ORIGINAL ARTICLE

# Registry of Transcatheter Aortic-Valve Implantation in High-Risk Patients

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## ABSTRACT

### BACKGROUND

Transcatheter aortic-valve implantation (TAVI) is an emerging intervention for the treatment of high-risk patients with severe aortic stenosis and coexisting illnesses. We report the results of a prospective multicenter study of the French national transcatheter aortic-valve implantation registry, FRANCE 2.

### METHODS

All TAVIs performed in France, as listed in the FRANCE 2 registry, were prospectively included in the study. The primary end point was death from any cause.

### RESULTS

A total of 3195 patients were enrolled between January 2010 and October 2011 at 34 centers. The mean (±SD) age was 82.7±7.2 years; 49% of the patients were women. All patients were highly symptomatic and were at high surgical risk for aortic-valve replacement. Edwards SAPIEN and Medtronic CoreValve devices were implanted in 66.9% and 33.1% of patients, respectively. Approaches were either transarterial (transfemoral, 74.6%; subclavian, 5.8%; and other, 1.8%) or transapical (17.8%). The procedural success rate was 96.9%. Rates of death at 30 days and 1 year were 9.7% and 24.0%, respectively. At 1 year, the incidence of stroke was 4.1%, and the incidence of periprosthetic aortic regurgitation was 64.5%. In a multivariate model, a higher logistic risk score on the European System for Cardiac Operative Risk Evaluation (EuroSCORE), New York Heart Association functional class III or IV symptoms, the use of a transapical TAVI approach, and a higher amount of periprosthetic regurgitation were significantly associated with reduced survival.

### CONCLUSIONS

This prospective registry study reflected real-life TAVI experience in high-risk elderly patients with aortic stenosis, in whom TAVI appeared to be a reasonable option. (Funded by Edwards Lifesciences and Medtronic.)

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Aortic stenosis is now the most frequently diagnosed valvular disease.[1,2] Surgical aortic-valve replacement is the definitive therapy for patients with severe symptomatic aortic stenosis.[2,3] Operative mortality is low among selected elderly patients but increases with the number and severity of coexisting illnesses.[4-6] A survey of hospitalized patients revealed the underreferral to surgery of those with severe symptomatic aortic stenosis.[7]

Transcatheter aortic-valve implantation (TAVI) was developed as an alternative to surgical aortic-valve replacement in this high-risk patient population. Ten years after the first implantation by Cribier and colleagues,[8] more than 50,000 patients have been treated by TAVI worldwide. There have been a number of reports from device-specific and national registries,[9-17] and one randomized trial has compared TAVI with medical therapy in patients in whom surgery was contraindicated[18] and with surgical aortic-valve replacement in high-risk patients.[19]

In 2010, a national TAVI coordination and monitoring program was set up in France to analyze patient characteristics and clinical outcomes in all centers performing TAVI. These procedures were performed with transfemoral, transapical, or subclavian approaches. This large registry reflects real-life experience, including all patients from all centers in France. Here, we report the results of our analysis of the characteristics and outcomes of the patients included in the registry.

## Methods

### Patients

As of January 2010, a total of 33 centers were authorized to perform TAVI by the French Ministry of Health on the basis of the presence of an on-site multidisciplinary team (consisting of an interventional cardiologist, a cardiothoracic surgeon, a cardiologist, an echocardiographer, an anesthetist, an imaging specialist, and a geriatrician); an annual volume of a least 200 surgical aortic-valve replacements; previous experience with balloon aortic valvuloplasty, TAVI, or both; and an even geographic distribution of centers throughout the country. The center in Monaco subsequently volunteered to participate, for a total of 34 centers.

On the basis of criteria specified by the French Ministry of Health, patients included in the registry were symptomatic adults with severe aortic stenosis who were not candidates for surgical aortic-valve replacement because of coexisting illnesses. Severe aortic stenosis was defined as an aortic-valve area of less than 0.8 $cm^2$, a mean aortic-valve gradient of 40 mm Hg or more, or a peak aortic jet velocity of 4.0 m per second or more. All patients had New York Heart Association (NYHA) class II, III, or IV symptoms. All patients who had undergone implantation on the basis of these criteria in France and Monaco since 2010 were prospectively included in the registry, without the use of exclusion criteria.

The French Aortic National CoreValve and Edwards (FRANCE 2) Registry was established under the French Societies of Cardiology and of Thoracic and Cardiovascular Surgery. Personnel at all centers underwent structured training. Supervisors monitored cases at each new institution until they were confident that clinicians had acquired sufficient expertise to perform safe independent implantation. Four centers were in the learning phase, and the first procedures were supervised; the others had already each performed more than five procedures.

Each multidisciplinary team could choose to implant one of two commercially available valves: the balloon-expandable Edwards SAPIEN or SAPIEN XT prosthesis (Edwards Lifesciences) or the self-expandable CoreValve (Medtronic). Both devices were implanted at 30 centers, and only the Edwards SAPIEN was implanted at 4 centers. We did not compare the femoral and nonfemoral access routes according to device availability, since both devices were available in the majority of the centers (88%).

At each center, the multidisciplinary team determined eligibility for TAVI on the basis of systematic clinical evaluation, angiographic assessment, multislice computed tomography, and echocardiography. All centers adopted a policy of using the transfemoral approach first, with criteria for the use of nontransfemoral approaches that were based on the size and degree of tortuosity, calcification, and atheroma of the aortoiliofemoral arterial tree, as assessed by the multidisciplinary team. SAPIEN devices were implanted by either the transfemoral or transapical route, and CoreValve devices by the transfemoral or subclavian route.

All patients provided written informed consent before undergoing the procedure, including con-

sent for anonymous processing of their data. The registry was approved by the institutional review board of the French Ministry of Health. Device manufacturers funded the registry but did not have any role in data collection or analysis or in the preparation of the manuscript.

### STUDY DEVICES AND PROCEDURES

The study design and the procedural characteristics for the two prostheses have been described previously.[15,20-23] Briefly, the Edwards SAPIEN device consists of bovine pericardial tissue mounted in a balloon-expandable, stainless-steel stent or, more recently, a cobalt–chromium, open-cell stent (SAPIEN XT). Three sizes are available (23, 26, and 29 mm) for aortic-valve annulus sizes of 18 to 27 mm. The 23-mm and 26-mm models can be implanted through either a transfemoral approach (Retroflex 3 delivery catheter, 22-French or 24-French introducer; or Novaflex delivery catheter, 18-French or 19-French introducer) or a transapical approach (Ascendra catheter, 24-French introducer). The 29-mm model requires a transapical approach.

The CoreValve prosthesis consists of porcine pericardial tissue, mounted in a self-expanding nitinol stent. Transfemoral and subclavian procedures were initially performed with an 18-French delivery catheter, later improved by an AccuTrak Stability Layer. Three sizes are available (26, 29, and 31 mm) for aortic-valve annulus sizes of 20 to 29 mm.

There were no prespecified recommendations with respect to the use of a transfemoral, transapical, or subclavian approach. Transarterial access was obtained percutaneously or after surgical cut-down, and transapical access by anterior minithoracotomy. Valve implantation was preceded by balloon dilation. Bursts of rapid ventricular pacing were used with the Edwards SAPIEN. The femoral access was closed surgically or percutaneously (Prostar XL, Abbott). All patients received aspirin (≤160 mg daily) and clopidogrel (300-mg loading dose, then 75 mg daily) before the procedure and aspirin alone after 1 month of dual therapy. The choice between general and local anesthesia for transfemoral implantation was left up to the individual team.

### STUDY END POINTS

The primary end point was death from any cause at 1 month, 6 months, and 1, 2, 3, 4, and 5 years. Secondary safety end points were major adverse cardiovascular or cerebrovascular events, cardiac events, cardiac or vascular surgery, bleeding or stroke during follow-up, and NYHA functional class. Secondary efficacy end points were the success rate and complications on the basis of Valve Academic Research Consortium (VARC) criteria,[24] with periodic echocardiographic assessment of aortic-valve function during the first 3 years, including evaluation of the mean gradient and valve area, as well as assessment for the presence and severity of aortic-valve or mitral-valve regurgitation. The severity of regurgitation was graded on a scale from 0 to 4, with higher grades indicating greater severity. Characteristics of the patients, access routes, and death rates were compared between 2010 and 2011.

### SURGICAL RISK FACTORS

We evaluated risk factors for cardiovascular surgery using the Society of Thoracic Surgeons (STS) score (on a scale from 0 to 100%, with higher numbers indicating greater risk and an STS score of more than 10% indicating very high surgical risk), and the logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE), which is calculated by a logistic-regression equation (on a scale from 0 to 100%, with higher scores indicating greater risk and a score of more than 20% indicating very high surgical risk).

### STUDY OVERSIGHT

The scientific committee was responsible for drawing up the protocol and case-report form. (For details, see the Supplementary Appendix, available with the full text of this article at NEJM.org.) Committee members had unrestricted access to the data after the database was locked, drew up the analysis plan, prepared all drafts of the manuscript, and made the decision to submit the manuscript for publication. They attest to the integrity of the study, completeness and accuracy of the data, and fidelity of the report to the protocol, which is available at NEJM.org. There were no data confidentiality agreements between companies and authors.

### DATA MANAGEMENT

Mortality was adjudicated by an independent clinical events committee (see the Supplementary Appendix). All adverse events were adjudicated according to the VARC classification system.[24] Postprocedural aortic regurgitation was assessed

by means of echocardiography. Data were recorded on a standardized electronic case-report form and sent to a central database (Axonal) over the Internet. Database quality control was performed by checking data against source documents for 10% of patients in randomly selected centers. All fields were examined for missing data or outliers, and teams were asked to complete or correct data wherever possible. Outlying data were checked and excluded if they were erroneous; such exclusion accounted for less than 1% of data.

### STATISTICAL ANALYSIS

Absolute numbers, percentages, and means (±SD) were computed to describe the population. Mortality was calculated with the use of Kaplan–Meier survival analysis. For comparisons between groups and univariate analysis of associated variables, we used Student's t-test analysis of variance or nonparametric tests for continuous variables and a chi-square test or Fisher's exact test for categorical variables. We used a univariate Cox model to analyze 1-year survival data, with a P value of less than 0.20 indicating statistical significance. We used a multivariate Cox model with stepwise regression, with adjustment for age, the approach route, logistic EuroSCORE, NYHA class, presence or absence of a history of cerebral vascular disease or myocardial infarction, number of patients included per study center, and presence or absence of periprosthetic regurgitation. The estimated hazard ratio was provided by the Cox model. All tests were two-sided. A P value of 0.05 was considered to indicate statistical significance. All analyses were performed with the use of SAS software, version 8.2.

## RESULTS

### PATIENTS

From January 2010 through October 2011, a total of 3195 patients underwent TAVI at 34 hospitals. Completeness of the data was checked against the national database maintained by the French health care authorities. The median follow-up was 114 days (interquartile range, 31 to 242), and follow-up was complete for 3188 patients (99.8%).

The mean number of patients who were enrolled in each hospital was 94 (range, 25 to 251). The mean age was 82.7±7.2 years (range, 24 to 101); 49% of patients were women. Severe aortic stenosis was confirmed in all cases, with a mean aortic-valve area of 0.7±0.2 $cm^2$ and a mean gradient of 48.1±16.5 mm Hg (Table 1). The mean aortic annulus diameter was 22.1±2.2 mm. The mean logistic EuroSCORE was 21.9±14.3%, and the mean STS score was 14.4±12.0%. A total of 835 patients (26.1%) had a logistic EuroSCORE of less than 20% and an STS score of less than 10% but had a coexisting condition for which surgery was contraindicated, including severe calcification of the aorta (in 8.3% of patients), a chest-wall deformity or damage by chest-wall irradiation (17.1%), or oxygen-dependent respiratory insufficiency or other coexisting condition not included in risk scores (51.4%); 7.4% of patients had a technical contraindication for extracorporeal circulation, and 15.8% opted to undergo TAVI rather than conventional surgery.

### PROCEDURAL CHARACTERISTICS

Most procedures were performed in a catheterization laboratory (74.7%), with the remainder performed in a hybrid room (15.3%) or an operating room (10.0%). Edwards SAPIEN devices were implanted in 66.9% of patients, and Medtronic CoreValve devices in the others. The implantation approach was transfemoral in 74.6% of patients, transapical in 17.8%, subclavian in 5.8%, and transaortic or transcarotid in 1.8%. Patients with coronary or peripheral arterial disease and those with an increased logistic EuroSCORE were more likely to undergo a transapical procedure (P<0.001 for both comparisons) (Table 2). Procedures were performed with the use of local anesthesia for 40.8% of femoral approaches, with surgical puncture-site closure in 24.0%. The mean duration of time in the intensive care unit was 4.9±4.8 days, and the mean hospital stay was 11.1±8.0 days. The procedural success rate (completion, with lowered mean gradient) was 96.9%, without significant differences among the approaches (P=0.35) (Table 3).

### PRIMARY END POINT

At 30 days, mortality from all causes on Kaplan–Meier analysis (primary end point) was 9.7% in the cohort as a whole (Table 3). Subsequent rates of death were 18.6% at 6 months (1545 patients) and 24.0% at 1 year (725 patients) (Fig. 1).

### SECONDARY END POINTS

Quality control did not show that centers underreported adverse events in the database, as com-

**Table 1. Characteristics of the Patients at Baseline.***

| Characteristic | All Patients (N=3195) | Edwards SAPIEN (N=2107) | Medtronic CoreValve (N=1043) |
|---|---|---|---|
| Age — yr | 82.7±7.2 | 82.9±7.2 | 82.3±7.2 |
| Male sex — no. (%) | 1630 (51.0) | 981 (46.6) | 626 (60.0) |
| Society of Thoracic Surgeons score — %† | 14.4±11.9 | 15.6±12.4 | 14.2±11.2 |
| Logistic EuroSCORE — %‡ | 21.9±14.3 | 22.2±14.3 | 21.3±14.3 |
| NYHA class III or IV — no./total no. (%) | 2376/3132 (75.9) | 1565/2072 (75.5) | 788/1035 (76.1) |
| Clinical history — no./total no. (%) | | | |
| Coronary artery disease | 1483/3093 (47.9) | 997/2046 (48.7) | 474/1025 (46.2) |
| Previous myocardial infarction | 508/3093 (16.4) | 347/2046 (17.0) | 158/1025 (15.4) |
| Previous CABG | 564/3093 (18.2) | 373/2046 (18.2) | 188/1025 (18.3) |
| Cerebrovascular disease | 308/3093 (10.0) | 205/2046 (10.0) | 101/1025 (9.9) |
| Aortic abdominal aneurysm | 148/3093 (4.8) | 98/2046 (4.8) | 50/1025 (4.9) |
| Peripheral vascular disease | 643/3093 (20.8) | 447/2046 (21.8) | 191/1025 (18.6) |
| Chronic obstructive pulmonary disease | 790/3093 (25.5) | 518/2046 (25.3) | 269/1025 (26.2) |
| Renal dialysis | 82/3093 (2.7) | 47/2046 (2.3) | 32/1025 (3.1) |
| Atrial fibrillation | 820/3083 (26.6) | 514/2038 (25.2) | 303/1024 (29.6) |
| Permanent pacemaker | 447/3135 (14.3) | 280/2073 (13.5) | 160/1034 (15.5) |
| Pulmonary hypertension | 478/2435 (19.6) | 324/1635 (19.8) | 151/787 (19.2) |
| Echocardiographic findings | | | |
| Aortic-valve area — $cm^2$ | 0.7±0.2 | 0.7±0.2 | 0.7±0.2 |
| Mean aortic-valve gradient — mm Hg | 48.1±16.5 | 48.6±16.5 | 47.1±16.4 |
| Left ventricular ejection fraction — % | 53.2±14.1 | 53.8±14.0 | 52.0±14.0 |
| Moderate or severe mitral regurgitation — no./total no. (%)§ | 58/2966 (2.0) | 37/1974 (1.9) | 21/972 (2.2) |
| Previous surgical aortic-valve replacement — no./total no. (%) | 49/3093 (1.6) | 18/2046 (0.9) | 31/1025 (3.0) |
| Life expectancy <1 yr — no./total no. (%) | 102/3093 (3.3) | 40/2046 (2.0) | 41/1025 (4.0) |
| Patient's decision to undergo TAVI — no./total no. (%) | 499/3165 (15.8) | 358/2096 (17.1) | 136/1039 (13.1) |

* Plus–minus values are means ±SD. Data regarding the type of valve were missing for 45 patients. CABG denotes coronary-artery bypass grafting, and NYHA New York Heart Association.

† The Society of Thoracic Surgeons score measures risk at the time of cardiovascular surgery on a scale from 0 to 100%, with higher numbers indicating greater risk. A score of more than 10% indicates very high surgical risk.

‡ The logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE), which measures patient risk at the time of cardiovascular surgery, is calculated by a logistic-regression equation. Scores range from 0 to 100%, with higher scores indicating greater risk. A logistic EuroSCORE of more than 20% indicates very high surgical risk.

§ Moderate or severe mitral regurgitation was defined as regurgitation of grade 3+ or higher.

pared with the medical files. The incidence of stroke was 3.4% at 30 days, 3.8% at 6 months, and 4.1% at 1 year, with rates of major stroke of 1.9%, 2.1%, and 2.2%, respectively. A new, permanent pacemaker was required more often in patients receiving CoreValve devices than in those receiving SAPIEN devices (24.2% vs. 11.5%). At 30 days, intraprosthetic aortic regurgitation was observed in 168 of 1822 patients (9.2%), with grade 1 regurgitation in 143 patients (7.8%), grade 2 in 22 (1.2%), and grade 3 in 3 (0.2%). Periprosthetic aortic regurgitation was observed in 1191 of 1846 patients (64.5%), with grade 1 regurgitation in 875 (47.4%), grade 2 in 301 (16.3%), and grade 3 in 15 (0.8%). Major vascular complications were reported in 156 patients (4.7%). Among all the groups, two valves were implanted during the procedure in 72 patients (2.3%), and in 12 patients (0.4%), the pro-

**Table 2. Characteristics of the Patients, According to TAVI Approach.***

| Characteristic | Transfemoral Approach (N=2361) | Transapical Approach (N=567) | Subclavian Approach (N=184) | P Value† |
|---|---|---|---|---|
| Age — yr | 83.0±7.2 | 81.5±7.4 | 82.2±6.7 | <0.001 |
| Male sex — no./total no. (%) | 1120 (47.4) | 332 (58.6) | 131 (71.2) | <0.001 |
| Logistic EuroSCORE — % | 21.2±14.7 | 24.8±14.7 | 20.3±15.2 | <0.001 |
| Society of Thoracic Surgeons score — % | 14.5±11.9 | 15.1±13.8 | 16.6±13.4 | 0.15 |
| NYHA class III or IV — no./total no. (%) | 1808/2323 (77.8) | 388/554 (70.0) | 130/182 (71.4) | <0.001 |
| Clinical history — no./total no. (%) | | | | |
| Coronary artery disease | 1018/2293 (44.4) | 325/547 (59.4) | 104/178 (58.4) | <0.001 |
| Previous myocardial infarction | 333/2293 (14.5) | 137/547 (25.0) | 33/178 (18.5) | <0.001 |
| Previous CABG | 348/2293 (15.2) | 164/547 (30.0) | 43/178 (24.2) | <0.001 |
| Previous balloon aortic valvuloplasty | 389/2293 (17.0) | 106/547 (19.4) | 39/178 (21.9) | 0.13 |
| Cerebrovascular disease | 219/2293 (9.6) | 60/547 (11.0) | 20/178 (11.2) | 0.50 |
| Aortic abdominal aneurysm | 59/2293 (2.6) | 54/547 (9.9) | 28/178 (15.7) | <0.001 |
| Peripheral vascular disease | 286/2293 (12.5) | 263/547 (48.1) | 74/178 (41.6) | <0.001 |
| Chronic obstructive pulmonary disease | 580/2293 (25.3) | 124/547 (22.7) | 63/178 (35.4) | 0.003 |
| Renal dialysis | 60/2293 (2.6) | 17/547 (3.1) | 4/178 (2.2) | 0.80 |
| Atrial fibrillation | 638/2287 (27.9) | 114/544 (21.0) | 56/178 (31.5) | 0.002 |
| Pulmonary hypertension | 364/1820 (20.0) | 72/429 (16.8) | 31/132 (23.5) | 0.16 |
| Severe aortic calcification | 127/2314 (5.5) | 10/556 (1.8) | 21/177 (11.9) | <0.001 |
| Harmful chest-wall irradiation | 144/2320 (6.2) | 29/553 (5.2) | 3/177 (1.7) | 0.02 |
| Chest-wall deformity | 62/2326 (2.7) | 6/557 (1.1) | 6/179 (3.4) | 0.06 |
| Previous surgical aortic-valve replacement | 37/2293 (1.6) | 8/547 (1.5) | 4/178 (2.2) | 0.72 |
| Life expectancy <1 yr — no./total no. (%) | 64/2293 (2.8) | 8/547 (1.5) | 8/178 (4.5) | 0.06 |
| Patient's decision to undergo TAVI — no./total no. (%) | 356/2349 (15.2) | 82/559 (14.7) | 23/182 (12.6) | 0.64 |

* Plus–minus values are means ±SD. Data for 83 patients who underwent transcarotid or transaortic approaches are not provided.
† P values are for the overall comparison among the three TAVI approaches.

cedure was converted to surgical aortic-valve replacement.

At 6 months, intraprosthetic aortic regurgitation was observed in 114 of 945 patients (12.1%), with grade 1 regurgitation in 96 (10.2%) and grade 2 in 18 (1.9%); periprosthetic regurgitation was observed in 618 of 983 patients (62.9%), with grade 1 regurgitation in 452 (46.0%), grade 2 in 158 (16.1%) and grade 3 in 8 (0.8%). At 1 year, intraprosthetic aortic regurgitation was observed in 43 of 458 patients (9.4%), with grade 1 regurgitation in 36 (7.9%), grade 2 in 6 (1.3%), and grade 3 in 1 (0.2%); periprosthetic regurgitation was observed in 285 of 426 patients (66.9%), with grade 1 regurgitation in 201 (47.2%), grade 2 in 79 (18.5%), and grade 3 in 5 (1.2%).

Mortality was significantly lower with the transfemoral approach than with the transapical approach; the respective rates of death were 8.5% and 13.9% at 30 days and 17.2% and 22.4% at 6 months (Fig. 1). There was no significant difference in the rate of procedural success according to approach. Complications as defined by VARC differed significantly among the approaches, except for stroke, minor and life-threatening bleeding, and aortic regurgitation (Table 3). The volume of implantation procedures that were performed at each study center had no significant effect on outcome.

On multivariate analysis, the factors that had a significant association with 1-year mortality were an increased logistic EuroSCORE (hazard ra-

**Table 3. Outcomes According to TAVI Approach and Device.***

| Outcomes | All Patients (N=3195) | Transfemoral Approach (N=2361) | Transapical Approach (N=567) | Subclavian Approach (N=184) | P Value† | Edwards SAPIEN (N=2107) | Medtronic CoreValve (N=1043) |
|---|---|---|---|---|---|---|---|
| Procedural success — no. (%) | 3095 (96.9) | 2293 (97.1) | 544 (95.9) | 178 (96.7) | 0.35 | 2044 (97.0) | 1018 (97.6) |
| Hospital stay — days | 11.1±8.0 | 10.5±8.1 | 13.3±7.8 | 11.6±6.0 | <0.001 | 10.9±7.5 | 11.3±8.9 |
| Death — no. (%) | | | | | | | |
| At 30 days | | | | | | | |
| From any cause | 293 (9.7) | 190 (8.5) | 77 (13.9) | 19 (10.1) | <0.001‡ | 195 (9.6) | 91 (9.4) |
| From cardiovascular cause§ | 212 (7.0) | 132 (5.9) | 59 (10.8) | 15 (8.7) | 0.73 | 141 (7.0) | 64 (6.7) |
| At 6 mo | | | | | | | |
| From any cause | 474 (18.6) | 321 (17.2) | 110 (22.4) | 32 (23.3) | 0.002‡ | 312 (18.1) | 155 (19.6) |
| From cardiovascular cause§ | 301 (11.7) | 197 (10.5) | 77 (15.7) | 18 (12.1) | 0.81 | 201 (11.5) | 93 (11.7) |
| At 1 yr | | | | | | | |
| From any cause | 528 (24.0) | 355 (21.7) | 129 (32.3) | 33 (25.1) | <0.001‡ | 352 (24.0) | 168 (23.7) |
| From cardiovascular cause§ | 324 (14.3) | 212 (12.7) | 84 (19.8) | 19 (14.4) | 0.79 | 217 (14.2) | 100 (14.3) |
| Implantation of two valves — no. (%) | 72 (2.3) | 47 (2.0) | 16 (2.9) | 5 (2.8) | 0.46 | 31 (1.4) | 37 (3.5) |
| Conversion to open surgery — no. (%) | 12 (0.4) | 16 (0.7) | 4 (0.7) | 0 (0.0) | 0.84 | 8 (0.4) | 4 (0.4) |
| Periprosthetic regurgitation at 30 days — no./total no. (%) | | | | | 0.09 | | |
| Grade 0 | 724/1915 (37.8) | 483/1418 (34.1) | 173/334 (51.8) | 37/112 (33.0) | | 515/1256 (41.0) | 203/642 (31.6) |
| Grade 1 | 875/1915 (45.7) | 671/1418 (47.3) | 131/334 (39.2) | 58/112 (51.8) | | 567/1256 (45.1) | 301/642 (46.9) |
| Grade 2 | 301/1915 (15.7) | 251/1418 (17.7) | 30/334 (9.0) | 15/112 (13.4) | | 169/1256 (13.5) | 128/642 (19.9) |
| Grade 3 | 15/1915 (0.8) | 13/1418 (0.9) | 0 | 2/112 (1.8) | | 5/1256 (0.4) | 10/642 (1.6) |
| Complications at 1 yr — no. (%) | | | | | | | |
| Stroke | | | | | | | |
| Major | 72 (2.3) | 51 (2.2) | 12 (2.1) | 5 (2.7) | 0.88 | 41 (1.9) | 27 (2.6) |
| Minor | 59 (1.8) | 36 (1.5) | 13 (2.3) | 8 (4.3) | 0.07 | 41 (1.9) | 18 (1.7) |
| Myocardial infarction | 37 (1.2) | 20 (0.8) | 10 (1.8) | 6 (3.3) | 0.004 | 16 (0.8) | 20 (1.9) |
| Bleeding | | | | | | | |
| Life-threatening | 39 (1.2) | 29 (1.2) | 8 (1.4) | 1 (0.5) | 0.76 | 32 (1.5) | 6 (0.6) |
| Major | 144 (4.5) | 36 (1.5) | 19 (3.4) | 6 (3.3) | <0.001 | 42 (2.0) | 16 (1.5) |
| Minor | 236 (7.4) | 161 (6.8) | 54 (9.5) | 13 (7.1) | 0.08 | 166 (7.9) | 70 (6.7) |
| Vascular complication | | | | | | | |
| Major | 150 (4.7) | 129 (5.5) | 11 (1.9) | 8 (4.3) | 0.002 | 57 (2.7) | 47 (4.5) |
| Minor | 160 (5.0) | 139 (5.9) | 9 (1.6) | 12 (6.5) | <0.001 | 60 (2.8) | 49 (4.7) |
| New pacemaker | 497 (15.6) | 359 (15.2) | 77 (13.6) | 47 (25.5) | <0.001 | 243 (11.5) | 252 (24.2) |
| Valve migration | 40 (1.3) | 28 (1.2) | 8 (1.4) | 2 (1.1) | 0.91 | 23 (1.1) | 17 (1.6) |

* Plus–minus values are means ±SD. Data for 83 patients who underwent transcarotid or transaortic approaches are not provided. Data regarding the type of valve were missing for 45 patients. Mortality was calculated with the use of Kaplan–Meier survival analysis.
† P values are for the overall comparison among the three TAVI approaches unless otherwise noted.
‡ Only the difference between the transfemoral approach and the transapical approach was significant.
§ Deaths from unknown causes were assumed to be deaths from cardiovascular causes.

tio per 1% increase, 1.37; 95% confidence interval [CI], 1.19 to 1.58), NYHA functional class III or IV versus class I or II (hazard ratio, 1.49; 95% CI, 1.09 to 2.03), transapical approach versus transfemoral approach (hazard ratio, 1.45; 95% CI, 1.09 to 192), and a periprosthetic regurgitation

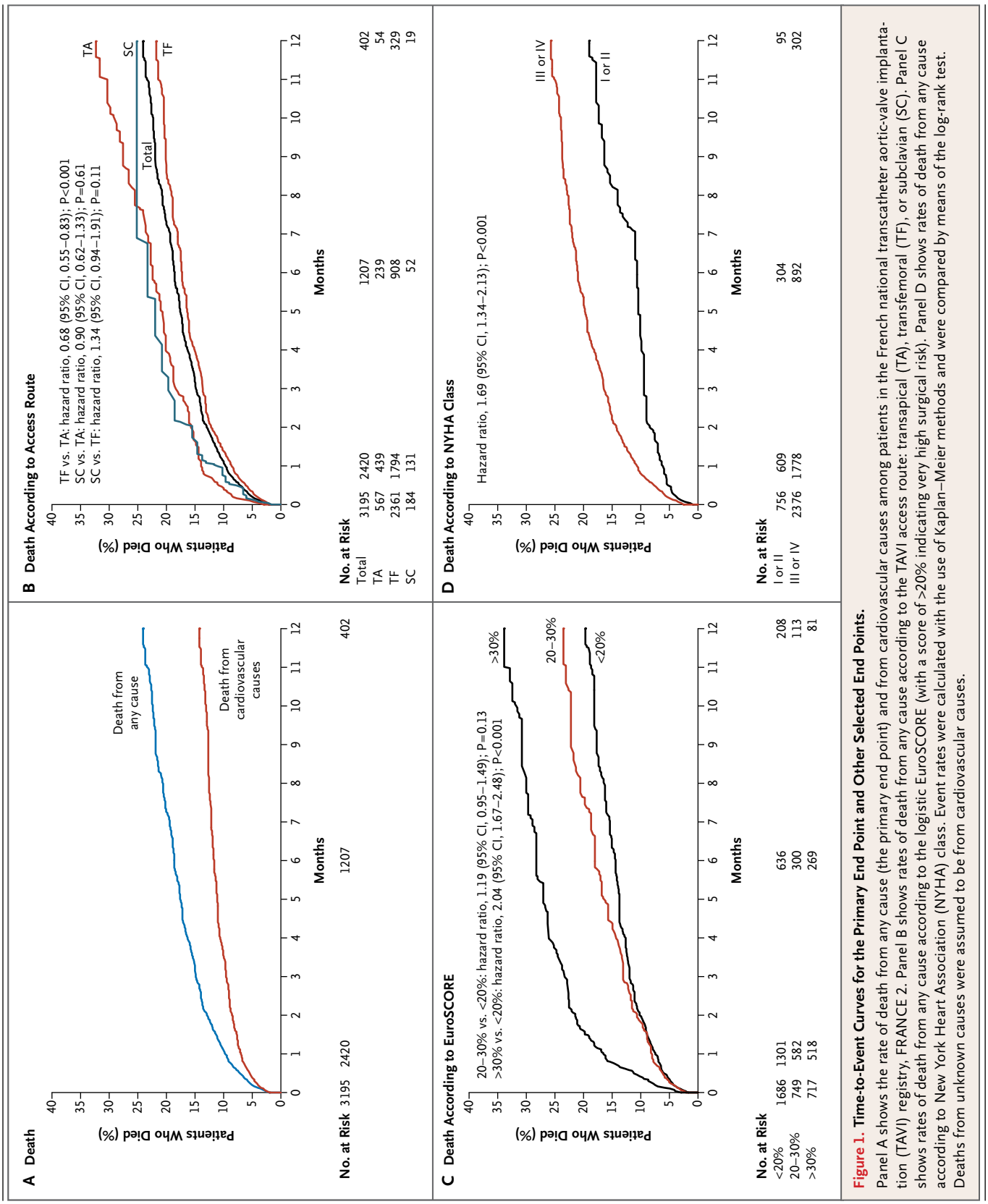


**Figure 1. Time-to-Event Curves for the Primary End Point and Other Selected End Points.**

Panel A shows the rate of death from any cause (the primary end point) and from cardiovascular causes among patients in the French national transcatheter aortic-valve implantation (TAVI) registry, FRANCE 2. Panel B shows rates of death from any cause according to the TAVI access route: transapical (TA), transfemoral (TF), or subclavian (SC). Panel C shows rates of death from any cause according to the logistic EuroSCORE (with a score of >20% indicating very high surgical risk). Panel D shows rates of death from any cause according to New York Heart Association (NYHA) class. Event rates were calculated with the use of Kaplan–Meier methods and were compared by means of the log-rank test. Deaths from unknown causes were assumed to be from cardiovascular causes.

grade of 2 or higher versus a grade of less than 2 (hazard ratio, 2.49; 95% CI, 1.91 to 3.25). At 1 year, 89.5% of surviving patients were asymptomatic or only mildly symptomatic (NYHA class I or II) (Fig. 2).

The numbers of patients who underwent TAVI were 1551 in 2010 and 1640 in 2011. From 2010 to 2011, there were significant reductions in the baseline logistic EuroSCORE (22.8±14.8 in 2010 vs. 20.9±13.8 in 2011), the use of the transapical route (301 of 1544 patients [19.5%] vs. 263 of 1623 patients [16.2%]), and the use of general anesthesia (1137 of 1550 patients [73.4%] vs. 1042 of 1604 patients [65.0%]) (P<0.001 for all comparisons); during the same period, the proportion of patients who preferred TAVI instead of conventional surgery increased significantly (223 of 1545 patients [14.4%] vs. 276 of 1616 patients [17.1%], P=0.04). There was no significant change in 30-day mortality from 2010 to 2011, as calculated by the Kaplan–Meier method (155 of 1551 patients [10.1%] died in 2010 and 138 of 1640 patients [9.2%] died in 2011, P=0.49).

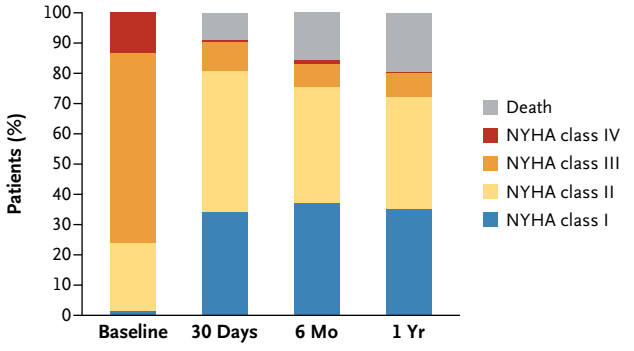


**Figure 2. NYHA Functional Status.**
Shown are the proportions of patients in each NYHA functional class on the basis of their symptoms at each time point. Data on death include deaths from all causes.

## DISCUSSION

We evaluated data from a national multicenter registry of a large consecutive series of patients undergoing TAVI, with quality control in randomly selected centers. The FRANCE 2 Registry captured every TAVI performed in all 34 active centers in France and Monaco, without selection bias. The data provided important information on TAVI in real-life practice in unselected centers; the team of cardiologists and surgeons at 30 of these centers had experience with TAVI.

Among the 3195 TAVIs that were performed, 80.4% were percutaneous and 19.6% were surgical; 17.6% of the procedures were performed with a transapical approach and 1.8% with a transaortic or transcarotid approach. A SAPIEN device was used in 66.9% of patients and a CoreValve device in 33.1%. The only comparable data available for the two types of valves were recently reported in registry studies in the United Kingdom[16] (with 47.1% of patients receiving a SAPIEN device and 31.1% undergoing a transapical procedure), in Germany[14] (with 15.6% receiving a SAPIEN device and 4.4% undergoing a transapical procedure), and in Belgium[17] (with 57.0% receiving a SAPIEN device and 14.3% undergoing a transapical procedure).

In our study, 30-day mortality was 9.7%, a rate that was similar to those reported previously by other registries, ranging from 5.4 to 11.5%.[9-11,13,14,16,17] In comparison, the rates of death reported in the Placement of Aortic Transcatheter Valves (PARTNER) trial (ClinicalTrials.gov number, NCT00530894) were 5.0% for the high-risk patients who were not candidates for surgical valve replacement (cohort B) and 5.2% for the high-risk patients who were candidates for surgical replacement (cohort A, as-treated analysis).[18,19]

The higher mortality associated with the transapical approach, as compared with the transfemoral approach, was similar to that reported in other studies.[13,16-18,25] The explanation is probably multifactorial. In our registry, patients undergoing the transapical procedure had a higher-risk profile than those undergoing the transfemoral procedure, as in other registries.[16,17,26] However, it is also possible that the learning curve for clinicians is steeper for the transapical approach than for the transfemoral approach.[26]

On multivariate analysis, the only independent predictors of 1-year mortality were increased risk on the logistic EuroSCORE, NYHA functional class III or IV, the use of a transapical approach, and periprosthetic regurgitation grade of 2 or more (on a scale of 0 to 4). The effect of the logistic EuroSCORE was also reported for the Edwards SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) registry[26] and the Italian registry.[11] The negative effect of periprosthetic regurgitation has been reported in studies of both the SAPIEN and CoreValve devices.[11,16,27,28] The 1-year survival rate of 76.0% in our registry was nearly the same

as the rates in the SOURCE and U.K. registries and in cohort A of the PARTNER trial.

In our study, one of the most common complications was the need for a permanent pacemaker (in 15.6% of patients). In the other registries, the rates were similar, with 13% in Belgium,[17] 16.3% in the United Kingdom,[16] 16.6% in Italy,[11] and 6.7% in SOURCE.[13] In the PARTNER trial, the reported rates were 3.4% for cohort B[18] and 3.8% for cohort A.[19] The proportion of patients who needed a permanent pacemaker was highest in the German registry (39.3%).[14] The higher rate of pacemaker placement with CoreValve implantation than with SAPIEN implantation in our study confirmed the findings in previous studies.[14,16,17] The incidence of stroke (4.1%) was similar to that in other registries and in the PARTNER trial, without a significant difference according to approach. Major vascular complications occurred more often in patients undergoing the transfemoral procedure (5.5%) than in those undergoing the transapical procedure (1.9%), a finding that was consistent with those in other registries.[13,16] Conversely, life-threatening or major bleeding was more frequent in patients undergoing the transapical procedure (4.8%) than in those undergoing the transfemoral procedure (2.7%). In the PARTNER trial,[18,19] rates of major bleeding (9.3% in cohort B and 16.8% in cohort A) and major complications (16.2% in cohort B and 9.3% in cohort A) were higher, a difference that is possibly due in part to different definitions (highlighting the need for a consensus definition of complications). Our data showed a substantial improvement in functional status.

Patient and procedural characteristics changed between 2010 and 2011. The Logistic EuroSCORE decreased significantly without an effect on 30-day mortality, as did the need for general anesthesia and the frequency of a transapical approach, probably because of the advent of the new transaortic approach and the decreased size of the Edwards valve-delivery systems. Patient choice in favor of TAVI increased significantly (from 14.4% to 17.1%, P=0.04). During the same period, the increase in the proportion of patients who declined surgical valve replacement even though they were candidates for surgery is a reflection of real-life practice, despite the national recommendations. The rapid increase in the use of TAVI entails a risk that candidates for conventional aortic-valve replacement will be treated percutaneously. The German registry[14] reported that 13% of patients had opted to undergo TAVI rather than conventional aortic-valve surgery, a rate that is alarming and clearly a case of off-label use of the procedure if the EuroSCORE is below 20%.

Our study has a number of limitations. Whereas our data on numbers of procedures and survival are extremely robust, those concerning complications are probably less so, since they were reported by the participating centers and were not independently adjudicated, owing to the lack of a central core laboratory for evaluating echocardiographic and neurologic assessments.

In conclusion, TAVI is a new therapeutic option for high-risk patients with severe aortic stenosis. Complication rates appear to be acceptable, considering the high frequency of coexisting illnesses in such patients. Further progress in patient-selection criteria, postprocedural care, and choice of optimal access are essential for improving results. TAVI appears to be a reasonable option in inoperable or high-risk patients with severe symptomatic aortic stenosis.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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## APPENDIX

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