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ORIGINAL ARTICLE

Predictive factors of early mortality after transcatheter aortic valve implantation: individual risk assessment using a simple score

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ABSTRACT

Objective Decision making for intervention in symptomatic aortic stenosis should balance the risks of surgery and of transcatheter aortic valve implantation (TAVI). We identified the factors associated with early mortality after TAVI and aimed to develop and validate a simple risk score.

Methods A population of 3833 consecutive patients was randomly split into two cohorts comprising 2552 and 1281 patients, used respectively to develop and validate a scoring system predicting 30-day or in-hospital mortality.

Results TAVI was performed using the Edwards Sapien prosthesis in 2551 (66.8%) patients and the Medtronic Corevalve in 1270 (33.2%). Approach was transfemoral in 2801 (73.4%) patients, transapical in 678 (17.8%), subclavian in 219 (5.7%) and other in 117 (3.1%). Early mortality was 10.0% (382 patients). A multivariate logistic model identified the following predictive factors of early mortality: age ≥90 years, body mass index <30 Kg/m^2, New York Heart Association class IV, pulmonary hypertension, critical haemodynamic state, ≥2 pulmonary oedemas during the last year, respiratory insufficiency, dialysis and transapical or other (transaortic and transcarotid) approaches. A 21-point predictive score was derived. C-index was 0.67 for the score in the development cohort and 0.59 in the validation cohort. There was a good concordance between predicted and observed 30-day mortality rates in the development and validation cohorts.

Conclusions Early mortality after TAVI is mainly related to age, the severity of symptoms, comorbidities and transapical approach. A simple score can be used to predict early mortality after TAVI. The moderate discrimination is however a limitation for the accurate identification of high-risk patients.

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) is now a well-established technique in patients who are at high risk for surgical aortic valve replacement (AVR).[1 2] Although surgical risk scores, such as the Euroscore or the Society of Thoracic Surgeons (STS) score, have limitations in the estimation of operative mortality, they are integrated into the decision-making process in order to choose the most appropriate intervention. Immediate results of TAVI can now be accurately assessed from large series.[3] However, only a few of them specifically analysed the factors associated with early mortality and were based on relatively small series.[4 5] In addition, there has not been any attempt to develop a scoring system to predict early mortality following TAVI.

We used the data from the French Aortic National CoreValve and Edwards (FRANCE 2) registry to analyse the predictive factors of early mortality after TAVI. We also aimed to develop and validate a simple scoring system aiming at predicting early mortality after TAVI.

METHODS

Population

Between 1 January 2010 and 31 December 2011, 3933 consecutive patients undergoing TAVI in the 33 French centres and in the Monaco centre were included in the FRANCE 2 registry. The criteria for the authorisation to perform TAVI, patient inclusion and the organisation of the FRANCE 2 registry were previously described.[6] Patients were selected for TAVI if they had severe, symptomatic aortic stenosis and if surgery was contraindicated or judged to be high risk by a multidisciplinary team.

The registry was approved by the Institutional Review Board of the French Ministry of Health. All patients gave written informed consent. Device manufacturers funded the registry but did not have any role in data collection or analysis or in the preparation of the manuscript.

For the purpose of the elaboration and validation of the score predicting early mortality, we excluded 35 patients for whom procedural data were missing and 65 patients in whom TAVI was performed because of degeneration of aortic bioprosthesis ('valve-in-valve' procedures). Therefore, the study population comprised 3833 patients.

Procedure

The two devices used were the balloon-expandable Sapien or Sapien XT prosthesis (Edwards Lifesciences) or the self-expandable CoreValve (Medtronic). Both devices were used in 30 centres, and only the Edwards Sapien was implanted in four centres. The balloon-expandable prostheses were

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used in 23 and 26 mm sizes with transfemoral approach using the Retroflex 3 or Novaflex delivery catheters, respectively, or the transapical approach using the Ascendra catheter. The 29 mm prosthesis was used only with the transapical approach. The balloon-expandable prosthesis was used in 26, 29 and 31 mm sizes with transfemoral or subclavian approaches.

The choice of the prosthesis, approach and type of anaesthesia was left at the discretion of the teams. The transfemoral approach was favoured as the first approach. Alternate approaches were transapical with the balloon-expandable prosthesis, subclavian with the self-expandable prosthesis and, less frequently, transaortic or transcarotid.

The performance of the procedures has been previously detailed.[6] All patients received aspirin (75–160 mg daily) and clopidogrel (300 mg loading dose and 75 mg daily) before the procedure and for 1 month after the procedure, and then a single antiplatelet drug regimen.

Endpoint

Mortality was adjudicated by an independent clinical events committee. The endpoint used for the elaboration and validation of the scoring system was all-cause mortality 30 days after the procedure or longer if the patient was not discharged, according to the recommendations of the Valvular Academic Research Consortium (VARC) classification system.[7]

Statistical analysis

Data were prospectively collected using a standardised electronic case report form and sent to a central database (Axonal). Quality control was performed by checking data against source documents for 10% of patients in randomly selected centres.

Continuous variables were expressed as mean± SD. Categorical variables were expressed as percentages and were grouped if needed according to risk progression.

The population of 3833 patients was split into two randomly selected cohorts: a development cohort of 2552 patients used for model building and a validation cohort of 1281 patients.[8 9] Model coefficients were not re-estimated and applied to the validation cohort. Univariate analysis was performed with a logistic model including the 56 variables listed in table 1.

Variables with $p<0.20$ in univariate analysis were entered in a multivariate adjusted logistic model with a backward selection procedure and a significance level of $p=0.05$. Continuous variables were kept continuous at this stage. Two-way interactions were studied between significant variables in multivariate analysis and selected if significant at the level of $p=0.01$.

We also tested a multilevel hierarchical logistic model including the covariates of the final model and the volume centre as a random effect to analyse the potential heterogeneity across centres. Volume centre was classified into <25, 25–50 and >50 procedures per year.

Then, continuous variables of the final model were categorised according to clinically relevant cut-off points. A score-based prediction rule for early mortality was developed from the multivariate model of the development cohort. Regression coefficients were multiplied by 10/3 and rounded to the nearest integer. The score was the sum of the points corresponding to each variable of the multivariate model.

The discrimination obtained with the final multivariate model, the multilevel hierarchical model and the score was assessed using the c-index and its 95% CI. Overall calibration was tested with the Hosmer–Lemeshow goodness-of-fit test. Calibration performance according to the score value was assessed by computing predicted mortality rates and observed

Table 1 Baseline and procedural characteristics of the development and validation cohorts

	Development cohort (n=2552)	Validation cohort (n=1281)
Age (years)	82.9±7.2 (2552)	83.0±7.2 (1281)
Female sex	1264/2552 (49.5)	631/1281 (49.3)
Height (cm)	163±8.9 (2549)	164±9.1 (1278)
Weight (kg)	70±14 (2551)	70±15 (1278)
Body surface area (m^2)	1.75±0.20 (2536)	1.75±0.21 (1270)
Body mass index (kg/m^2)	26.0±5.1 (2549)	26.0±4.8 (1278)
High-risk conditions for surgery		
Porcelain aorta	201/2548 (7.9)	100/1179 (7.8)
Thoracic deformation	53/2548 (2.1)	33/1279 (2.6)
Radiation therapy	137/2548 (5.4)	86/1279 (6.7)
Other comorbidities not included in risk scores	1520/2548 (59.7)	753/1279 (58.9)
Refusal of surgery	243/2548 (9.5)	137/1279 (10.7)
Functional status		
NYHA class		
I–II	627/2540 (24.7)	316/1274 (24.8)
III	1593/2540 (62.7)	778/1274 (61.1)
IV	320/2540 (12.6)	180/1274 (14.1)
At least two episodes of APE during the last year	289/2545 (11.4)	162/1279 (12.7)
Angina pectoris	378/2552 (14.8)	231/1281 (18.0)
Unstable angina*	71/2544 (2.8)	45/1279 (3.5)
Syncope	221/2552 (8.7)	89/1281 (7.0)
ECG		
Atrial fibrillation	636/2520 (25.2)	340/1264 (26.9)
Pacemaker	359/2541 (14.1)	180/1276 (14.1)
Right bundle branch block	243/2497 (9.7)	130/1249 (10.4)
Left bundle branch block	298/2497 (11.9)	150/1249 (12.0)
Risk factors		
Active smoking	77/2552 (3.0)	50/1281 (3.9)
Hypertension	1773/2552 (69.5)	880/1281 (68.7)
Diabetes	659/2552 (25.8)	327/1281 (25.5)
Dyslipidemia	1228/2552 (48.1)	608/1281 (47.5)
Comorbidities		
Prior myocardial infarction	385/2552 (15.1)	182/1281 (14.2)
Coronary artery stenosis >50%	1187/2494 (47.6)	579/1256 (46.1)
Extent of coronary disease		
1-vessel disease	497/1182 (42.0)	252/577 (43.7)
2-vessel disease	354/1182 (30.0)	160/577 (27.7)
3-vessel disease	331/1182 (28.0)	165/577 (28.6)
Prior coronary bypass grafting	460/2552 (18.0)	218/1281 (16.8)
Prior cardiac surgery*	497/2544 (19.5)	239/1279 (18.7)
Prior balloon aortic valvuloplasty	415/2552 (16.3)	219/1281 (17.7)
Lower limb arteritis	514 /2552 (20.1)	274/1281 (21.4)
Abdominal aortic aneurysm	112/2552 (4.4)	62/1281 (4.8)
Peripheral artery disease*	685/2544 (26.9)	394/1279 (30.8)
Respiratory insufficiency†	620/2552 (24.3)	326/1281 (25.5)
Chronic obstructive pulmonary disease*	587/2545 (23.1)	290/1279 (22.7)
Hemoglobin (g/dL)	12.1±1.7 (2468)	12.0±1.7 (1230)
Creatinine clearance (mL/min)‡	48.1±24.2 (2471)	47.9±23.7 (1233)
Dialysis	56/2552 (2.2)	42/1281 (3.3)
Prior cerebrovascular accident	246/2552 (9.6)	134/1281 (10.5)
Neurological dysfunction*	198/2544 (7.8)	99/1279 (18.7)
Severe chronic neuropathy	32/2552 (1.2)	23/1281 (1.8)

Continued

Table 1 Continued

	Development cohort (n=2552)	Validation cohort (n=1281)
Life expectancy <1 year	59/2552 (2.3)	31/1281 (2.4)
Oral anticoagulation	611/2552 (23.9)	318/1281 (24.8)
Antiplatelet drug	1656/2552 (64.9)	824/1281 (64.3)
Echocardiographic data		
Annular diameter (mm)	22.1±2.2 (2357)	22.1±2.2 (1181)
Mean gradient (mm Hg)	48±16 (2493)	49±17 (1237)
Valve area (cm^2)	0.67±0.18 (2416)	0.67±0.19 (1210)
LVEF (%)	53±14 (2518)	53±14 (1257)
Aortic regurgitation		
0	143/2550 (5.6)	71/1281 (5.5)
1	950/2550 (37.2)	462/1281 (36.1)
2	1027/2550 (40.3)	520/1281 (40.6)
≥3	430/2550 (16.9)	228/1281 (17.8)
Mitral regurgitation		
0	135/2550 (5.3)	64/1281 (5.0)
1	783/2550 (30.7)	425/1281 (33.2)
2	1092/2550 (42.8)	555/1281 (43.3)
≥3	540/2550 (21.2)	237/1281 (18.5)
Systolic PAP (mm Hg)	45±14 (1994)	45±14 (981)
Systolic PAP >60 mm Hg*	664/2544 (26.1)	317/1279 (24.8)
Procedure		
Critical preoperative state*	97/2544 (3.8)	59/1279 (4.6)
Emergency intervention	62/2544 (2.4)	27/1279 (2.1)
General anaesthesia	1754/2551 (68.8)	890/1280 (69.5)
Prosthesis		
Edwards Sapien	1696/2544 (66.7)	855/1277 (66.9)
Medtronic Corevalve	848/2544 (33.3)	422/1277 (33.1)
Approach		
Transapical	449/2537 (17.7)	229/1278 (17.9)
Transfemoral	1866/2537 (73.6)	935/1278 (73.2)
Subclavian	142/2537 (5.6)	77/1278 (6.0)
Other	80/2537 (3.1)	37/1278 (2.9)

Values are mean ± SD (available data) or n (%).
*Definitions according to the Euroscore.
†Obstructive or non-obstructive symptomatic respiratory disease.
‡According to the Cockroft–Gault formula.
APE, acute pulmonary oedema; NYHA, New York Heart Association; PAP, pulmonary artery pressure.

mortality rates with 95% CI and visually represented using calibration plots.[8] Analyses were performed with SAS statistical software (SAS Institute, Cary, North Carolina, USA, V.9.3) and R software (R foundation for statistical computing, Vienna, Austria, V.2.12.0).

RESULTS

Population study

Patient characteristics are described in table 1 for the development and validation cohorts. Age was ≥90 in 435 patients (11.4%) and ≥80 in 2776 (72.4%). Mean logistic Euroscore was 21.5±13.8 in the development cohort and 21.9±14.1 in the validation cohort.

Procedure

The type of prosthesis and the approach are detailed in table 1. Other approaches were transaortic in 103 patients and transcarotid in 14. Prosthesis implantation was successful in 3698 patients (97.2%).

Early mortality

Follow-up was complete in 3831 patients (99.9%). There were 382 early deaths (10.0%), including 253 (9.9%) in the development cohort and 129 (10.1%) in the validation cohort.

Death occurred on the day of the procedure in 84 cases (22.0%), between the second day and the end of the first week in 110 cases (28.8%), during the second week in 59 (15.4%), the third week in 49 (12.8%), between day 21 and day 30 in 52 (13.6%) and after day 30 in 28 (7.4%).

When dividing the 2 years of the study into eight trimesters, early mortality rates varied between 8.6 and 11.5% and there was no difference between the eight trimesters (p=0.85). There was no difference in early mortality rates according either to the centre (p=0.27) or the annual volume centre: 10.0% in the 5 centres performing <25 procedures, 10.9% in the 10 centres performing 25–50 procedures and 9.9% in the 19 centres performing >50 procedures (p=0.89).

Early mortality was 8.0% (142/1774) with the transfemoral approach using the Edwards Sapien prosthesis, 9.3% (95/1019) with the transfemoral approach using the Medtronic CoreValve prosthesis, 8.8% (19/217) with the subclavian approach using the Medtronic CoreValve prosthesis, 15.1% (102/677) with the transapical approach using the Edwards Sapien prosthesis and 12.8% (15/117) with other approaches. There was no interaction between the type of prosthesis and the approach in relation to early mortality (p=0.30).

Predictive factors of early mortality

Predictive analysis of early mortality was performed in the 2552 patients from the development cohort. Univariate analysis is detailed in table 2.

Multivariate analysis identified nine independent predictive factors of early mortality (see online supplementary table S2). No interaction was significant. The c-index obtained with the final logistic model in the development cohort without coding of continuous variables was 0.68 (95% CI 0.65 to 0.72). The c-index obtained with the multilevel hierarchical model was 0.69 (95% CI 0.65 to 0.72), showing no effect of the heterogeneity across centres on the prediction. There was no significant difference between predicted and observed mortality (p=0.60). The c-index obtained with the logistic Euroscore was 0.59 (95% CI 0.55 to 0.64).

Score building

The scoring system was derived from the final multivariate model in the development cohort. The final model is detailed in online supplementary table S3.The score was calculated by adding each component and ranged theoretically from 0 to 21 (table 3). In the development cohort, the score ranged between 0 and 14.

The relationship between the score value and predicted early mortality is shown in figure 1. The OR associated with a one-point increase of the score was 1.33 (95% CI 1.25 to 1.40). The c-index was 0.67 (95% CI 0.64 to 0.71) for the score in the development cohort. The p value of the Hosmer–Lemeshow test was 0.40. Predicted and observed early mortality rates according to score values are detailed for the development cohort in figure 2 and in the online supplementary table S4.

Score validation

The predictive model and the score were tested in the validation cohort.

Table 2 Predictive factors of early (30-day or in-hospital) mortality after TAVI

	Alive (n=2299)	Dead (n=253)	Unadjusted OR (95% CI)	p Value
Age (years)	82.7±7.2 (2299)	84.1±6.4 (253)	1.03 (1.01 to 1.05)	0.002
Female sex	1135/2299 (49.4)	129/253 (51.0)	1.07 (0.82 to 1.38)	0.63
Height (m)	1.63±0.89 (2297)	1.63±0.88 (252)	0.99 (0.98 to 1.01)	0.28
Weight (kg)	69.9±14.5 (2299)	66.0±13.2 (252)	0.98 (0.97 to 0.99)	<0.0001
Body mass index (kg/m^2)	26.2±5.1 (2297)	24.9±4.5 (236)	0.94 (0.92 to 0.97)	<0.0001
High-risk conditions for surgery				
Porcelain aorta	180/2295 (7.8)	21/253 (8.3)	0.94 (0.59 to 1.51)	0.80
Thoracic deformation	43/2295 (1.9)	10/253 (4.0)	0.46 (0.23 to 0.94)	0.03
Radiation therapy	123/2295 (5.4)	14/253 (5.5)	0.97 (0.55 to 1.71)	0.91
Other comorbidities not included in risk scores	1364/2295 (59.4)	156/253 (61.7)	0.91 (0.70 to 1.19)	0.49
Refusal of surgery	213/2295 (9.3)	30/253 (11.8)	0.76 (0.51 to 1.14)	0.19
Functional status				
NYHA class				<0.0001
I–II–III	2026/2289 (88.5)	194/251 (77.3)	1	
IV	263/2289 (11.5)	57/251 (22.7)	2.26 (1.64 to 3.12)	
At least two episodes of APE during the last year	239/2292 (10.4)	50/253 (19.8)	2.12 (1.51 to 2.96)	<0.0001
Angina pectoris	337/2299 (14.7)	41/253 (16.2)	1.13 (0.79 to 1.60)	0.51
Unstable angina*	63/2291 (2.8)	8/253 (3.2)	1.16 (0.55 to 2.44)	0.71
Syncope	188/2299 (8.2)	33/253 (13.0)	1.68 (1.14 to 2.50)	0.009
ECG				
Atrial fibrillation	562/2272 (24.7)	74/248 (29.8)	1.29 (0.97 to 1.73)	0.08
Pacemaker	326/2290 (14.2)	33/251 (13.2)	0.91 (0.62 to 1.34)	0.64
Right bundle branch block	219/2253 (9.7)	24/244 (9.8)	1.01 (.65 to 1.58)	0.95
Left bundle branch block	266/2253 (11.8)	32/244 (13.1)	1.13 (0.76 to 1.68)	0.55
Risk factors				
Active smoking	68/2299 (3.0)	9/253 (3.6)	1.21 (.60 to 2.46)	0.60
Hypertension	1603/2299 (69.7)	170/253 (67.2)	0.89 (0.67 to 1.17)	0.41
Diabetes	600/2299 (26.1)	59/253 (23.3)	0.86 (0.63 to 1.17)	0.34
Dyslipidemia	1125/2299 (48.9)	103/253 (40.7)	0.72 (0.55 to 0.93)	0.01
Comorbidities				
Prior myocardial infarction	338/2299 (14.7)	47/253 (18.6)	1.32 (0.95 to 1.86)	0.10
Coronary artery stenosis >50%	1067/2254 (47.3)	120/240 (50.0)	1.11 (0.85 to 1.45)	0.43
Extent of coronary disease				0.72
1-vessel disease	450/1063 (42.3)	47/119 (39.5)	1	
2-vessel disease	319/1063 (30.1)	35/119 (29.4)	1.05 (0.66 to 1.66)	
3-vessel disease	294/1063 (27.6)	37/119 (31.1)	1.20 (0.76 to 1.90)	
Prior coronary bypass grafting	412/2299 (17.9)	48/253 (19.0)	1.07 (0.77 to 1.49)	0.68
Prior cardiac surgery*	447/2291 (19.5)	50/253 (19.8)	1.02 (0.73 to 1.41)	0.92
Prior aortic valvuloplasty	357/2299 (15.5)	58/253 (22.9)	1.62 (1.18 to 2.22)	0.003
Lower limb arteritis	446/2299 (19.4)	68/253 (26.7)	1.53 (1.14 to 2.05)	0.005
Abdominal aortic aneurysm	102/2299 (4.4)	10/253 (4.0)	0.88 (0.46 to 1.72)	0.72
Peripheral artery disease*	611/2291 (26.7)	74/253 (29.3)	1.14 (0.85 to 1.51)	0.38
Respiratory insufficiency†	536/2299 (23.3)	84/253 (33.2)	1.64 (1.24 to 2.16)	0.0005
Chronic obstructive pulmonary disease*	519/2292 (22.6)	68/253 (26.9)	1.26 (0.94 to 1.69)	0.13
Hemoglobin (g/dL)	12.1±1.7 (2224)	12.1±1.7 (244)	1.00 (0.92 to 1.08)	0.95
Creatinine clearance (mL/min)‡	48.3±24.6 (2229)	45.7±20.6 (242)	1.00 (0.99 to 1.00)	0.06
Dialysis	44/2299 (1.9)	12/253 (4.7)	2.55 (1.33 to 4.90)	0.004
Prior cerebrovascular accident	220/2299 (9.6)	26/253 (10.3)	1.08 (0.71 to 1.66)	0.72
Neurological dysfunction*	175/2291 (7.6)	23/253 (9.1)	1.21 (0.77 to 1.91)	0.41
Severe chronic neuropathy	31/2299 (1.4)	1/253 (0.4)	0.29 (0.04 to 2.14)	0.20
Life expectancy <1 year	49/2299 (2.1)	10/253 (4.0)	1.89 (0.95 to 3.78)	0.07
Oral anticoagulation	548/2299 (23.8)	63/253 (24.9)	1.06 (0.78 to 1.43)	0.71
Antiplatelet drug	1489/2299 (64.8)	167/253 (66.0)	1.06 (0.80 to 1.39)	0.69
Echocardiographic data				
Annular diameter (mm)	22.1±2.2 (2132)	22.3±2.1 (225)	1.03 (0.97 to 1.10)	0.31
Mean gradient (mm Hg)	48.6±16.4 (2246)	46.4±18.0 (247)	0.99 (0.98 to 1.00)	0.06
Valve area (cm^2)	0.67±0.18 (2177)	0.68±0.19 (239)	1.28 (0.61 to 2.67)	0.51
LVEF(%)	53.5±14.1 (2267)	51.5±14.8 (251)	0.99 (0.98 to 1.00)	0.04

Continued

Table 2 Continued

	Alive (n=2299)	Dead (n=253)	Unadjusted OR (95% CI)	p Value
Aortic regurgitation				0.88
0	129/2297 (5.6)	14/253 (5.5)	1	
1	855/2297 (37.2)	95/253 (37.6)	1.02 (0.57 to 1.85)	
2	922/2297 (40.1)	105/253 (41.5)	1.05 (0.58 to 1.89)	
≥3	391/2297 (17.0)	39/253 (15.4)	0.92 (0.48 to 1.75)	
Mitral regurgitation				0.10
0	121/2297 (5.3)	14/253 (5.5)	1	
1	712/2297 (31.0)	71/253 (28.1)	0.86 (0.47 to 1.58)	
2	992/2297 (43.2)	100/253 (39.5)	0.87 (0.48 to 1.57)	
≥3	472/2297 (20.5)	68/253 (26.9)	1.25 (0.68 to 2.29)	
Systolic PAP (mm Hg)	45.1±14.1 (1787)	46.9±14.1 (207)	1.01 (1.00 to 1.02)	0.10
Systolic PAP >60 mm Hg*	579/2291 (25.3)	85/253 (33.6)	1.50 (1.13 to 1.97)	0.004
Procedure				
Critical preoperative state*	73/2291 (3.2)	24/253 (9.5)	3.19 (1.97 to 5.15)	<0.0001
Emergency intervention	51/2291 (2.2)	11/253 (4.4)	2.00 (1.03 to 3.88)	0.04
General anaesthesia	1559/2298 (67.8)	195/253 (77.1)	1.59 (1.17 to 2.16)	0.003
Prosthesis				0.10
Edwards Sapien	1519/2296 (66.2)	177/248 (71.4)	1	
Medtronic Corevalve	777/2296 (33.8)	71/248 (28.6)	0.78 (0.59 to 1.05)	
Approach				0.0001
Transfemoral or subclavian	1835/2288 (80.2)	173/249 (69.5)	1	
Transapical	384/2288 (16.8)	65/249 (26.1)	1.80 (1.32 to 2.44)	
Other	69/2288 (3.0)	11/249 (4.4)	1.69 (0.88 to 3.26)	

Univariate analysis in the development cohort of 2552 patients. Values are mean ± SD (available data) or n (%).
*Definitions according to the Euroscore.
†Obstructive or non-obstructive symptomatic respiratory disease.
‡According to the Cockroft–Gault formula.
APE, acute pulmonary oedema; NYHA, New York Heart Association; PAP, pulmonary artery pressure; TAVI, transcatheter aortic valve implantation.

The c-index was 0.59 (95% CI 0.54 to 0.64) for the final multivariate model and 0.59 (95% CI 0.54 to 0.64) for the score in the validation cohort. The corresponding p values of the Hosmer–Lemeshow test were 0.50 with the final multivariate model and 0.50 with the score. Predicted and observed early mortality rates according to score values are detailed for the validation cohort in figure 3 and in the online supplementary table S5. The good calibration was also shown by the fact that the line fitting the data was close from the diagonal line for predicted mortality up to 20%.

DISCUSSION

In this large nationwide registry comprising all TAVI procedures performed with different devices and approaches, eight patient-related and one procedure-related variables were identified as predictive factors of early mortality. It was possible to derive a simple multivariate score to estimate early mortality after TAVI. However, its moderate discrimination limits its ability to reliably identify patients at high risk of early death after TAVI.

Population

The present study population reflects contemporary TAVI practices in high-risk patients. A strength of this registry is to include all consecutive procedures performed with the two most commonly used prosthetic devices and all approaches.[10] We excluded TAVI procedures performed for bioprosthesis degeneration, which is an off-label indication, and is the subject of specific studies.[11]

Early mortality after TAVI

Early all-cause mortality is a standardised endpoint proposed by the VARC and is consistent with guidelines for reporting mortality after cardiac valve interventions.[7 12] Mortality at 30 days or longer if the patient was not discharged is also the usual endpoint for assessing early mortality in surgical databases and with risk scores.[13 14]

The 10.0% early mortality rate is consistent with other multicentre registries, ranging from 5.4 to 12.4%.[4 5 15–18] A meta-analysis on more than 16 000 procedures reported a 30-day mortality rate of 8.1%.[3]

The absence of difference in mortality rates according to centres, volume activity and between trimesters can be related to the fact that 30 of the 34 centres had previous experience with TAVI.[6]

Predictive factors of early mortality

Older age was associated with a modest but significant increase in early mortality.

The relationship between low body mass index (BMI) and increased early mortality is an original finding with regards to TAVI. This shows that early mortality is increased not only in patients with BMI<18.5, but also in those with normal weight, as compared with overweight patients with a BMI≥30. Consistent findings have been reported after AVR for aortic stenosis, with the lowest early postoperative mortality rates in patients with a BMI around 30.[19] A BMI<24 was a predictive factor of 6-month mortality after AVR in octogenarians.[20] Weight loss is also a component included in the frailty scoring systems.

The two comorbidities identified as predictive factors of 30-mortality after TAVI were respiratory insufficiency and dialysis, which is consistent with valve surgery.[21]

Four factors were directly related to the severity of hemodynamic consequences of aortic stenosis, that is, recent acute pulmonary oedema (APE), New York Heart Association (NYHA) class IV, pulmonary hypertension and critical state, which comprises conditions related to poor hemodynamic status according to

Table 3 Predictive factors of early (30-day or in-hospital) mortality after TAVI

	Adjusted OR (95% CI)	p Value	Points for score (/21)
Age (years)			
<90	1		0
≥90	1.53 (1.02 to 2.30)	0.04	1
Body mass index (kg/m²)			
≥30	1		0
18.5–29.9	1.51 (1.01 to 2.27)	0.047	1
<18.5	2.27 (1.09 to 4.74)	0.03	3
NYHA class IV	1.79 (.26 to 2.54)	0.001	2
Pulmonary oedema (APE)			
<2 APE last year	1		0
≥2 APE last year	1.61 (1.12 to 2.30)	0.01	2
Pulmonary hypertension (systolic PAP ≥60 mm Hg)	1.45 (1.08 to 1.94)	0.01	1
Critical state*	2.39 (1.42 to 4.02)	0.001	3
Respiratory insufficiency†	1.64 (1.22 to 2.20)	0.001	2
Dialysis	2.88 (1.46 to 5.66)	0.002	4
Approach			
Transfemoral or subclavian	1		0
Transapical	2.02 (1.47 to 2.78)	<0.0001	2
Other	2.18 (1.11 to 4.28)	0.02	3

Multivariate analysis in the development cohort and definition of the score.
APE, acute pulmonary oedema; NYHA, New York Heart Association; PAP, pulmonary artery pressure; TAVI, transcatheter aortic valve implantation.
*Any one or more of the following: ventricular tachycardia or fibrillation or aborted sudden death, preoperative cardiac massage, preoperative ventilation before arrival in the anaesthetic room, preoperative inotropic support, intra-aortic balloon counterpulsation or preoperative acute renal failure (anuria or oliguria <10 mL/h).
†Obstructive or non-obstructive symptomatic respiratory disease.

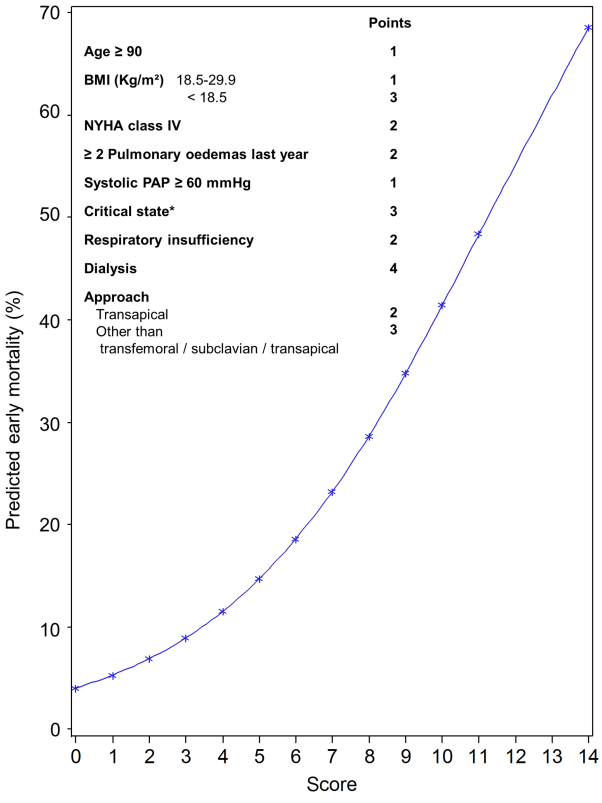

Figure 1 Relationship between the score value and predicted early mortality after transcatheter aortic valve implantation.

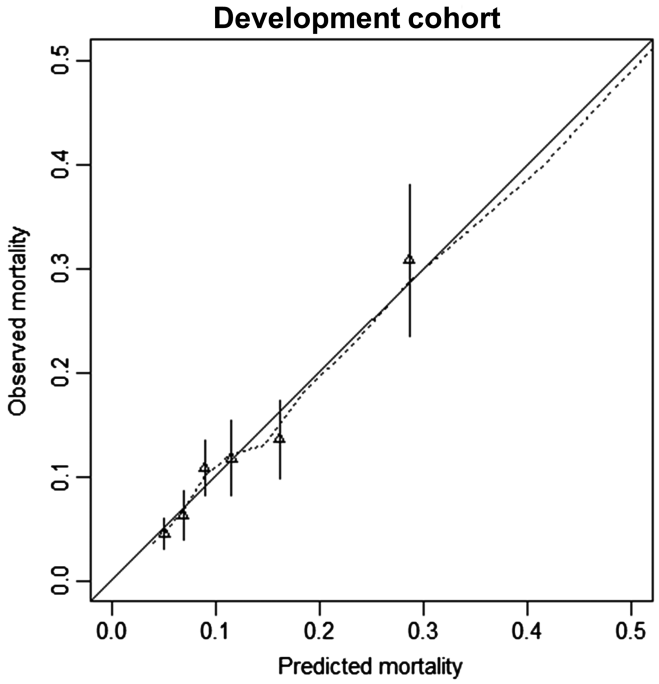

Figure 2 Calibration plot showing the predicted probability versus observed early mortality after transcatheter aortic valve implantation in the development cohort. The diagonal line represents the perfect calibration. Observed mortality is represented with 95% CI.

the definition of the Euroscore.[13] Pulmonary hypertension and the need for hemodynamic support were also associated with early mortality in the Canadian registry of TAVI.[4] In the present series, haemodynamic indices were strong predictive factors of early mortality after TAVI. This points out the importance of a timely intervention to reduce the procedural risk and may suggest a role for

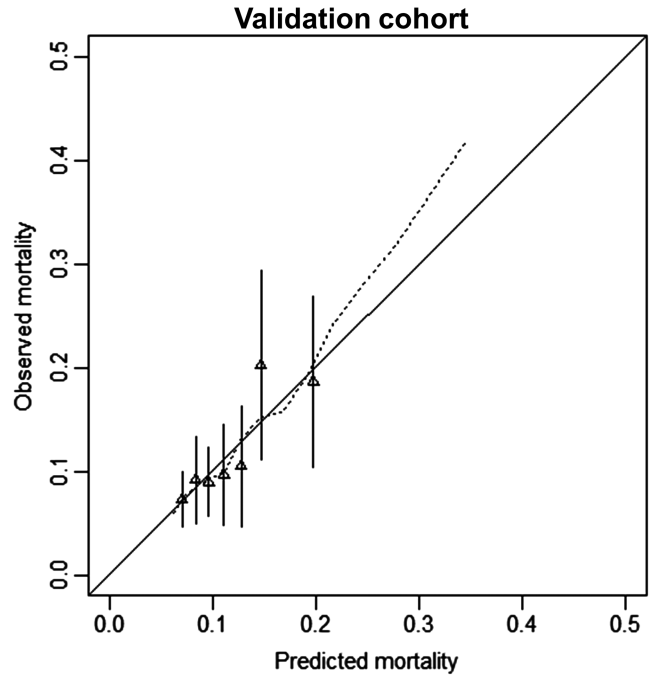

Figure 3 Calibration plot showing the predicted probability versus observed early mortality after transcatheter aortic valve implantation in the validation cohort. The diagonal line represents the perfect calibration. Observed mortality is represented with 95% CI.

balloon aortic valvuloplasty as a bridge to TAVI in patients with poor hemodynamic condition. Impaired LVEF was associated with early mortality in univariate but not in multivariate analysis. This illustrates a strong confounding effect between EF and NYHA class or pulmonary hypertension. The transapical approach and other approaches (transaortic and transcarotid) were associated with a higher early mortality. On the other hand, there were no differences between the transfemoral and subclavian approaches. Increased mid-term mortality with transapical approach has also been shown in another registry.[17] The interpretation of the relationship between approach and mortality should be cautious. Thoracotomy may be harmful in high-risk patients. However, since the transfemoral approach was favoured in the FRANCE 2 registry, transapical and other approaches were likely to be used in sicker patients. In addition, the modalities of pain control influence postprocedural mortality.[22] Even a multivariate analysis cannot control for all potential known and unknown confounding factors in this setting. There were no differences between the two prosthetic devices, as also shown in other recent analyses.[3]

Scoring system

The risk score combining nine variables enables early mortality to be estimated for any given patient. Although score values theoretically range between 0 and 21, no patient had a risk score >14, showing that patients combining all predictive factors of early mortality were denied the procedure according to clinical judgement of the heart team.

The score achieved, however, only a moderate discrimination, as attested by the value of the c-index of 0.67 in the development sample and 0.59 in the validation sample. Although predictive analyses of early and mid-term mortality after TAVI have been reported, they did not comprise a specific validation sample allowing for an unbiased estimation of their predictive performance.[8] Surgical risk scores achieved a better discrimination, with c-indexes around 0.80.[13 14] The German aortic valve risk score is specific to aortic stenosis and achieves a c-index of 0.81 but comprises 95% of AVR and only 573 TAVI procedures.[23] Unpublished analyses from the SOURCE (for Edwards SAPIEN Aortic Bioprosthesis European Outcome) registry mentioned comparable values of c-index obtained with multivariate predictive models of early mortality (0.61 for transapical and 0.70 with transfemoral approach).[24] In a population of patients aged ≥70 undergoing cardiac surgery, the c-index was 0.65 with the Euroscore and 0.67 with the STS score, attesting for limited discrimination performance of scores in specific populations of high-risk patients.[25] Whatever TAVI or surgery is considered, very high-risk patients represent a small and particularly heterogeneous group, in which it is difficult to collect all variables and to estimate the contribution of each variable influencing early mortality. That is the reason why recent recommendations emphasise the importance of clinical judgment.[1 2] Finally, a number of postprocedural complications may increase early mortality after TAVI.[7] This may contribute to limit the predictive performance of a model based on preprocedural patient characteristics.

With regard to calibration, there was a good overall concordance between the numbers of predicted and observed deaths. The analysis of score calibration according to the score value shows a good concordance between predicted and observed deaths for predicted early mortality rates <20%, which corresponds to >90% of the patients. The concordance between predicted and observed mortality in very high-risk patients is difficult to ascertain given the small number of patients. This is consistent with the limitations of risk scores in surgical AVR.[26] Even if the recent Euroscore II achieves a good discrimination, its calibration properties are weaker in patients with a predicted mortality >30%.[27]

Study limitations

The lack of standardised definition for certain comorbidities may introduce some heterogeneity, particularly for respiratory insufficiency. However, only one series used predefined spirometric criteria to analyse the impact of pulmonary disease after TAVI.[28]

The assessment of the predictive performance of the score is limited by the lack of external validation. Nevertheless, the validation of the score in a randomly selected cohort limits the risk of overestimation with the predictive value of the score.

The FRANCE 2 registry did not collect indices assessing functional or cognitive capacity, particularly indices of frailty. Taking such indices into account may improve the discrimination.

Since this score was developed from a cohort of patients at high risk for surgery, it cannot be extrapolated to patients at intermediate risk, who are currently considered as candidates for surgical AVR but are the subject of specific trials.

CONCLUSION

The analysis based on a contemporary registry allows for a better knowledge of patients who are at high risk of early mortality after TAVI. Four of the eight patient-related characteristics are related to the consequences of aortic stenosis, that is, NYHA class IV, previous APE, pulmonary hypertension and critical state, thereby highlighting the importance of timely indication of TAVI. The scoring system combining predictive factors allows an easy estimation of early mortality after TAVI performed with current devices and approaches. This score may contribute to decision making by a multidisciplinary team in high-risk patients with aortic stenosis. Despite a good concordance between predicted and observed mortality, the moderate discrimination illustrates the difficulties in achieving a reliable prediction of early outcome after TAVI in an individual patient. Improvement in patient selection will also require predictive analyses of mid-term outcome.

Key messages

What is already known on this subject

Immediate results of transcatheter aortic valve implantation (TAVI) can now be assessed from large numbers of patients. The assessment of early mortality is an important component of decision making. Only a limited number of relatively small series specifically analysed the factors associated with early mortality. No scoring system has been developed to predict early mortality following TAVI.

What this study adds

This study identified nine predictive factors of early mortality after TAVI. It also describes a simple scoring system that can contribute to individualise risk assessment, although its moderate discrimination performance limits its ability to accurately identify patients at high risk of early death after TAVI.

How might this impact on clinical practice

Four of the eight patient-related characteristics are related to the consequences of aortic stenosis, that is, New York Heart Association class IV, previous acute pulmonary oedema, pulmonary hypertension and critical state. Their impact on early mortality after TAVI highlights the importance of timely indication. Despite limited predictive performance, the proposed score can be useful in decision making in high-risk patients with severe, symptomatic aortic stenosis.

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Collaborators FRANCE 2 Investigators: see supplementary table S1.

Contributors BI participated in the conception of the FRANCE 2 registry, designed the score study, participated in data analysis and drafted the manuscript. CL performed the statistical analysis. DH and AV revised the manuscript content critically. Other authors contributed to the design of the FRANCE 2 registry and revised the manuscript. All authors approved the final version of the submitted manuscript.

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Heart

Predictive factors of early mortality after transcatheter aortic valve implantation: individual risk assessment using a simple score

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