was designed to assess initial post commercial clinical transcatheter aortic valve implantation results of the Edwards SAPIEN valve in consecutive patients in Europe. Cohort 1 consists of 1038 patients enrolled at 32 centers. One-year outcomes are presented. Patients with the transapical approach (n=575) suffered more comorbidities than transfemoral patients (n=463) with a significantly higher logistic EuroSCORE (29% versus 25.8%; *P*=0.007). These groups are different; therefore, outcomes cannot be directly compared. Total Kaplan Meier 1-year survival was 76.1% overall, 72.1% for transapical and 81.1% for transfemoral patients, and 73.5% of surviving patients were in New York Heart Association (NYHA) class I or II at 1 year. Combined transapical and transfemoral causes of death were cardiac in 25.1%, noncardiac in 49.2%, and unknown in 25.7%. Pulmonary complications (23.9%), renal failure (12.5%), cancer (11.4%), and stroke (10.2%) were the most frequent noncardiac causes of death. Multivariable analysis identified logistic EuroSCORE, renal disease, liver disease, and smoking as variables with the highest hazard ratios for 1-year mortality whereas carotid artery stenosis, hyperlipidemia, and hypertension were associated with lower mortality.

Conclusion—The SOURCE Registry is the largest consecutively enrolled registry for transcatheter aortic valve implantation procedures. It demonstrates that with new transcatheter aortic techniques excellent 1-year survival in high-risk and inoperable patients is achievable and provides a benchmark against which future transcatheter aortic valve implantation cohorts and devices can be measured. (***Circulation***. 2011;124:425-433.)

Key Words: aortic valve stenosis ■ heart valve prosthesis implantation ■ registries

The Edwards SAPIEN valve was approved for commercial use in the European Union; the transfemoral (TF) delivery in August 2007 and transapical (TA) delivery in January 2008. One-year results of small controlled feasibility trials[1] and single-center experience[1–3] using this device have been reported previously. However, midterm outcomes of larger series of patients are still outstanding.

The Edwards SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry was created to obtain clinical data involving the Edwards SAPIEN valve during the first years of commercial activity in Europe. The background of the registry, as well as the 30-day results of Cohort 1, have been described previously.[4,5] We now present the 1-year outcomes of this cohort.

Methods

Since May 2009, further data collection has occurred, which allows us to present 100% of the procedural data, 99.9% of the 30-day data, and 98% of the 1-year outcomes. This is higher than the previously published report where 98% of 30-day outcomes were reported,

which resulted in minor variations of the baseline demographic data compared with the previous publication.[4]

Events and values collected are site reported, and there are no core laboratories. The principal investigators (M.R.T., O.W.) reviewed and adjudicated all clinical and adverse events reported into the Medidata RAVE electronic database (Medidata Solutions Inc, New York, NY). No functional assessment of the Edwards SAPIEN valve has been reviewed for this manuscript. The devices implanted during this time were the SAPIEN Transcatheter Heart Valve sizes 23 mm and 26 mm requiring 22F and 24F introducer sheaths for the TF approach and 26F introducer sheaths for the TA approach (Edwards Lifesciences LLC, Irvine, CA).

Statistical Analysis

Continuous variables are presented as mean±SD and were compared between groups using the Student *t* test. Categorical variables are provided as frequencies and percentages and were compared using the Fisher exact test. Univariable factors were binary, with the exception of scaled Logistic EuroSCORE.

Survival analysis is performed by Kaplan–Meier (KM), with patients being censored as of the last date known alive. Proportional hazards regression was used to analyze the impact of covariates. The Harrell overall c index was used to measure how well the model fits against data, with an index approaching 1 giving the best fit. The complete range of data was included in these analyses; both death dates and follow-up dates past the exact 1-year point were included. For the analysis of the relationship between EuroSCORE and survival a pairwise comparison of each stratum was also performed using a Bonferroni adjusted log-rank test.

Proportional hazards regression models were constructed using an automated iterative forward selection/backward elimination algorithm (the selection=stepwise option in SAS), with thresholds of $P=0.05$ for both entry into and removal from the model. The overall model is then compared with each inclusion of additional variables. Unlike forward selection regression, if a previously selected variable, on inclusion of additional variables, is shown not to add value to the overall model, the variable is excluded.

Although TA and TF patients appear to be different, some pooled analyses are presented. These are valid only to the extent that the TA/TF distribution in the SOURCE Registry is reflective of future clinical practice. A *P* value <0.05 was considered statistically significant. All statistical analysis was performed using SAS, version 9.1 or higher (SAS Institute Inc, Cary, NC). The principal investigators had full access to and take responsibility for the integrity of the data presented in the article. All authors have read and agree to the manuscript as written.

Results

Demographic and Baseline Characteristics

Cohort 1 comprises 463 TF patients and 575 TA patients. Baseline demographics and risk factors are shown in Table 1. Although gender distribution and presence of pulmonary disease were similar for both populations, statistically significant differences were observed with respect to age, renal dysfunction, peripheral vascular disease, carotid artery stenosis >50%, incidence of coronary artery disease, porcelain aorta, prior coronary artery bypass grafting and mitral valve disease. In addition, the difference in logistic EuroSCORE (25.8% for the TF and 29.1% for the TA group; $P=0.0007$) is an indication that the TA cohort represents a higher-risk population. Therefore, these groups are considered different and outcomes cannot be directly compared.

One-Year Survival

The 1-year KM survival curves for the entire patient cohort and the TA and TF cohorts are shown in Figure 1. The 1-year

Table 1. Baseline Demographics and Risk Factors

	TF (n=463)	TA (n=575)	P
Age, mean (SD), y	81.7 (6.7)	80.7 (7.0)	0.02
Female, n (%)	255 (55.1)	321 (55.8)	0.08
Pulmonary disease, n (%)	114 (24.6)	172 (29.9)	0.06
Renal insufficiency/failure, n (%)	118 (25.5)	187 (32.5)	0.02
Logistic EuroSCORE, mean (SD), %	25.8 (14.4)	29.1 (16.2)	0.0007
Peripheral vascular disease, n (%)	49 (10.6)	161 (28.0)	<0.0001
Carotid artery stenosis (>50%), n (%)	33 (7.1)	99 (17.2)	<0.0001
Coronary artery disease, n (%)	220 (47.5)	317 (55.1)	0.02
Porcelain aorta, n (%)	21 (4.5)	65 (11.3)	0.0001
Prior CABG, n (%)	81 (17.5)	155 (27.0)	0.0003
Mitral valve disease, n (%)	73 (15.8)	184 (32.0)	<0.0001
Mitral valvuloplasty, n (%)	2 (0.4)	4 (0.7)	0.70
Liver disease, n (%)	13 (2.8)	18 (3.1)	0.86
Hyperlipidemia/hypercholesterolemia, n (%)	222 (48.0)	306 (53.2)	0.09
Other cardiovascular conditions, n (%)	43 (9.3)	89 (15.5)	0.004
Noncardiovascular conditions: none, n (%)	145 (31.3)	96 (16.7)	<0.0001
Cardiomyopathy, n (%)	10 (2.2)	10 (1.7)	0.66
PTCA/stent, n (%)	105 (22.7)	154 (26.8)	0.13
Systemic hypertension, n (%)	291 (62.9)	388 (67.5)	0.13
Smoking, n (%)	74 (16.0)	134 (23.3)	0.004
Coagulopathy, n (%)	6 (1.3)	7 (1.2)	1.00
NYHA class IV (yes/no), n (%)	68 (14.7)	78 (13.6)	0.65

TF indicates transfemoral; TA, transapical; CABG, coronary artery bypass grafting; PTCA, percutaneous transluminal coronary angioplasty; and NYHA, New York Heart Association. Percentages are based on the No. of nonmissing values available.

KM survival for the entire cohort was 76.1%, 72.1% in TA patients and 81.1% in TF patients.

Relationship Between EuroSCORE and Survival

The relationship between logistic EuroSCORE and 1-year survival after transcatheter aortic valve implantation (TAVI) was examined. The results are displayed in Figure 2A and 2B. In the TA patients, 170 (29.6%) had a logistic EuroSCORE of <20, 285 (49.6%) had a logistic EuroSCORE of between 20 and 40, and 119 (20.7%) had a logistic EuroSCORE of ≥40. In the TF patients, 170 (36.7%) had a logistic EuroSCORE of <20, 225 (48.6%) had a logistic EuroSCORE of between 20 and 40, and 66 (14.3%) a logistic EuroSCORE of >40. Survival in patients with a logistic EuroSCORE of <20 was similar for the TA and TF patients (78.4% for TA and 80.9% for TF).

Causes of Death Between 30 Days and 1 Year

There were 179 patients who died between 30 days and 1 year. The causes of death in these patients are shown in Figure 3. Only 25.1% (45/179) of the deaths were definitely
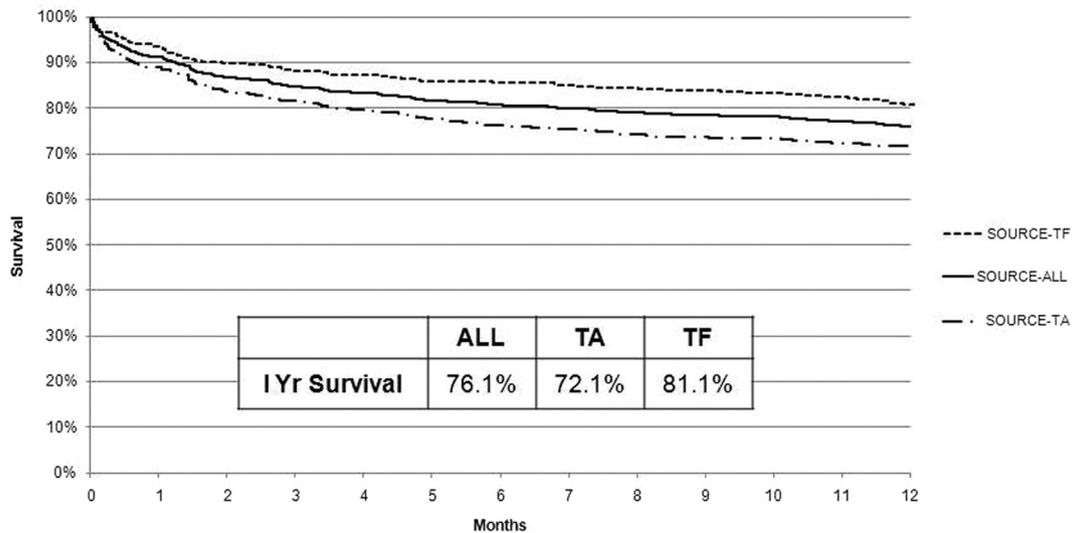
Figure 1. Kaplan–Meier 1-year survival curves. Yr indicates year; TA, transapical; and TF, transfemoral.

cardiac in nature, with heart failure being the most common cause (62.2%) within this group. Almost half of the deaths (49.2%, 88/179) were noncardiac in origin, with the 4 most common causes being pulmonary disease (23.9%, 21/88), renal failure (12.5%, 11/88), cancer (11.4%, 10/88), and stroke (10.2%, 9/88)). The cause of death was unknown in 25.7% (46/179) of the patients.

Univariable and Multivariable Analysis of 1-Year Mortality

Univariable Analysis
Univariable analysis was performed to assess associations between preprocedural risk factors and 1-year mortality. The results of risk factors that were statistically significant are displayed in Tables 2 and 3. For TA, the most statistically important risk factor was the logistic EuroSCORE ($P<0.0001$, hazard ratio [HR]=1.21 associated with a 10% increase in EuroSCORE). However, those with the highest HRs were renal insufficiency/failure (HR=1.72, $P=0.0005$) liver disease (HR=2.52, $P=0.005$), and cardiomyopathy (HR 2.43, $P=0.03$). Counterintuitively, the presence of a carotid artery stenosis of >50% appeared to be associated with a lower mortality (HR=0.55, $P=0.02$). For TF, the most statistically important factor was NYHA class IV symptoms (HR=2.42, $P=0.0002$). Other factors with high HRs were again renal insufficiency/failure (HR=2.09, $P=0.0005$) and liver disease (HR=2.69, $P=0.02$). Univariable factors in the TF patients with the lowest HRs and therefore associated with the lowest mortalities were hyperlipidemia (HR=0.51, $P=0.002$) and hypertension (HR=0.58, $P=0.008$).

Multivariable Analysis
Multivariable analysis results are shown in Tables 4 and 5. The logistic EuroSCORE was the most statistically important factor associated with higher mortality for TA ($P=0.0001$, HR=1.19 associated with a 10% increase in EuroSCORE). However, similar to the univariable analysis, the HRs were highest for liver disease (HR=2.89, $P=0.001$), renal insufficiency/failure (HR=1.44, $P=0.02$), and other cardiovascular condi-

tions (HR=1.47, $P=0.04$). The presence of a carotid artery stenosis continued to be associated with a lower mortality in the multivariable analysis (HR=0.48, $P=0.002$). For TF, statistically important factors associated with higher mortality were scaled logistic EuroSCORE (HR=1.19, $P=0.01$), renal insufficiency/failure (HR=2.09, $P=0.001$), smoking (HR=2.42, $P=0.0003$), and liver disease (HR=2.47, $P=0.04$). Hypertension (HR=0.53, $P=0.004$), hyperlipidemia (HR=0.61, $P=0.03$) and carotid artery stenosis (HR=0.07, $P=0.004$) continued to be associated with a lower 1-year mortality.

Relationship Between Perioperative Vascular Complications and Survival
Although major vascular access complications were less frequent in TA patients (2.1% versus 12.3%), at the 1-year time point there was a difference between vascular complications and the occurrence of 1-year mortality for both approaches (TF 1-year survival 83.9% without a vascular complication and 72.2% with a vascular complication; TA 1-year survival 73.2% without a vascular complication and 47.4% with a vascular complication) (Figure 4).

Freedom From Major Adverse Events (Stroke, Permanent Pacemaker, Myocardial Infarction, Vascular Complications, Endocarditis, and Reoperation) at 1 Year
One-year KM freedom from stroke (95.5%), myocardial infarction (98.6%), reoperation (97.0%), endocarditis (99.0%), and pacemaker implantation (91.5%) for the entire cohort was high. The events noted occurred after 30 days. There are no clinically relevant differences in the event rates for TA and TF patients.

Valve Performance and Function
The SOURCE Registry is a clinical registry and no systematic echocardiographic evaluation of valve function was required. No cases of aortic stenosis due to leaflet dysfunction were reported at 1 year. Three cases of increased aortic regurgitation (AR) were reported. One case of apparent movement of the valve at 3
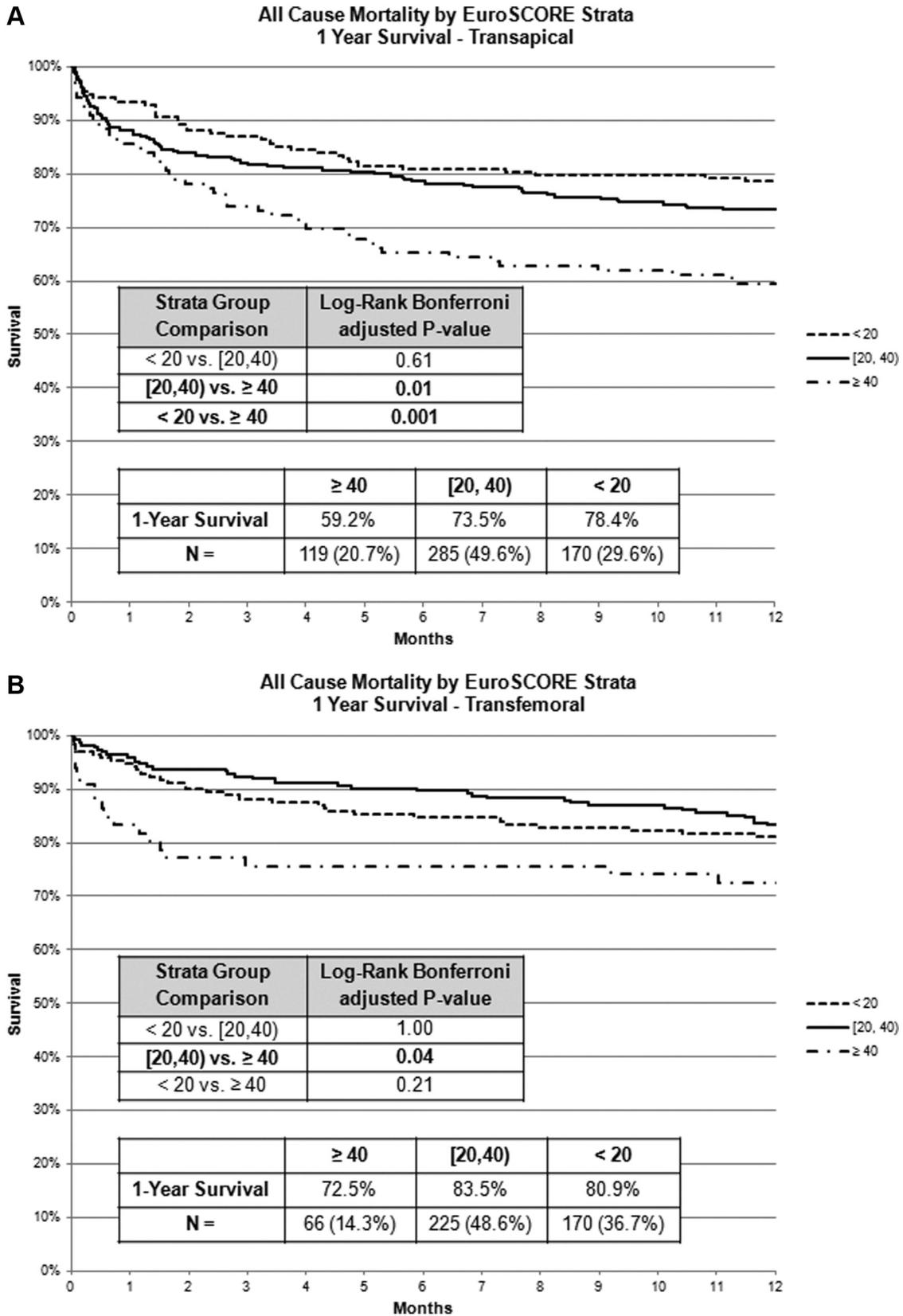
A

All Cause Mortality by EuroSCORE Strata
1 Year Survival - Transapical

Strata Group Comparison	Log-Rank Bonferroni adjusted P-value
< 20 vs. [20,40)	0.61
[20,40) vs. ≥ 40	0.01
< 20 vs. ≥ 40	0.001

	≥ 40	[20, 40)	< 20
1-Year Survival	59.2%	73.5%	78.4%
N =	119 (20.7%)	285 (49.6%)	170 (29.6%)

Legend: - - - - < 20 ; ——— [20, 40) ; - · - ≥ 40

B

All Cause Mortality by EuroSCORE Strata
1 Year Survival - Transfemoral

Strata Group Comparison	Log-Rank Bonferroni adjusted P-value
< 20 vs. [20,40)	1.00
[20,40) vs. ≥ 40	0.04
< 20 vs. ≥ 40	0.21

	≥ 40	[20,40)	< 20
1-Year Survival	72.5%	83.5%	80.9%
N =	66 (14.3%)	225 (48.6%)	170 (36.7%)

Legend: - - - - < 20 ; ——— [20, 40) ; - · - ≥ 40

Figure 2. A, Relationship between EuroSCORE and survival for TA group. **B**, Relationship between EuroSCORE and survival for TF group. Yr indicates year; TA, transapical; and TF, transfemoral.
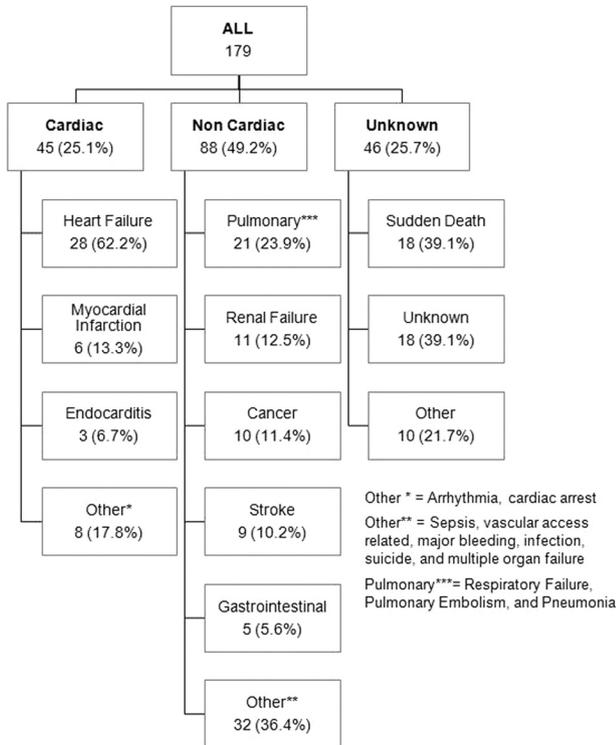
Figure 3. Causes of late deaths (30 days to 1 year; n=179/1038).

weeks in a patient with a previous surgical mitral valve replacement was reported, with upward movement and slanting/tilting resulting in important central and paravalvular leak.[6] In addition, 2 patients were reported as having increased central AR at 1 year as confirmed by echocardiogram.

Changes in Functional Status

Before receiving TAVI, 77.6% of TA patients and 76.3% of TF patients were in NYHA class III or IV. At 1-year follow-up, 69% of the surviving TA patients and 78.4% of the surviving TF patients were in NYHA functional class I or II.

Table 2.   Univariable Analysis for Transapical TAVI (Variables That Have a *P* Value <0.05 and/or Are Factors in Multivariable Analysis Are Displayed)

Variable	*P*	HR	95% Confidence Limits	
Scaled logistic EuroSCORE (%/10)	<0.0001	1.21	1.11	1.32
Renal insufficiency/failure	0.0005	1.72	1.27	2.34
EuroSCORE ≥30	0.0008	1.69	1.24	2.28
Liver disease	0.005	2.52	1.33	4.80
Other cardiovascular conditions	0.005	1.69	1.17	2.43
Noncardiovascular conditions: none	0.01	0.54	0.33	0.87
Carotid artery stenosis (>50%)	0.02	0.55	0.34	0.90
Coronary artery disease	0.02	1.45	1.06	1.98
EuroSCORE ≥20	0.02	1.53	1.06	2.20
Cardiomyopathy	0.03	2.43	1.07	5.50
PTCA/stent	0.05	1.39	1.00	1.91

TAVI indicates transcatheter aortic valve implantation; HR, hazard ratio; and PTCA, percutaneous transluminal coronary angioplasty.

Table 3.   Univariable Analysis for Transfemoral TAVI (Variables That Have a *P* Value <0.05 and/or Are Factors in Multivariable Analysis Are Displayed)

Variable	*P*	HR	95% Confidence Limits	
NYHA class IV (yes/no)	0.0002	2.42	1.53	3.84
Renal insufficiency/failure	0.0005	2.09	1.38	3.17
Noncardiovascular conditions: none	0.001	0.40	0.23	0.70
Hyperlipidemia/hypercholesterolemia	0.002	0.51	0.33	0.78
Systemic hypertension	0.008	0.58	0.39	0.87
Mitral valvuloplasty	0.008	6.70	1.65	27.24
Smoking	0.01	1.86	1.16	2.98
Scaled logistic EuroSCORE (%/10)	0.01	1.18	1.03	1.34
Liver disease	0.02	2.69	1.17	6.15
Carotid artery stenosis (>50%)	0.04	0.13	0.02	0.90
Coagulopathy	0.10	2.63	0.83	8.31

TAVI indicates transcatheter aortic valve implantation; HR, hazard ratio; and NYHA, New York Heart Association.

Discussion

For nearly 50 years, surgical aortic valve replacement was the gold standard for treatment of patients with aortic stenosis.[7] Because of encouraging early results from various centers and registries, TAVI is increasingly seen as an alternative treatment in high-risk patients.[8–10] Currently, no randomized data have been published on how TAVI compares with surgical aortic valve replacement or on the comparison of the TA versus the TF approach.

The SOURCE Registry was created to gather outcome data on the Edwards SAPIEN bioprosthesis, for both the TF and TA approaches, during the early phase of commercialization of the product in Europe. The aim was to create a robust data set that could be used to assess procedural results in the real world, document 1-year outcomes, and potentially predict outcomes in terms of a TAVI risk score. Thirty-day results were published previously.[4,5]

The SOURCE Registry is the largest series of consecutively implanted TAVI patients with 1-year clinical outcomes. The 1-year survival for Cohort 1 patients in the SOURCE Registry is >76%. In the patients treated with the TF approach, the survival is >80%. Transapical patients have

Table 4.   Multivariable Analysis: Variables Associated With Mortality for Transapical TAVI

Parameter	*P*	HR	95% Confidence Limits	
Scaled logistic EuroSCORE (%/10)	0.0001	1.19	1.09	1.30
Liver disease	0.001	2.89	1.51	5.53
Renal insufficiency/failure	0.02	1.44	1.05	1.98
Carotid artery stenosis (>50%)	0.002	0.48	0.30	0.76
Other cardiovascular conditions	0.04	1.47	1.02	2.11

c-index=0.6576.

TAVI indicates transcatheter aortic valve implantation; HR, hazard ratio.

Table 5. Multivariable Analysis: Variables Associated With Mortality, Transfemoral TAVI

Parameter	P	HR	95% Confidence Limits	
Renal insufficiency/failure	0.001	2.09	1.34	3.26
Hyperlipidemia/hypercholesterolemia	0.03	0.61	0.39	0.95
Systemic hypertension	0.004	0.53	0.35	0.82
Smoking	0.0003	2.42	1.51	3.90
Scaled logistic EuroSCORE (%/10)	0.01	1.19	1.04	1.36
Liver disease	0.04	2.47	1.04	5.85
Carotid artery stenosis (>50%)	0.004	0.07	0.01	0.43
Coagulopathy	0.009	5.09	1.49	17.39

c-index=0.7062.

TAVI indicates transcatheter aortic valive implantation; HR, hazard ratio.

a 1-year survival of >70%, which represents a significant improvement compared with previously reported early multicenter monitored results.[11] In addition, in a comparable risk group of patients defined by a logistic EuroSCORE <20, 1-year survival in TA patients is not different from that of the TF patients. Surviving patients had an important improvement in functional status. Before receiving TAVI, the majority of TA patients were in NYHA class III or IV (77.6%) whereas at 1 year 69% of the surviving TA patients were in NYHA I or II. Similarly, 76% of TF patients were in functional class III or IV before receiving TAVI, and in the surviving TF patients at 1 year 78.4% were in functional class I or II.

Prior Edwards Lifesciences Transcatheter Heart Valve clinical studies include Registry of EndoVascular Implantation of Valves in Europe (REVIVE), TRanscatheter EndoVascular Implantation of VALves (REVIVAL), The initial multicenter feasibility trial for TA-AVI (TRAVERCE), and Placement of AoRtic TraNscathetER Valves trial in Europe (PARTNER EU).

This data set, when pooled, includes 281 TA patients and 222 TF patients recruited between January 2006 and January 2008.[11,12] (S. Kodali, MD, unpublished data, 2008). The KM 1-year survival curves for these historical pooled TA and TF patients were 58.1% and 74.9%, respectively (M. Thomas, MD, unpublished data, 2010). The survival rates for TA of 72.1% and TF of 81.1% reported in the current study therefore compare favorably.

There are currently no randomized trial results comparing TAVI with high-risk surgery, which may provide these results a degree of context. Therefore, only reports from risk-adjusted outcomes in octogenarians who underwent surgical aortic valve replacement can be used for comparison. Leontyev et al[13] reported the results of surgical aortic valve replacement on octogenarians with varying EuroSCOREs. Patient groups were split into those with a logistic EuroSCORE of <10, 10 to 20, and >20 (which most closely resembles the TAVI population). The 30-day survival was similar in the 3 groups, ranging from 92.5% to 89.3%. However, the 1-year survival underwent a linear decline dependent on EuroSCORE, starting with a survival of 90% for those with a EuroSCORE of <10, to 78% for those with a EuroSCORE of 10 to 20, and 69% for those with a EuroSCORE of >20. This mortality pattern is similar to the TAVI patients in Cohort 1, making it likely that the late mortality during the first postoperative year is not explained by the procedure but by comorbidities. The overall 1-year survival of 76.1% for the TAVI patients in Cohort 1 is encouraging in this context, but a direct comparison is impossible.

Univariable and multivariable regression analysis was used to assess the association of preprocedural morbidities with 1-year outcomes (Tables 2 through 5). In the multivariable analysis, logistic EuroSCORE, renal failure, liver failure, and smoking were all associated with increased mortality. There are some factors that have statistically appeared to be associated with decreased 1-year mortality. These are the presence of a carotid stenosis, hypertension, and hyperlipidemia.

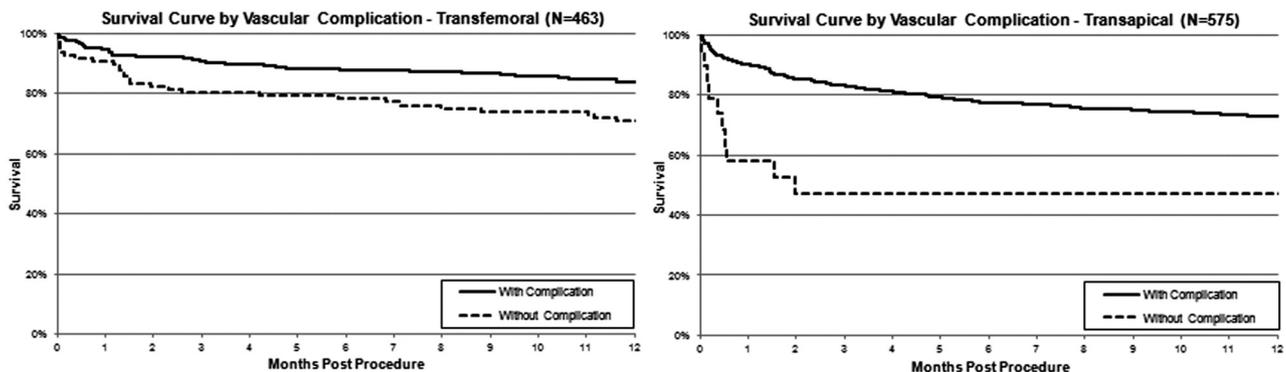| Approach	Estimated 1-Year Survival in Pts who did not have vascular access complications	Estimated 1-Year Survival in Pts who did have vascular access complications	P-Value
Transfemoral	83.9%	72.2%	0.01
Transapical	73.2%	47.4%	0.02

Figure 4. Association between early vascular access complications and 1-year mortality. Pts indicates patients; TF, transfemoral; and TA, transapical.

This is initially counterintuitive, given that these factors are generally associated with diffuse multisite atherosclerosis. These findings could, of course, represent the play of chance, but it is interesting that these are comorbidities that require the intervention of medical therapy. The association between these medical therapies (eg, lipid-lowering agents and anti-hypertensive agents) and 1-year outcomes of TAVI merits further investigation.

The logistic EuroSCORE and Society of Thoracic Surgeons scores were established as a mortality risk assessment of open cardiac surgery. Unfortunately, their utility in TAVI is very much open to question,[14–16] resulting in an urgent need to produce a TAVI risk score that will have a similar utility for TAVI patients. This may take time to develop, and the task will likely involve the collection of data on thousands of TAVI patients, similar to the extensive data that generated the EuroSCORE algorithm (19 030 patients), the latest Society of Thoracic Surgeons cardiac surgery risk score for isolated aortic valve surgery (67 292 patients), and the original Society of Thoracic Surgeons score for coronary artery bypass grafting (80 881 patients).[17–19] Harmonization of data collection between various trials and registries, with standardized definitions of end points, such as those proposed by the Valvular Academic Research Consortium would be ideal.[20] Finally, these scores relate to outcomes at 30 days, which may not reflect the appropriate time frame of risk in this patient population, especially in terms of cost-effectiveness. The total SOURCE Registry (Cohort 1 and 2) consists of 2344 patients.(M. Thomas, MD, unpublished data, 2010). Accordingly, any potential risk score based on the SOURCE Registry must be viewed as tentative. Thus far, the c statistics for the receiver operator curves of various multivariable models for the entire cohort at 30 days (TF: c=0.70; TA: c=0.61) and the Harrell c-index for Cohort 1 at 1 year (TF: c=0.71; TA: c=0.66) have been disappointing for these very reasons.(M. Thomas, MD, unpublished data, 2010, and O. Wendler, MD, unpublished data, 2010, respectively). Frailty was not assessed in the SOURCE registry. Validated frailty scores are available,[21] and this type of data will be collected in future registries of the Edwards Transcatheter Heart Valve and is likely to be a key variable in a future TAVI risk score.

The difficulties of predicting 1-year mortality becomes evident with the analysis of causes of death between 30 days and 1 year in the current registry. Approximately a quarter (25.1%) of the deaths were definitively cardiac related, with the majority of deaths in this group due to heart failure (62.2%). This suggests that noncardiac comorbidities are an important determinant of survival at 1 year. The most important noncardiac causes were pulmonary disease, renal failure, cancer, and stroke. In addition, in this elderly population with multiple comorbidities it may be difficult to precisely determine the cause of death. The cause of death was unknown in 25% of this population. Sudden death (39.1%) was the primary causality attributed to unknown cause of death. Within the new Valvular Academic Research Consortium definitions,[20] these patients would be allocated to cardiac death. A number of these patients were "found dead in bed." Academically, it may

be appropriate to classify a 95-year-old who is found dead in bed as having a cardiac death, but the clinical relevance and relationship to the device and underlying aortic pathology is less clear.

The 30-day incidence of stroke of 2.5% and the KM freedom from stroke at 1 year of 95.5% demonstrate that the stroke event rate between 30 days and 1 year is low (n=19). Although preoperative risk factors for stroke were more important in the TA group, the incidence is not different between the TA and TF patients. Two recent studies by Kahlert[22] and Ghanem[23] detected new cerebral lesions in 73% to 84% (presumably embolic) of patients after TAVI. These were clinically silent in the overwhelming majority of cases, but this area merits further investigation. Importantly, of the 19 patients in the SOURCE Registry who had a stroke between 30 days and 1 year, 4 had a confirmed hemorrhagic stroke. Because the absolute duration and need for dual antiplatelet therapy in these elderly patients undergoing TAVI is unknown, careful attention should be given to any bleeding events so that the risk/benefit ratio of the antiplatelet therapy can be assessed.

The 3 patients with increased AR merit further comment. The patient with apparent movement of the prosthesis after implantation had a previous mitral valve replacement in situ.[6] This patient had mild AR documented post procedure but returned 3 weeks later with severe paravalvular AR and moderate valvular AR. The patient was converted to open surgical aortic valve replacement and unfortunately died on day 7 after a stroke. The exact sequence of events in this patient remains unclear but underlines the caution required in placing a transcatheter aortic heart valve in the presence of a previously surgically treated mitral valve. The cause of the increased AR in the other 2 patients is also unclear. The site reported that in both cases the prostheses were placed in a correct position. Both prostheses had a circular configuration in the echos performed postoperatively. No obvious morphological sign of leaflet damage was seen during echocardiography at 1-year-follow-up. Therefore, the mechanism of AR in these cases remains to be elucidated. Aortic regurgitation had increased in both patients (in one from non to mild to moderate; and in the other from trace to moderate AR). Both patients had clinically improved at 1-year follow-up, moving from NYHA III to II, and neither patient required further intervention.

The final question to be asked is, can these results be further improved? The SOURCE Registry data suggest that if the risk profile of the patients is reduced, the 1-year survival will be better. This will be achieved by refining what is acceptable in terms of comorbidities. The data also demonstrate that avoidance of vascular complications will influence the subsequent 1-year mortality. The newest Edwards TF and TA devices have a lower French profile, and the hope is that fewer vascular complications and further improvements in the 1-year mortality will be achieved.

Recently, the PARTNER US trial reported a large 1-year mortality advantage of TAVI compared with medical therapy in surgically inoperable aortic stenosis patients.[24] One-year survival in the TAVI arm was 69.3% compared with 49.3% in the medically treated arm (P<0.001). The SOURCE Registry

1-year survival of 76.1% is slightly better than in the PARTNER patients and may reflect the fact that the Euro-SCOREs were slightly lower in SOURCE than in the TAVI arm of PARTNER (25.8% versus 26.4%) and patients in the SOURCE Registry were not required to be a surgical turn-down. It is therefore possible that the actual risk of patients in the SOURCE Registry may be lower, although no direct comparisons can be made.

Limitations of the SOURCE Registry

The SOURCE Registry is a clinical registry and contains limited functional assessment of the Edwards SAPIEN valve. All adverse events were self-reported by the participating centers; no adjudication of adverse events via source documentation was assessed. However, review and adjudication of all serious adverse events and adverse events in the electronic database were performed by the principal investigators.

Conclusions

Kaplan–Meier 1-year survival for Cohort 1 from the SOURCE Registry shows an improvement compared with historical controls. Survival for the TF approach is now >80%. There has been an important improvement in the TA patients, with survival now similar to historical TF controls. Lower-risk patients have similar survival at 1 year for TF and TA. The SOURCE Registry data set may facilitate the development of a TAVI risk score, which should lead to improved patient selection for the procedure. This risk score and avoidance of vascular complications by lower-profile devices is expected to result in further improvements in 1-year survival. The 1-year results of Cohort 1 of the SOURCE Registry provides a benchmark against which future TAVI cohorts and new TAVI devices may be measured.

Disclosures

Drs Thomas and Wendler are the principal investigators for the SOURCE Registry and consultants to Edwards Lifesciences LLC. The Herzzentrum in Leipzig (Dr Walther's institution during the collection of these data) is an official Edwards training center. Drs Lefèvre, Himbert, and Eggebrecht are proctors for Edwards Lifesciences LLC. Dr Lefèvre is a principal investigator of the PARTNER EU study, and R. Schwarz is an employee of Edwards Lifesciences. The other authors report no conflicts.

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CLINICAL PERSPECTIVE

Cohort 1 of the Edwards SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry describes the outcomes at 30 days and 1 year of >1000 consecutive patients undergoing transcatheter aortic valve implantation using the Edwards SAPIEN valve. The 30-day results have previously been published and have established the procedural results of the technique in a large group of patients in a multicenter registry. The 1-year data describe the outcomes in the largest group of transcatheter aortic valve implantation patients at this time point. This combined data will allow the interventional community to adequately consent transcatheter aortic valve implantation patients on the basis of robust data and will also be a benchmark against which future patient groups and any new devices may be measured.

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One-Year Outcomes of Cohort 1 in the Edwards SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry: The European Registry of Transcatheter Aortic Valve Implantation Using the Edwards SAPIEN Valve

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