SOURCE 3: 1-year outcomes post-transcatheter aortic valve implantation using the latest generation of the balloon-expandable transcatheter heart valve

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Aims
Transcatheter aortic valve implantation (TAVI) has developed from a procedure for patients with aortic stenosis inoperable or high risk for surgery, into a treatment option even for intermediate risk elderly patients. This development has been facilitated by the clinical learning curve and constant improvements of transcatheter heart valves used. We present total 1-year results of SOURCE 3, the European post-approval multicentre registry of the latest generation balloon expandable SAPIEN 3™ (Edwards Lifesciences, Irvine, CA, USA).

Methods and results
Participating centres have submitted their consecutive experience with the SAPIEN 3, dependent on patients consent. Data were prospectively collected and all end point-related outcomes adjudicated according to VARC-2 definitions by an independent committee. Between July 2014 and October 2015, in total 1946 patients (mean age 81.6 ± 6.7 years, 52% male) were enrolled in 80 centres from 10 European countries. At 1 year, all-cause mortality was 12.6%, cardiovascular mortality 8.0%, stroke 3.1%, disabling stroke 1.4%, and rate of new pacemakers 13.2%. Causes of death were 62.0% cardiovascular and 38.0% non-cardiovascular, with heart failure (13.4%) and pulmonary complications (12.7%) being the main reasons for fatal outcomes. Multivariable analysis identified New York Heart Association Class IV and renal insufficiency as predictors of mortality, while higher BMI’s improved survival. Severe (zero) and moderate paravalvular leakage (2.6%) was rare at 1 year.

Conclusion
In SOURCE 3, we observe a low complication rate and mortality at 1 year. Given the low incidence of higher degree paravalvular leakages, this variable did no longer affect outcome.

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Keywords
Aortic stenosis • Transcatheter aortic valve implantation • Balloon expandable valve • SAPIEN 3 • Predictors of mortality • Causes of death
Introduction

Over the last decade, transcatheter aortic valve implantation (TAVI) has progressed from being a procedure solely for inoperable and high-risk patients for surgical aortic valve replacement, to an alternative treatment option in elderly patients with even intermediate risk. At its introduction, the key for success was to find technical solutions to perform the procedure safely. Nowadays, with the knowledge that specific post-operative events such as vascular complications and paravalvular leakage (PVL) affect short- and mid-term survival, the goal is also to reduce these events to make long-term outcomes predictable for individual patients.

The most recent modifications to the 3rd-generation of the SAPIENTM transcatheter heart valve (THV), the SAPIEN 3TM (both Edwards Lifesciences, Irvine, CA, USA), have been reported previously. They have been developed to potentially improve implantation, facilitate transfemoral access, and reduce strokes, vascular complications and PVLs. Outcome in Europe using the SAPIEN 3 is currently assessed through the post-approval SOURCE 3 (SAPIEN 3 Aortic Bioprosthesis European Outcome) Registry, to observe safety and performance under ‘real-world’ conditions. While outcomes from registries usually have their own limitations and are seen to be inferior compared to randomized trials, they provide additional value in that they represent experience from what clinicians call the ‘Real World’. Therefore, SOURCE 3 does not only provide information on how the 3rd-generation balloon-expandable valve performs but also makes it feasible to reflect on contemporary heart team decisions on TAVI strategies and their outcome in an all-comers cohort of patients.

Thirty-day results of SOURCE 3 have recently been published and demonstrated high-procedural success with low risk of early complications and mortality. Here we present the outcomes and predictors of the total 1-year results of the SOURCE 3 Registry.

Methods

Registry design and purpose of this report

SOURCE 3 is an European post-approval multicentre and observational registry, aimed to evaluate the safety and performance of the SAPIEN 3 THV in ‘real-life’ practice for 5 years, as previously described in detail. It has been approved by the local ethics committees, and respective health authorities, if applicable of the participating countries, and all the patients who have provided written informed consent.

An independent clinical events committee (CEC) reviewed and adjudicated all key clinical events according to Valve Academic Research Consortium 2 (VARC-2) criteria (a list of CEC members is provided in Supplementary material online, File S1). Post-index procedure vascular complications, acute kidney injury, and bleeding were adjudicated up to 30 days. Other events, such as death, transient ischaemic attack, rehospitalization for valve-related symptoms or worsening congestive heart failure post-discharge, new conduction abnormalities and pacemakers, myocardial infarction, new onset of atrial fibrillation and other TAVI-related complications were adjudicated over 1 year. Events of death were adjudicated by an independent CEC to determine if the cause was of cardiovascular or non-cardiovascular origin. All strokes were reviewed and characterized by an independent neurologist (see Supplementary material online, File S1) into disabling or non-disabling stroke.

Study population

Eighty centres in 10 European countries are registered in SOURCE 3 (centres listed in Supplementary material online, File S2). As per the indication for use and the ESC/EACTS guidelines, patients for whom TAVI was deemed the best treatment option were selected on the basis of the clinical consensus of the ‘Heart Team’, a multidisciplinary team of cardiac surgeons, interventional cardiologists, anaesthetists, and imaging specialists. The appropriate size of SAPIEN 3 (23 mm, 26 mm, or 29 mm) was determined based on pre-procedural echocardiographic and/or computed tomographic findings. The devices were delivered via transfemoral (TF) or other alternative access approaches (non-transfemoral (Non-TF): i.e. transapical, transaortic, transsubclavian, or transcarotid), as described in detail previously.

Intervention and purpose

Patients underwent echocardiographic measurements, electrocardiogram recordings and a global clinical status evaluation including New York Heart Association (NYHA) functional class assessment at baseline, discharge, 30-days and 1-year post-index procedure. Echocardiographic data presented were site reported. Electrocardiographic records were analysed by a cardiologist at each centre and conduction abnormalities assessed on the basis of VARC-2 definitions.

Transcatheter heart valve and delivery devices

All patients were treated using the SAPIEN 3 THV. Details of the device have been highlighted in previous publications.

Data collection and statistical analysis

All data were entered in the electronic data capture system by the participating centres and monitored by the Sponsor.

The modality of TAVI treatment, TF, or Non-TF, was decided by the local heart teams, based on the patient’s condition. Due to this selection bias, the two cohorts are very different in terms of their baseline characteristics as highlighted in Table 1 (the P-values in this table serve descriptive purpose only to highlight the differences of baseline characteristics between the TF and Non-TF cohort). For that reason a direct comparison of the post-TAVI outcomes was not performed.

Continuous variables are presented as mean ± standard deviation or median [Q1, Q3] and were compared between groups using the two-sample t-tests or Mann–Whitney U test. Categorical variables are given as frequencies and percentages, and were compared using Fisher’s exact test. Kaplan–Meier (KM) analyses were performed using the log-rank test. A paired analysis was conducted on haemodynamic parameters (mean gradient, peak gradient, effective orifice area, left-ventricular ejection fraction).

Univariate Cox proportional hazard models were performed to obtain the hazard ratio estimates on all-cause mortality using patient baseline characteristics, procedural and post-procedural variables (listed in Supplementary material online, File S3). Univariate P-values <0.2 were further selected as the starting subset for multivariable stepwise Cox proportional hazards model for all-cause mortality. Proportional hazards were checked in the subset and highly correlated variables were further removed. Thereafter, a multivariable stepwise Cox proportional hazard model was computed for all-cause mortality.

All statistical analyses were performed using SAS, version 9.3 (SAS Institute Inc, Cary, NC, USA).
Results

Patients and procedural characteristics

Patients with severe, symptomatic aortic stenosis, consecutively treated using the SAPIEN 3, were enrolled between July 2014 and October 2015. Compared to the previous cohort, investigated at 30 days (n = 1947), 1 withdrawal of consent occurred, resulting in a total number of 1946 patients for this 1-year analysis. Most patients (n = 1694, 87.1%) were treated using TF approach, while 12.9% of patients (n = 252) underwent TAVI through Non-TF access (transapical 72%, transaortic 21%, transsubclavian 2%, transcortid 5%).

The mean age was 81.6 ± 6.7 years and major comorbidities were frequent, resulting in a mean logistic EuroSCORE I (logES) of 18.3 ± 13.2%. Patients were predominantly male (52%) and 73.3% of patients were in NYHA Class III/IV at enrolment. As detailed in Table 1, Non-TF patients presented with a higher risk profile compared to the TF cohort.

The majority of TF patients underwent the procedure under conscious sedation (1014/1694, 59.9%), while the remaining cohort was treated under general anaesthesia. Implantation success was 98.5% (1915/1946) in all patients. A pre-TAVI balloon dilatation was completed in 50.5% of all patients and post-TAVI dilatations in 10.7% (207/1943) of the total cohort (TF: 10.4%, Non-TF: 12.7%).
Procedural complications were previously reported, with unplanned valve-in-valve procedures in 0.7% (14/1946), conversion to open heart surgery in 0.6% (11/1946) and supportive use of cardio-pulmonary bypass during the TAVI procedure in 0.3% (6/1945) (Table 2).

One-year clinical outcomes
Follow-up for patients was 100% complete. The KM estimate for all-cause mortality at 1-year was 12.6% for the total cohort, 11.8% after TF, and 18.5% after Non-TF access (Table 2). Mortality was lower in patients with logES of <10 (10.3%) compared to those with logES >30 (19.6%; \( P = 0.0002 \), Figure 1). Cardiovascular mortality was 8.0% overall, 7.5% in TF patients and 11.3% in Non-TF patients. In patients who were converted to open-heart surgery (\( n = 11 \)) or in whom cardiopulmonary bypass was used during TAVI (\( n = 6 \)), 1-year mortality was high with 63.6% (\( n = 6 \)) and 50% (\( n = 3 \)), respectively.

The KM event rate for stroke was 3.1%, which were disabling in 1.4%. Other CEC adjudicated post-TAVI complications included new pacemaker implantations (13.2%), new onset of atrial fibrillation (7.9%), myocardial infarction (0.9%), endocarditis (1.3%), and valve thrombosis (0.4%). Rehospitalization for valve-related symptoms or worsening congestive heart failure was recorded in 8.1% of patients (Table 2).

Causes of deaths
A total of 245/1946 patients (12.6%) died during the 1st year from cardiovascular (\( n = 152/245, 62.0% \)) or non-cardiovascular events (\( n = 93/245, 38.0% \)). Most common causes for cardiovascular deaths were heart failure (21.7%), sudden cardiac death (10.5%), and endocarditis (7.9%). A new pacemaker implantation post-TAVI did not affect sudden cardiac death at 1 year. In patients, who suffered from post-TAVI endocarditis, the 1-year mortality was 50% (\( n = 12 \)). Most common causes for non-cardiovascular deaths were of pulmonary (30.1%), cancer (22.6%) and sepsis (15.1%) origin (Table 3).

Predictors of all-cause 1-year mortality
Univariate analysis was performed to assess associations between patient’s baseline characteristics, procedural and post-procedural complications, and 1-year mortality (a summary of all variables analysed are listed in Supplementary material online, File S3). The results of risk factors with \( P < 0.2 \) (continuous variable, and levels of categorical variables with \( P < 0.2 \), which were also later used for the multivariable analysis, are displayed in Table 4. Strongest patient’s characteristics to predict 1-year mortality were logES, renal insufficiency moderate to severe tricuspid regurgitation, and atrial fibrillation. Female gender, higher mean aortic gradients, and body mass index were identified as indicators of improved survival. TF access and post-procedural characteristics such as acute kidney injury, length of stay in intensive care, and recovery time, were among the

### Table 2 One-year clinical outcomes

| End points                        | Total \( N = 1946 \) | TF \( N = 1694 \) | Non-TF \( N = 252 \) |
|-----------------------------------|----------------------|------------------|----------------------|
| All-cause mortality %             |                      |                  |                      |
| 30 days                           | 2.2 [1.6, 3.0]       | 1.9 [1.4, 2.7]   | 4.0 [2.2, 7.2]       |
| 1 year                            | 12.6 [11.2, 14.2]    | 11.8 [10.3, 13.4]| 18.5 [14.2, 23.9]    |
| Cardiovascular mortality %        |                      |                  |                      |
| 30 days                           | 1.6 [1.1, 2.3]       | 1.5 [1.0, 2.2]   | 2.4 [1.1, 5.3]       |
| 1 year                            | 8.0 [6.8, 9.3]       | 7.5 [6.3, 8.9]   | 11.3 [7.9, 16.0]     |
| All stroke %                      |                      |                  |                      |
| 30 days                           | 1.4 [1.0, 2.1]       | 1.2 [0.8, 1.9]   | 2.8 [1.3, 5.8]       |
| 1 year                            | 3.1 [2.4, 4.0]       | 2.7 [2.0, 3.6]   | 5.6 [3.3, 9.5]       |
| Disabling stroke %                |                      |                  |                      |
| 30 days                           | 0.5 [0.3, 1.0]       | 0.5 [0.2, 0.9]   | 0.8 [0.2, 3.1]       |
| 1 year                            | 1.4 [0.9, 2.0]       | 1.1 [0.7, 1.7]   | 3.6 [1.8, 7.1]       |
| Transient ischaemic attack %      |                      |                  |                      |
| 30 days                           | 0.6 [0.3, 1.1]       | 0.6 [0.3, 1.1]   | 0.8 [0.2, 3.2]       |
| 1 year                            | 1.2 [0.8, 1.8]       | 1.2 [0.7, 1.8]   | 1.3 [0.4, 3.9]       |
| Myocardial infarction %           |                      |                  |                      |
| 30 days                           | 0.3 [0.1, 0.7]       | 0.2 [0.1, 0.6]   | 0.8 [0.2, 3.1]       |
| 1 year                            | 0.9 [0.6, 1.5]       | 0.8 [0.5, 1.4]   | 1.8 [0.7, 4.6]       |
| New onset of atrial fibrillation %|                      |                  |                      |
| 30 days                           | 6.3 [5.3, 7.5]       | 5.6 [4.6, 6.8]   | 11.6 [8.2, 16.2]     |
| 1 year                            | 7.9 [6.8, 9.2]       | 7.1 [5.9, 8.4]   | 13.3 [9.7, 18.2]     |
| New permanent pacemaker %         |                      |                  |                      |
| 30 days                           | 12.1 [10.7, 13.6]    | 12.4 [10.9, 14.0]| 10.4 [7.2, 14.8]     |
| 1 year                            | 13.2 [11.7, 14.8]    | 13.6 [12.0, 15.3]| 10.4 [7.2, 14.8]     |
| Endocarditis %                    |                      |                  |                      |
| 30 days                           | 0.3 [0.1, 0.6]       | 0.2 [0.1, 0.6]   | 0.4 [0.1, 2.8]       |
| 1 year                            | 1.3 [0.9, 2.0]       | 1.3 [0.9, 2.0]   | 1.2 [0.4, 3.8]       |
| Valve thrombosis %                |                      |                  |                      |
| 30 days                           | 0.1 [0.0, 0.4]       | 0.1 [0.0, 0.4]   | 0.4 [0.1, 2.8]       |
| 1 year                            | 0.4 [0.2, 0.8]       | 0.3 [0.1, 0.7]   | 0.8 [0.2, 3.2]       |
| Rehospitalisation %a              |                      |                  |                      |
| 30 days                           | 1.0 [0.6, 1.5]       | 1.0 [0.6, 1.6]   | 0.8 [0.2, 3.2]       |
| 1 year                            | 8.1 [6.9, 9.5]       | 8.0 [6.8, 9.5]   | 8.7 [5.7, 13.2]      |

All events are CEC adjudicated; values are Kaplan–Meier estimates (%) [95% confidence interval].

TF, transfemoral.

*aRehospitalisations for valve-related symptoms or worsening congestive heart failure.
Figure 1 Overall survival, for the total cohort and for patients with a baseline EuroSCORE I < 10 and >30.

Table 3 Main causes of mortality at 1 year

| Cardiovascular deaths | Total                  | 152/245* (62.0%) | Non-cardiovascular deaths | Total                  | 93/245* (38.0%) |
|-----------------------|------------------------|-------------------|----------------------------|------------------------|-----------------|
| Main causes of cardiovascular deaths |                        |                   | Main causes of non-cardiovascular deaths |                        |                 |
| Heart failure         | 33/152 (21.7%)         |                   | Pulmonary                  | 28/93 (30.1%)          |                 |
| Sudden cardiac death  | 16/152 (10.5%)         |                   | Cancer                     | 21/93 (22.6%)          |                 |
| Endocarditis          | 12/152 (7.9%)          |                   | Sepsis                     | 14/93 (15.1%)          |                 |
| Stroke                | 9/152 (6%)             |                   | Cachexia                   | 9/93 (9.7%)            |                 |
| Haemorrhagic          | 3/152 (2.0%)           |                   | Multi-system organ failure | 6/93 (6.5%)            |                 |
| Undetermined          | 1/152 (0.7%)           |                   | Bleeding                   | 4/93 (4.3%)            |                 |
| Ischaemic             | 5/152 (3.3%)           |                   | Gastro-intestinal          | 3/93 (3.2%)            |                 |
| Vascular injury/access site-related complications | 7/152 (4.6%) |                   | Accidental/trauma          | 3/93 (3.2%)            |                 |
| Thromboembolism       | 4/152 (2.6%)           |                   | Renal failure              | 2/93 (2.2%)            |                 |
| Bleeding              | 3/152 (2.0%)           |                   | Other causes*              | 3/93 (3.2%)            |                 |
| Cardiac tamponade     | 3/152 (2.0%)           |                   |                            |                        |                 |
| Cardiogenic shock     | 3/152 (2.0%)           |                   |                            |                        |                 |
| Unknown causeb        | 39/152 (25.7%)         |                   |                            |                        |                 |
| Other causesc         | 23/152 (15.1%)         |                   |                            |                        |                 |

*Number of deaths overall at 1 year.

All deaths, including those of unknown cause were adjudicated.

All procedural complications have been described previously; this table presents causes of death occurring at a rate ≥2% in the two categories cardiovascular and non-cardiovascular, over 1 year. Causes of deaths <2% are summarized under ‘other causes’.
strongest predictors of 1-year mortality after performing TAVI (Table 4).

Eighteen variables with \( P < 0.2 \) from the univariate analysis were selected to enter the stepwise Cox proportional hazards model. Final results of the multivariable analysis identified pre-procedural (NYHA Class IV and renal insufficiency), procedural (longer procedure time; skin-to-skin), and post-procedural indicators (acute kidney injury, length of stay in intensive care) as independent predictors for 1-year mortality. Higher body mass index remained a protective predictor of survival (Table 4).

Functional evaluation

While most patients were in NYHA Class III/IV at baseline (73.3%), the procedure significantly improved functional capabilities of patients as assessed 30 days after the procedure, with most patients (87.3%) in NYHA class I/II. This improvement was sustained at 1-year with most patients in NYHA class I/II (87.1%). The difference, previously observed at 30 days between the TF and Non-TF cohort, with slower functional recovery in patients who underwent TAVI through Non-TF access, has now disappeared (Figure 2).

Haemodynamics

Mean transaortic gradients significantly decreased and mean effective orifice areas significantly increased after the index procedure. Both parameters remained stable up to 1-year, as did the left-ventricular ejection fraction (Table 5). At 1-year, PVLs were classified of none/trace degree in 72.2% of patients and 25.2% were classified with mild PVLs, while moderate PVLs were rare (2.6%) and no patient experienced severe PVL (Figure 3).

Discussion

One-year outcomes of SOURCE 3, the largest registry on TAVI using the SAPIEN 3, demonstrate that the low 30-day mortality and high-procedural success rate previously reported, translated to a low all-cause mortality at 1 year. Survival according to risk profile, measured using logES, is significantly higher at 1 year in patients with logES < 10 compared to those with logES > 10 (Figure 1).

Main causes of deaths were of cardiovascular origin (62%). Non-cardiovascular fatal complications were observed in 38% of the total cohort of these elderly high-risk patients. Independent predictors of 1-year mortality were found in baseline characteristics (NYHA Class IV and renal insufficiency), procedural characteristics (duration of the procedure), as well as post-procedural characteristics (acute kidney injury, length of stay in intensive care after the procedure). Interestingly, higher BMIs predicted improved 1-year survival, which given the advanced age of patients in SOURCE 3 was not surprising.

Comparison to other transcatheter aortic valve implantation registries

Two registries have also reported on the 1-year outcomes for the latest generation self-expanding THV technology. However, the number of patients enrolled in the REPRISE II Study on the Lotus™ THV (Boston Scientific, Marlborough, MA, USA) \( (n = 120) \) and the DISCOVER Study on the Direct Flow™ THV (Direct Flow Medical, Santa Rosa, CA, USA) \( (n = 100) \) are small. All cause 1-year mortality was comparable to our findings (REPRISE 10.9%, DISCOVER 10%), while major stroke at 1-year was higher in DISCOVER (8%), major bleeding was higher in REPRISE II (21%). The rate of new pacemaker implantations at 1-year was 31.9% (REPRISE) and 21% (DISCOVER) and thus increased compared to SOURCE 3. Neither of the studies provided detailed analysis of predictors for 1-year outcomes or causes of death.

The ADVANCE Study with the CoreValve™ THV (Medtronic, Minneapolis, MN, USA) is larger, with a total of 1015 patients enrolled. All-cause mortality was higher (17.9%), with similar rates of major stroke at 1-year (2.2%) compared to SOURCE 3. Independent predictors of 1-year mortality included mean baseline transaortic valve gradient, postoperative acute kidney injury, and aortic regurgitation at discharge, which has been discussed by the authors to reflect the higher rate of moderate and severe aortic regurgitation of 15.6% at discharge after the index procedure.

Comparison to other SAPIEN 3 registries

Interestingly, the 1-year mortality in SOURCE 3 is very similar compared to the North American experience (PARTNER II) with the SAPIEN 3 (all-cause mortality 14.4%, cardiovascular mortality 8.1% vs. SOURCE 3 12.6% and 8.0%). Differences of all-cause and cardiovascular mortality between TF and Non-TF access groups were higher in PARTNER II, when compared to SOURCE 3.
II, Non-TF access, higher STS score, and disabling strokes were found to be independent predictors of 1-year mortality.

The similarities in the 30-day and 1-year outcomes of the North American and European experience are reassuring and may indicate that the present balloon-expandable THV technology has evolved towards more predictable implantation results, which are independent of operator variability.

**Limitations**

SOURCE 3 is a clinical registry and all outcomes, including those on PVL, are self-reported by the participating centres. Monitoring was conducted by Edwards Lifesciences and 100% of adverse events were monitored on-site.

The modality of TAVI treatment, TF or Non-TF, was decided by the local Heart Teams, based on patients’ condition. Due to this selection bias, the two cohorts are very different in terms of their baseline characteristics as highlighted in Table 1. For that reason, their post-TAVI outcomes could not be compared to each other directly and do not allow conclusions on how the access route itself affects outcomes.

In SOURCE 3, the EuroSCORE I is used to describe the predicted risk of patients for surgical aortic valve replacement. While this makes the comparison with previous SOURCE registries easier, comparison with newer TAVI investigations, in which the STS score or EuroSCORE II are used, is more challenging.

In individuals who suffered from strokes a routine neurological assessment was not performed in all patients. Strokes are self-reported and no routine neurological assessment was performed in all patients.

### Table 4  Predictors of mortality at 1 year

|                          | Univariate model | P-value | Multivariable model | P-value |
|--------------------------|------------------|---------|---------------------|---------|
|                          | HR (95% CI)      |         | HR (95% CI)         |         |
| **Baseline characteristics** |                  |         |                     |         |
| Gender female            | 0.77 (0.6, 0.99) | 0.042   |                     |         |
| Body mass index          | 0.97 (0.94, 1)   | 0.021   | 0.98 (0.96, 1.00)   | 0.027   |
| Baseline NYHA IV         | 2.37 (0.83, 6.81)| 0.109   | 2.53 (1.25, 5.12)   | 0.010   |
| Baseline NYHA III        | 2.23 (0.83, 6.01)| 0.12    |                     |         |
| Left ventricular ejection fraction ≤35% | 1.76 (1.24, 2.48) | 0.001   |                     |         |
| Left ventricular ejection fraction | 0.99 (0.98, 1) | 0.003   |                     |         |
| Mean aortic valve gradient | 0.98 (0.98, 0.99)| <0.0001 |                     |         |
| Logistic EuroSCORE I     | 1.02 (1.01, 1.03)| <0.0001 |                     |         |
| Logistic EuroSCORE I >_20| 1.73 (1.24, 2.42)| 0.001   |                     |         |
| Country Germany          | 1.73 (1.2, 2.99) | 0.051   |                     |         |
| Myocardial infarction    | 1.29 (0.9, 1.85) | 0.16    |                     |         |
| Renal insufficiency      | 2.04 (1.59, 2.63)| <0.0001 | 1.3 (1.06, 1.59)    | 0.010   |
| Mitral regurgitation mod-severe | 1.62 (1.1, 2.37) | 0.014   |                     |         |
| Tricuspid regurgitation mod-severe | 2.19 (1.48, 3.23)| <0.0001 |                     |         |
| Congestive heart failure | 1.28 (0.99, 1.65)| 0.059   |                     |         |
| Coronary artery disease  | 1.49 (1.15, 1.93)| 0.002   |                     |         |
| Diabetes                 | 1.2 (0.92, 1.56) | 0.19    |                     |         |
| Chronic obstructive pulmonary disease | 1.39 (1.02, 1.89)| 0.04    |                     |         |
| Insulin dependent diabetes mellitus | 1.35 (0.94, 1.94)| 0.105   |                     |         |
| Previous pacemaker implantation | 1.31 (0.92, 1.87)| 0.14    |                     |         |
| Atrial fibrillation      | 1.77 (1.35, 2.33)| <0.0001 |                     |         |
| **Procedural characteristics** |                  |         |                     |         |
| Device size (29 mm)      | 1.49 (1.09, 2.04)| 0.014   |                     |         |
| Anaesthesia type conscious sedation to general anaesthesia | 2.37 (0.88, 6.42) | 0.09    |                     |         |
| Volume of contrast media | 0.998 (0.99, 1.00)| 0.18    |                     |         |
| Procedure time (skin to skin) | 1.002 (0.99, 1.01)| 0.15    | 1.005 (1.00, 1.01)| <0.0001 |
| Transfemoral access      | 0.61 (0.44, 0.84)| 0.003   |                     |         |
| New pacemaker at procedure | 0.09 (0.01, 0.67)| 0.019   |                     |         |
| Paravalvular leak at discharge mod-severe | 0.09 (0.00, NA)| 0.97    |                     |         |
| **Post-procedural characteristics** |                  |         |                     |         |
| Days from implant to discharge | 1.04 (1.03, 1.05)| <0.0001 |                     |         |
| Length of stay in intensive care unit | 1.07 (1.05, 1.08)| <0.0001 | 1.05 (1.04, 1.06)| <0.0001 |
| Major vascular complications (up to 30 days) | 2.59 (1.69, 3.98)| <0.0001 |                     |         |
| Acute kidney injury (up to 7 days) | 3.13 (1.93, 5.05)| <0.0001 | 1.93 (1.32, 2.83)| 0.0007  |

CI, confidence interval; HR, hazard ratio; NYHA, New York Heart Association.
**Figure 2** Categorization of patients by NYHA functional class.

**Figure 3** Categorization of patients by PVL grade.
Table 5  Haemodynamic outcomes at baseline, 30 days, and 1 year, with paired analysis on mean change from baseline to 1 year

|                      | Mean ± SD (N) | Baseline | 30 days | 1 year | Mean change from baseline to one year |
|----------------------|---------------|----------|---------|--------|--------------------------------------|
| Mean aortic gradient (mmHg) | 44.1 ± 16.0 (858) | 11.8 ± 5.1 (568) | 12.3 ± 5.1 (858) | -31.9 ± 15.93 (858) |
| Peak aortic gradient (mmHg) | 71.4 ± 23.8 (728) | 21.3 ± 9.2 (465) | 21.9 ± 9.0 (728) | -49.5 ± 23.75 (728) |
| Effective orifice area (cm²) | 0.73 ± 0.210 (434) | 1.64 ± 0.46 (263) | 1.70 ± 1.40 (434) | 0.97 ± 1.41 (434) |
| Left ventricular ejection fraction (%) | 55.5 ± 13.3 (830) | 57.3 ± 11.6 (588) | 57.9 ± 11.3 (830) | 2.4 ± 11.20 (830) |

However, strokes, as all clinical events, were subsequently CEC adjudicated (details are in Supplementary material online, File S1).

Conclusions

SOURCE 3 is a large, ‘real-world’ registry, which confirms the good performance and safety of the SAPIEN 3 at 1-year post-TAVI. The results will inform medical teams in their discussions to identify the optimal treatment option for their patients with aortic stenosis. It provides further evidence on the indication of TAVI and is important for the evaluation of this technique towards lower risk patients. However, longer follow-up is vital to get a better understanding about the durability of this new THV.

Supplementary material

Supplementary material is available at European Heart Journal online.

Author’s contributions

O.W. and A.V. wrote the first draft of the manuscript, which was revised and approved by all co-authors. This manuscript was prepared using a clinical extract of completed and adjudicated 1-year follow-up results from the SOURCE 3 Registry. The Registry is in active follow-up and interim analyses were completed for this report. The authors are aware of the data and leave full responsibility for data completeness and analysis accuracy with the Sponsor.

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