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Long-Term Outcomes After Transcatheter Aortic Valve Implantation in High-Risk Patients With Severe Aortic Stenosis

The U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry

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Objectives The objective was to define the characteristics of a real-world patient population treated with transcatheter aortic valve implantation (TAVI), regardless of technology or access route, and to evaluate their clinical outcome over the mid to long term.

Background Although a substantial body of data exists in relation to early clinical outcomes after TAVI, there are few data on outcomes beyond 1 year in any notable number of patients.

Methods The U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry was established to report outcomes of all TAVI procedures performed within the United Kingdom. Data were collected prospectively on 870 patients undergoing 877 TAVI procedures up until December 31, 2009. Mortality tracking was achieved in 100% of patients with mortality status reported as of December 2010.

Results Survival at 30 days was 92.9%, and it was 78.6% and 73.7% at 1 year and 2 years, respectively. There was a marked attrition in survival between 30 days and 1 year. In a univariate model, survival was significantly adversely affected by renal dysfunction, the presence of coronary artery disease, and a nontransfemoral approach; whereas left ventricular function (ejection fraction <30%), the presence of moderate/severe aortic regurgitation, and chronic obstructive pulmonary disease remained the only independent predictors of mortality in the multivariate model.

Conclusions Midterm to long-term survival after TAVI was encouraging in this high-risk patient population, although a substantial proportion of patients died within the first year. (J Am Coll Cardiol 2011;58:2130–8) © 2011 by the American College of Cardiology Foundation

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Symptomatic severe aortic stenosis carries a poor prognosis (1,2). Surgical aortic valve replacement (AVR) has, until recently, been the only effective treatment in adults with severe symptomatic aortic stenosis. For patients who are selected for isolated surgical aortic valve replacement the overall perioperative risk is low (3,4). However, the operative risk is increased for elderly patients, for patients with concomitant coronary artery disease or severely reduced left ventricular (LV) function and also for patients with comorbid conditions such as cerebral and peripheral vascular disease, renal failure, and respiratory dysfunction (3,4).

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Transcatheter aortic valve implantation (TAVI) was developed as an alternative to AVR in this high-risk patient population. The first implant in man was performed by Cribier (5) in 2002, using a balloon expandable frame and equine valve. Currently, 2 devices are under post-marketing surveillance in Europe: the balloon-expandable Edwards SAPIEN prosthesis (Edwards Lifesciences, Irvine, California) and the self-expandable CoreValve revalving prosthesis (Medtronic, Minneapolis, Minnesota). A substantial body of data now exists in relation to the early clinical outcomes after TAVI but there are few data on outcome beyond 1 year in any notable number of patients. A number of observational clinical studies demonstrated the feasibility (6,7) of TAVI leading its use as an alternative treatment in these patients (8–10). There are a number of reports that have emanated from post-marketing device specific and national registries (11–17). In general, these have been limited to selected centers, largely focused on 1 or another technology and usually have been dependent of industry funding. To date, none of these registries has reported significant numbers of patients with long-term follow-up.

Cohort B of the PARTNER (Placement of Aortic Transcatheter Valve) trial compared the outcome after TAVI compared with medical therapy in a very high risk patient population considered unsuitable for surgery (18). One-year survival and cardiac symptoms were significantly and markedly better in the TAVI arm, with only 5 patients needing to be treated to prevent 1 death at 12 months. There was, however, a higher incidence of stroke and major vascular complications. Cohort A of the PARTNER trial compared TAVI to AVR in a high-risk population in whom both therapies were considered clinically acceptable (19). This study showed noninferiority of TAVI to AVR for the primary endpoint of all cause 1-year mortality but an increased risk of stroke at 30 days and 1 year in the TAVI arm. This trial took place in tightly defined and highly selected patients in highly selected centers with a single technology (Edwards SAPIEN).

Abbreviations and Acronyms

AR = aortic regurgitation
AVR = aortic valve replacement
CAD = coronary artery disease
CCAD = Central Cardiac Audit Database
COPD = chronic obstructive pulmonary disease
LV = left ventricular
NYHA = New York Heart Association
TAVI = transcatheter aortic valve implantation

In 2007, as the first patients in the United Kingdom were being considered for TAVI, a national program was established to coordinate and monitor the practice and dissemination of TAVI. The purpose of this project was to define the characteristics and clinical outcomes of the patient population treated with TAVI (regardless of technology or access route) in every (i.e., nonselected) center undertaking TAVI. In this paper, we report the outcomes (survival status as of December 12, 2010) of all TAVI procedures undertaken in England and Wales between the first implant in January 2007 until the end of December 2009.

Methods

A total of 25 centers throughout England and Wales developed active TAVI programs between January 2007 and December 2009. All centers underwent structured training, comprising didactic sessions, simulator training, and visits to experienced centers to observe cases. Proctors attended cases at the new institution until the institution, proctors, and the manufacturing company were confident that sufficient expertise had been acquired to permit safe and independent implantation. The following technologies were available to these units: the Medtronic CoreValve system (approved for commercial use in the European Union in May 2007) and the Edwards SAPIEN valve (the transfemoral delivery system approved in November 2007 and transapical in January 2008).

All potential patients went through a systematic process of clinical evaluation, angiographic and echocardiographic assessment. Patient selection was effected in each individual unit through a multidisciplinary team process. These teams consisted not only of cardiac surgeons and interventional cardiologists but also of many other medical specialties and allied professionals. Most centers used devices from only 1 manufacturer. The decision as to the access route to be used was determined by the multidisciplinary team. All centers adopted a "transfemoral first" selection policy with criteria for a nontransfemoral approach based upon the multidisciplinary team's consideration of the size and also the degree of tortuosity, calcification, and atheroma of the aortoilio-

Lifesciences. Dr. Spyt is a consultant for Edwards Lifesciences. Dr. MacCarthy is a proctor for Edwards Lifesciences. Dr. Wendler is a consultant and proctor for Edwards Lifesciences. Dr. Hildick-Smith is a proctor for Medtronic. Dr. Blackman is a proctor for Medtronic CoreValve. Dr. Levy is a proctor for Medtronic CoreValve. Dr. Brecker is a proctor for Medtronic CoreValve. Dr. Mullen has received consultancy and research grants from Medtronic; and consultancy, teaching grants, and research grants from Edwards LifeSciences. All other authors have reported they have no relationships relevant to the contents of this paper to disclose.

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femoral arterial tree. The SAPIEN implants were either by the transfemoral or transapical routes, and the CoreValve by transfemoral, subclavian, or occasionally direct aortic access. There was a small volume of cross-referral between centers, of patients who were deemed to be more suitable for 1 particular device, when this was not available at the original center.

In 2007, the Society for Cardiothoracic Surgery in Great Britain and Ireland and the British Cardiovascular Intervention Society agreed a dataset of demographics, risk factors, and outcome measures to be collected on all patients. The Central Cardiac Audit Database (CCAD) (20) established a web-based system for data entry, encryption, and transfer (the dataset and definitions are provided in Online Table 1). A total of 25 centers throughout England and Wales developed TAVI programs between January 2007 and December 2009 (see Online Appendix for contributing hospitals). All 25 units have submitted their data to CCAD on all patients treated, retrospectively for patients treated before establishing the database and prospectively thereafter. To the end of December 2009, data from all cases treated in England and Wales were entered into the database. No patient having a TAVI was excluded from analysis.

Mortality tracking was undertaken by the National Health Service Central Register by using unique patient identifiers. It is a legal requirement for all deaths in the United Kingdom to be registered with this body. It is not possible to effect any form of burial/cremation or similar process for the deceased without such registration. Thus, tracking yields very robust results. Survival status for the whole cohort of patients was determined through the NHS Central Register as of December 12, 2010.

Periprocedural and post-procedural complications were self-reported according to definitions defined within the national dataset (Supplementary Table 1) with post-implantation aortic regurgitation (AR) assessed visually according to standard angiographic criteria at the termination of the implantation procedure.

All of these processes were performed in compliance with current U.K. Data Protection and Information Governance legislation. All patients provided signed, informed consent.

Data cleaning. All fields were examined for missing data or extreme values, and contributing units were asked to complete or correct data where possible. Extreme data were verified and excluded only if found to be erroneous.

Statistics. Categorical data were presented as percentages, and comparison between groups done by the chi-square test or the Fisher's exact test. Numerical data were presented as mean ± SD or median (interquartile range), and comparisons done with the 2-sample *t* test or the 2-sample Wilcoxon rank-sum (Mann-Whitney) test. Time-to-event data analysis was done using the Cox proportional hazards model. The Kaplan-Meier survival curves were drawn to assess differences between groups for the time to an event data. For the Cox model, univariate analysis of each of the possible predictors of the outcome were tested. Those variables that were significant at $p < 0.05$, and the presence of peripheral vascular disease were included in a multivariate model to determine the independent predictors of the outcome variables. The analysis was done using Stata version 10.1 statistical software (StataCorp, College Station, Texas).

Results

Demographic and baseline characteristics. Completeness of valid data was 99.6% for demographic data, 96.4% for risk factors, 97.4% for procedural variables, and 98.5% for in hospital outcomes. Eighteen of the 25 units had valid data completeness of >98%. Mortality tracking was achieved in 100% of patients with survival status reported as of December 12, 2010. Follow-up ranged from 11 months to 46 months.

Data from 877 implants in 870 patients were submitted to the CCAD. In 7 patients, a subsequent TAVI was performed as a vale-in-valve procedure at a later date to the original implant. In the analysis of survival, the second procedure was censored.

The Registry thus contains the records of 870 patients. The number of implants per year increased from 66 in 2007, to 273 in 2008, and to 538 in 2009. The median number of implants per center was 24 (range 5 to 114). Baseline demographics and risk factors are shown in Table 1. Significant concomitant coronary artery disease (CAD [defined as ≥50% stenosis affecting >1 major epicardial coronary artery]) was present in 410 patients (48%).

The majority (69%) of implants were by the transfemoral route. More than one-half of the SAPIEN implants were transapical, in contrast to almost 90% of CoreValve implants being through the transfemoral route (Table 1). The presence of peripheral vascular disease, CAD, prior cardiac surgery, renal dysfunction, and New York Heart Association (NYHA) functional class III or IV symptoms were significantly more common in patients having TAVI by a nonfemoral approach compared with a transfemoral approach (Table 1). The median logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) was 18.5%, and was lower in the transfemoral cohort (17.1%) than in the nontransfemoral cohort (21.4%; $p < 0.0001$).

There were similar numbers of CoreValve and SAPIEN implants (459 vs. 410; unknown in 8); and 41% of all CoreValve and 28% of all SAPIEN implants were proctored. Patients treated with the SAPIEN valve tended to be older and were more likely to be in NYHA functional class III/IV and to have a greater likelihood of having coronary and peripheral vascular disease (Table 1) than were CoreValve treated patients.

Procedural parameters and outcomes. Periprocedural parameters and outcomes are defined in Table 2. Procedural success was achieved in 846 patients (97.2%). Implantation was unsuccessful in 8 cases, and emergency

Table 1 Demographics

Variables	All Patients (n = 870)	Transfemoral Route (n = 599)	Other Routes (n = 271)	p Value	Medtronic CoreValve (n = 452)	Edwards SAPIEN (n = 410)	p Value
Male	456/870 (52.4)	311/599 (51.9)	145/271 (53.5)	0.66	235/452 (52.0)	217/410 (52.9)	0.78
Age, yrs	81.9 ± 7.1	81.7 ± 7.4	82.3 ± 6.6	0.32	81.3 ± 7.4	82.6 ± 6.7	0.007
AV peak gradient	80.9 ± 27.2	82.1 ± 27.8	77.9 ± 25.7	0.05	83.4 ± 28.5	77.5 ± 25.0	0.003
LVEF ≥50%	553/865 (64.0)	382/597 (64.0)	171/268 (63.8)		288/452 (63.7)	262/406 (64.5)	
LVEF 30%–49%	238/865 (27.0)	166/597 (28.0)	72/268 (26.9)	0.85	123/452 (27.2)	112/406 (27.6)	0.82
LVEF <30%	74/865 (9.0)	49/597 (8.0)	25/268 (9.3)		41/452 (9.1)	32/406 (7.9)	
NYHA functional class I/II	199/866 (23.0)	156/597 (26.1)	43/269 (16.0)	0.001	118/452 (26.1)	80/406 (19.7)	0.03
NYHA functional class III/IV	667/866 (77.0)	441/597 (73.9)	226/269 (84.0)		334/452 (73.9)	326/406 (80.3)	
Coronary disease	394/828 (47.6)	249/574 (43.4)	145/254 (57.1)	<0.001	194/436 (44.5)	198/384 (51.6)	0.04
Any previous cardiac surgery	259/853 (30.4)	160/586 (27.3)	99/267 (37.1)	0.004	129/439 (29.4)	126/406 (31.0)	0.60
PVD	241/832 (29.0)	110/563 (19.5)	131/269 (48.7)	<0.001	109/423 (25.8)	130/401 (32.4)	0.04
Diabetes mellitus	196/861 (22.8)	137/595 (23.0)	59/266 (22.2)	0.79	101/450 (22.4)	92/403 (22.8)	0.89
COPD	239/834 (28.7)	158/574 (27.5)	81/260 (31.2)	0.28	120/438 (27.4)	115/388 (29.6)	0.48
Creatinine >200 mmol/l	55/863 (6.7)	32/588 (5.4)	25/265 (9.4)	0.03	28/444 (6.3)	28/401 (7.0)	0.69
Logistic EuroSCORE	18.5 (11.7–27.9)	17.1 (11.0–25.5)	21.4 (14.4–33.6)	<0.001	18.1 (11.1–27.9)	18.5 (12.4–27.7)	0.34

Values are n/N (%), mean ± SD, or median (interquartile range).

AV = aortic valve; COPD = chronic obstructive pulmonary disease; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LVEF = left ventricular ejection fraction; PVD = peripheral vascular disease.

conversion to an AVR occurred in 6 patients (0.7%), all of whom had a SAPIEN implant via a transapical approach (2.2% of transapical implants) (Table 2).

Post-procedural (30-day) complications. The incidence of major complications is described in Table 2. The incidence of stroke and myocardial infarction was 4.1% and 1.3%, respectively. The requirement for a new permanent pacemaker was significantly more common with CoreValve implants than with SAPIEN (24.4% vs. 7.4%; $p < 0.0001$). Some degree of paravalvar AR (angiographic grade ≥1) occurred in 61% of patients, with this being moderate to severe (AR >2) in 13.6%. Moderate to severe leaks were significantly more common with the CoreValve device. Major vascular complications were reported in 6.3% of patients, and occurred predominantly in the transfemoral cohort (8.4%).

Early survival. Survival for the whole cohort at 30 days was 92.9%. There was a higher 30-day mortality among patients receiving a nontransfemoral implant compared with patients receiving a transfemoral TAVI ($p = 0.03$) (Table 2). There were some significant demographic differences between these cohorts (Table 2).

Midterm and long-term survival. The Kaplan-Meier survival curve for the whole population is shown in Figure 1. Survival at 1 year and 2 years was 78.6% and 73.7% at 1 and 2 years, respectively (with 651 and 213 patients alive and at risk at 1 and 2 years follow-up, respectively). There was a marked attrition in survival between 30 days and 6 months, with 9.6% of patients dying during this period and a further 4.7% between 6 months and 1 year. There was no difference in survival at 1 year between patients in the SAPIEN cohort compared with the CoreValve cohort. There was a signifi-

Table 2 Outcomes

Variables	All Patients (n = 870)	Transfemoral Route (n = 599)	Other Routes (n = 271)	p Value	Medtronic CoreValve (n = 452)	Edwards (n = 410)	p Value
Procedural success	846/870 (97.2)	583/599 (97.3)	263/271 (97.1)	0.82	444/452 (98.2)	402/410 (98.1)	0.84
All-cause mortality at end of follow-up	249/870 (28.6)	153/599 (25.5)	96/271 (35.4)	0.003	122/452 (27.0)	122/410 (29.8)	0.37
30-day survival, % dead	62/870 (7.1)	33/599 (5.5)	29/271 (10.7)	0.006	26/452 (5.8)	35/410 (8.5)	0.11
1-yr survival, % dead	186/870 (21.4)	111/599 (18.5)	75/271 (27.7)	0.002	93/452 (21.7)	89/410 (20.6)	0.68
2-yr survival, % dead	229/870 (26.3)	135/599 (22.5)	94/271 (36.7)	<0.001	108/452 (23.9)	116/410 (28.3)	0.14
MACCE, in hospital	90/870 (10.3)	56/599 (9.4)	34/271 (12.6)	0.15	42/452 (9.3)	48/410 (11.7)	0.25
Stroke, in hospital	35/864 (4.1)	24/594 (4.0)	11/270 (4.1)	0.98	18/448 (4.0)	17/408 (4.2)	0.91
MI	11/864 (1.3)	6/594 (1.0)	5/270 (1.9)	0.31	5/447 (1.1)	6/409 (1.5)	0.65
AR moderate/severe	115/849 (13.6)	91/585 (15.6)	24/264 (9.1)	0.01	76/439 (17.3)	39/405 (9.6)	0.001
Surgical conversion	6/850 (0.7)	0/592 (0)	6/268 (2.2)	0.001*	0/450 (0)	6/402 (1.5)	0.01*
Major vascular complication	55/869 (6.3)	50/598 (8.4)	5/271 (1.9)	<0.001	28/451 (6.2)	26/410 (6.3)	0.94
Repeat procedure	7/870 (0.8)	7/599 (1.2)	0/271 (0)	0.11*	7/452 (1.6)	0/410 (0)	0.02*
Pacemaker	141/867 (16.3)				110/451 (24.4)	30/408 (7.4)	<0.001

Values are n/N (%). *Fisher exact test.

AR = aortic regurgitation; MACCE = major adverse cardiovascular and cerebrovascular events; MI = myocardial infarction.

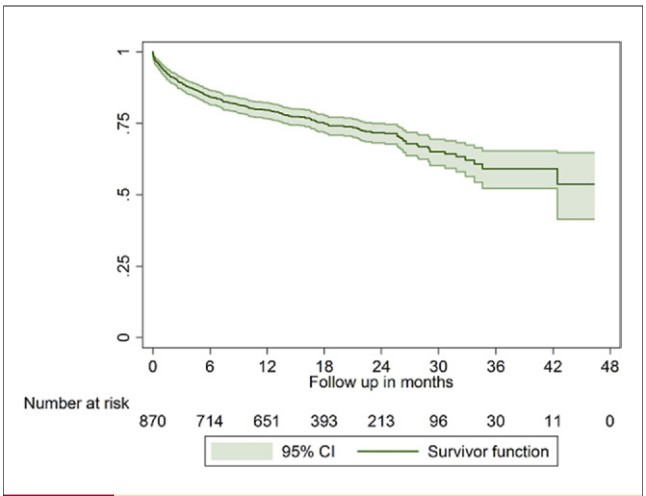

Figure 1 **Survival Curves for Whole Cohort of 870 Patients**

Event rate was calculated by the Kaplan-Meier method. **Shaded area** indicates 95% confidence interval (CI); **darker line** indicates survivor function.

cant difference in survival between the transfemoral and the nontransfemoral route of implantation (Fig. 2). Actual 1-year mortality was 18.5% with transfemoral and 22.7% with nontransfemoral. This difference persisted at 2 years, with a mortality of 22.5% in the transfemoral cohort compared with 36.7% in the nontransfemoral cohort (Table 2).

The predictors of mortality (at 1 year post-implant) within the univariate and multivariate analyses are shown in Table 3. In the univariate model, survival was significantly adversely affected by LV dysfunction, renal dysfunction, the presence of concomitant coronary artery disease or chronic obstructive pulmonary disease (COPD), the presence of moderate or severe AR, and a nontransfemoral approach. Age, NYHA functional class, or type of device implanted did not affect survival. Left ventricular function (ejection fraction <30%), the presence of COPD, and the presence of moderate or severe AR (Table 3) were the only independent predictors of mortality in the multivariate model. As noted in the preceding text, the early survival advantage in the patients treated with CoreValve implants was no longer apparent at 1 year.

There was no difference in survival at 1 year between cohorts of patients with a logistic EuroSCORE of 0 to 20 and 21 to 40, but a marked and significant reduction in midterm survival for patients with a logistic EuroSCORE of >40 (Fig. 3). There was no difference in survival between proctored and nonproctored cases, or between the first 20 patients having implants in any individual unit and that in subsequent patients.

Discussion

This national, multicenter study reports a large consecutive and all-inclusive series of patients diagnosed with severe symptomatic aortic stenosis who underwent TAVI. They were all deemed to be at high risk for conventional surgery, on the basis of the clinical judgment of the multidisciplinary team within each individual unit. The U.K. TAVI Registry is unique in that it has captured every TAVI performed at all the 25 active units within England and Wales, and thus includes the entire "learning curve" and early experience of adopting centers without any publication bias that might be induced by center selection. The data reported here provide the first results from the U.K. Registry and encompasses a substantial number of implants with both the Medtronic CoreValve and the Edwards SAPIEN valve. All previously reported TAVI registries are device specific or from selected centers. These data from the U.K. Registry reflect the largest series of consecutive cases reported to date of midterm and long-term outcomes after TAVI with >200 patients alive and at risk 2 years post-implant. The minimum follow-up was >11 months.

Principle findings. In this cohort of patients the 30-day mortality was 7.1%. The rate observed in this registry was similar to that reported in previous registries: Canadian registry, 10.4% (12); SOURCE (SAPIEN Aortic Bioprosthesis European Outcome) registry, 8.5% (15); FRANCE (French Aortic National CoreValve and Edwards) registry, 12.7% (11); German registry, 8.2% (16); and Italian registry, 5.4% (13). In the PARTNER B cohort, 30-day mortality was 5%, and it was 5.2% in the PARTNER A cohort (as treated analysis) (18,19). This (7.1%) mortality allied to a significant reduction in 30-day mortality that occurred with time (30-day mortality for the 2009 cohort was 4.3%) is an encouraging statistic in relation to the further dissemination of TAVI.

The majority (>85%) of nontransfemoral approach cases were effected by a transapical approach. The higher mortality in the nontransfemoral cohort, compared with the

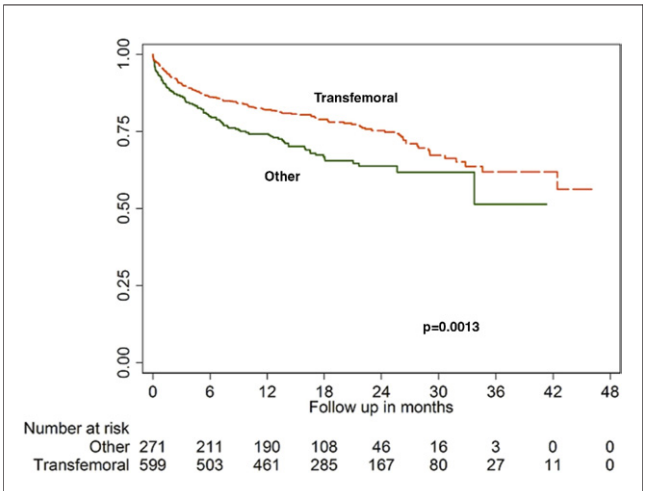

Figure 2 **Survival Curves by Access Route**

Survival curves for transfemoral access route **(orange broken line)** and nontransfemoral route **(green solid line)**. Event rates calculated by the Kaplan-Meier method and compared with the use of the log-rank test.

Table 3 Predictors of Mortality at 1 Year

Variables	Alive (n = 684)	Dead (n = 186)	Univariate Model	p Value	Multivariate Model	p Value
Edwards SAPIEN	321/680 (47.2)	89/182 (48.9)	1.00			
Medtronic CoreValve	359/680 (52.8)	93/182 (51.1)	0.95 (0.70–1.29)	0.75		
Route, other	196/684 (28.7)	75/186 (40.3)	1.00			
Route, transfemoral	488/684 (71.3)	111/186 (59.7)	0.65 (0.48–0.88)	0.006	0.73 (0.52–1.04)	0.08
AR moderate/severe	83/674 (12.3)	32/175 (18.3)	1.49 (1.00–2.21)	0.048	1.66 (1.10–2.51)	0.016
Major vascular complication	39/684 (5.7)	16/185 (8.7)	1.42 (0.82–2.45)	0.21		
Permanent pacemaker	108/683 (15.8)	33/184 (17.9)	1.21(0.83–1.77)	0.32		
Male	355/684 (59.9)	101/186 (54.3)	1.19 (0.88–1.61)	0.25		
Age, yrs	81.8 ± 7.3	82.3 ± 6.4	1.01 (0.99–1.03)	0.52		
AV gradient	81.1 ± 27.1	79.9 ± 27.8	0.996 (0.990–1.002)	0.20		
LVEF ≥50%	459/680 (67.5)	94/185 (50.8)	1.00		1.00	
LVEF 30%–49%	169/680 (24.9)	69/185 (37.3)	1.93 (1.40–2.66)	<0.001	1.49 (1.03–2.16)	0.03
LVEF <30%	52/680 (7.6)	22/185 (11.9)	1.89 (1.16–3.07)	0.01	1.65 (0.98–2.79)	0.06
NYHA functional class I/II	160/680 (23.5)	39/186 (21.0)	1.00			
NYHA functional class III/IV	520/680 (76.5)	147/186 (79.0)	1.14 (0.79–1.63)	0.50		
Coronary disease	301/653 (46.1)	93/175 (53.1)	1.38 (1.01–1.87)	0.04	1.23 (0.88–1.73)	0.23
Any previous cardiac surgery	202/667 (30.3)	57/186 (30.7)	1.04 (0.75–1.43)	0.83		
PVD	179/654 (27.4)	62/178 (34.8)	1.28 (0.91–1.75)	0.16		
Diabetes mellitus	146/675 (21.6)	50/136 (26.9)	1.36 (0.98–1.89)	0.07		
COPD	176/654 (26.9)	63/180 (35.0)	1.40 (1.02–1.93)	0.04	1.41 (1.00–1.98)	0.05
Creatinine >200 mmol/l	38/668 (5.7)	19/185 (10.3)	1.84 (1.14–2.97)	0.012	1.55 (0.90–2.68)	0.11

Values are n/N (%), mean ± SD, or hazard ratio (95% confidence interval).
CI = confidence interval; HR = hazard ratio; other abbreviations as in Tables 1 and 2.

femoral cohort, is comparable to that seen in almost all studies (15,18). Although a nontransfemoral approach conferred a significantly increased risk of death at 30 days and at 1 year and 2 years of follow-up and was a predictor of an adverse outcome in the univariate analysis, it was not an independent predictor of mortality at 1 year. The explanation is probably multifactorial. It is clear that the nontransfemoral cohort of patients has a more adverse risk profile than patients who can be treated by the femoral approach, but it is also possible that aspects of the transapical procedure per se may confer an increased risk.

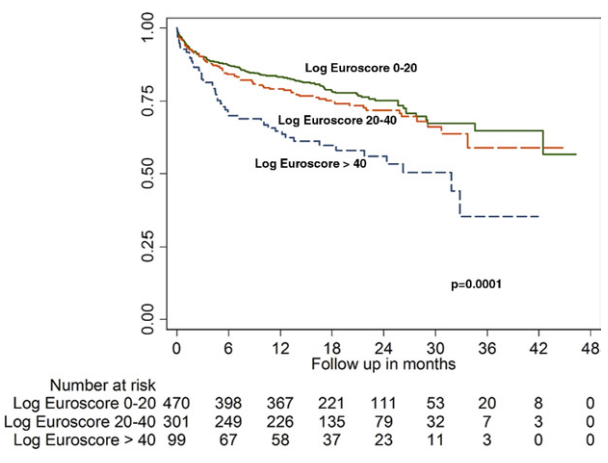

Figure 3 Survival Curves by Log EuroSCORE

Survival curves by logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE [Log Euroscore]): **green solid line** = 0 to 20; **orange broken line** = 20 to 40; **blue broken line** = >40. Event rates calculated by the Kaplan-Meier method and compared with the use of the log-rank test.

We report midterm survival after TAVI in a large cohort of patients for whom mortality tracking was achieved in 100% of cases. Kaplan-Meier survival was 78.6% and 73.7% at 1 and 2 years, respectively. The numbers of patients "at risk" in the Kaplan-Meier analyses were 651 and 213 at 1 year and 2 years, respectively (in comparison to 260 and 67, respectively, in the PARTNER cohort A (19).

In addition to death occurring within 30 days of procedure, there was a marked ongoing attrition in the first 6 months post-implant (with 9.6% of patients dying between 30 days and 6 months and 4.7% dying between 6 months and 1 year). This high attrition in the first year post-implant is also seen in the SOURCE registry and the Italian registries and in both cohorts of the PARTNER trial; for example, 18% of patients died after a TAVI between 30 days and 1 year in PARTNER A. It is of interest that there was an almost identical rate of attrition in the control (AVR) group. Our data show that this high rate of attrition decreases substantially after 1 year, with 21.4% of patients dying within the first year but only 4.9% (of the original cohort) between 1 and 2 years. This pattern of survival closely matches that reported in the U.K. Surgical Database for octogenarians undergoing either AVR or AVR with concomitant coronary artery bypass grafting, with a high rate of attrition in the first 6 months followed by an ongoing constant risk of dying of 5% to 6% per year over the next 3 years (4).

The demonstration that there was no survival difference between patient cohorts with logistic EuroSCORE of 0 to 20 and 21 to 40 reaffirms the relative lack of utility in this scoring system in risk/outcome prediction for this group of patients and confirms the need for more sophisticated and procedure specific (rather than generic) scoring systems (21). In the cohort with a logistic EuroSCORE > 40, it is again interesting to note that the 30-day mortality was not significantly different from the logistic EuroSCORE 0 to 20 and 21 to 40 cohorts but that midterm mortality was significantly inferior. Almost 25% of the logistic EuroSCORE >40 cohort of patients died between 30 days and 6 months. The poor outcome during this 30-day to 6-month period for these very high risk patients warrants further investigation, in particular to determine whether patients who are likely not to survive to 6 months or even 1 year can be prospectively identified.

In the univariate analysis, impaired LV ejection fraction, transfemoral access, CAD, the presence of moderate or severe AR, COPD, and renal dysfunction had an adverse impact on survival. However, interestingly, neither age, NYHA functional class, nor the presence of peripheral vascular disease were significantly associated with survival. In the multivariate analysis, the only independent predictors of survival were an LV ejection fraction <30%, the presence of moderate or severe AR, and COPD.

These data encompass the learning curve of all units with this technique. The observation that 30-day and midterm mortality was equivalent in proctored cases and in nonproctored cases, and in the first 20 cases compared with subsequent cases in each unit, reflects well on the process of education, training, and mentorship established by both of the companies with current commercially available devices. It also suggests good judgment of both the centers and proctors as to when a unit is able to progress to stand-alone implantation. Further growth and dissemination of TAVI should retain this robust training structure in addition to a strict multidisciplinary approach.

The incidence of early stroke is not surprising, given the patient population, and is comparable to other registries and to the PARTNER trial. The finding of magnetic resonance imaging evidence of (albeit seemingly silent) cerebral perfusion defects in 84% of TAVI patients (22) highlights the need to evaluate neurological outcomes in these patients, including cognitive function. Embolic protection devices may have a role in ameliorating the incidence of stroke, but at present it remains a major concern and represents an obstacle to the application of TAVI in lower risk patients.

The significantly higher rate of permanent pacemaker requirement with CoreValve implantation confirms previous reports (23,24) and is likely due to the presence of the stent within the subvalvar LV outflow tract with impingement on the left branch of the Bundle of His. Not surprisingly, the presence of pre-procedural right bundle branch block conveys a very high risk of permanent pacemaker implantation after CoreValve implantation (25).

In 61% of patients, there was a degree of paravalvular AR that would traditionally have been regarded as suboptimal or even unacceptable after AVR. The finding that the degree of post-implant AR was an independent predictor of survival at 1 year is an important observation and requires further detailed study. Whether the regurgitation is responsible for this adverse outcome or is merely a marker for other adverse features cannot be assessed from this registry. The presence of moderate or severe AR was more common in the Medtronic CoreValve cohort. There is some evidence that the degree of AR remains stable or even reduces during the first year post-implant (26). The influence of this residual AR on parameters such as the incidence of endocarditis and hemolysis and the effect on LV mass regression are unknown and will need to be further evaluated. A reduction in the incidence and severity of paravalvular AR represents an obvious target for technical improvements in the design of transcatheter valves and of implantation techniques.

The observation that COPD was an independent predictor of outcome is perhaps surprising. In patients with aortic stenosis and COPD, it can be difficult to be certain as to the precise contribution of each pathology in an individual patient with progressive severe breathlessness. For patients in whom COPD predominates, the relief of aortic stenosis may not change the clinical outcome as much as in other patient groups, and that may in part explain this observation.

Comparison of the incidence of major vascular complications between case series is complicated by differing definitions. The incidence of major iliofemoral complications in 1 study (in the same patients) was shown to vary between 4% and 13% depending upon the definitions used (27) The data fields collected in the U.K. Registry (see Appendix) would be expected to capture the major, but not the less serious, vascular complications. Despite this, the reported rate of 8.4% among transfemoral patients in our series is high, though comparable to other reports (27–29) Further studies are required to identify the risk factors for and precise nature of these peripheral vascular complications. It is hoped that improvements in technology and technique and in the selection of the optimal access route for implantation will reduce the rate of this complication in the future.

A substantial proportion of patients being considered for TAVI have concomitant CAD. In this registry, 410 (47%) patients had CAD (defined as ≥50% stenosis affecting ≥1 major epicardial coronary artery). The optimal management of CAD in the setting of TAVI is not well defined. Hybrid percutaneous coronary intervention was undertaken in only 55 patients (14% of those patients with CAD). Thus, in this registry, patients with concomitant CAD have been predominantly been managed by TAVI alone, with a low incidence of early myocardial infarction. The presence of concomitant CAD was identified as a risk factor in the univariate analysis but was not an independent predictor of survival at 1 year. This is an interesting observation given

the marked survival differences seen after conventional surgery in elderly patients who require AVR and coronary artery bypass graft surgery compared with patients undergoing isolated AVR (4). The optimal management of concomitant CAD is not well defined and is another area in relation to this patient population that requires further study.

Strengths and limitations of the study. Like all registries, ours is only as good and credible as the quality of the data within it. Data completeness in this registry was good, but whereas data on the numbers of procedures and survival outcome are believed to be extremely robust, those concerning morbidity and complications are likely less so. Although internal consistency checks have been applied, these data are self-reported and have not been systematically validated or independently adjudicated.

The definitions used in the dataset are not directly comparable to those in other published reports. The Society of Thoracic Surgeons score could not be calculated from the dataset. The recent publication of the VARC (Valvular Academic Research Consortium-consensus of event definition) definitions should go some way to improving the comparability of data from future studies (30).

Value of the study. The U.K. TAVI program was established to capture and report outcomes on TAVI procedures performed within the United Kingdom. In this, the first report from this registry, the short-term and midterm outcomes of the 870 patients undergoing TAVI until the end of 2009 are reported. It is unique in that it is comprehensive, has captured data from all consecutive patients in all of the clinically active units, encompasses a substantial number of implants with both commercially available technologies utilizing all of the described access routes, and has robust (100%) overall mortality tracking. It is also the first report of outcomes beyond 1 year for a substantial number of patients (>850) and demonstrates encouraging midterm outcomes for patients who are still alive I year after TAVI. These real-world data are complementary to the data emanating from the PARTNER randomized trials.

Conclusions

To summarize, outcomes after TAVI for this high-risk patient population of patients with severe aortic stenosis were encouraging. Although 30-day mortality was acceptable, there was a significant attrition between 30 days and 12 months, predominantly in the highest risk cohort. The rate of reduction in survival fell markedly after 1 year. These data, in conjunction with those from other registries and from the PARTNER trial, suggest that it would be appropriate to compare TAVI with surgical AVR in the setting of a randomized trial in a less high risk cohort of patients.

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Key Words: aortic stenosis ■ registry ■ transcatheter aortic valve implantation.

APPENDIX

For a list of hospitals contributing patients to this study and a supplementary table of the dataset and definitions, please see the online version of this article.