Transapical TAVI: Survival, Hemodynamics, Devices and Machine Learning. Lessons Learned After 10-Year Experience

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Abstract: Aim of this single-center, retrospective study was to assess early and long-term clinical and hemodynamic results of transapical aortic valve implantation (TA-TAVI), and to identify predictors of survival at follow-up. All patients undergoing TA-TAVI for severe aortic valve stenosis at our institution were reviewed. A hybrid approach based on machine-learning techniques was employed to identify survival predictors, using a bagging-decision-tree algorithm and a Random-Forest algorithm, respectively. Two-hundred-thirty-four consecutive patients underwent

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TA-TAVI (March 2009-May 2019). All cause 30-day mortality was 5.1%. Device success was 95.7%. Median follow-up time was 35.2 months. Kaplan-Meier overall survival rates at 2, 5, and 8 years were 75%, 44%, and 15%, respectively. Structural-valve-deterioration occurred in 25 patients (11.3%) overall. The strongest predictors of survival at follow-up were age, body-mass-index, and ejection fraction. TA-TAVI provided valid early and long-term outcomes. These data support its choice as an optimal alternative access whenever the transfemoral route is not feasible. (Curr Probl Cardiol 2023;48:101734.)

Introduction

Transcatheter aortic valve implantation (TAVI) is a safe and effective treatment for severe symptomatic aortic valve stenosis, especially in elderly and high/intermediate surgical risk patients.[1,2] Although the transfemoral (TF) access is the most popular since it can be performed in a completely percutaneous fashion and with local anesthesia only, the transapical (TA) route is generally considered one of the main alternative accesses because it's antegrade, it allows an easy valve crossing and also an excellent control during valve deployment.[3] Aim of this single center, retrospective study was to describe 10-year experience of TA-TAVI by analyzing early and long-term clinical and hemodynamic results of all transcatheter heart valves generations that have been used with this approach in clinical practice.

Patients and Methods

All patients who underwent TA-TAVI for severe symptomatic native aortic valve stenosis at our institution were reviewed. The analysis excluded patients who underwent TA-TAVI for either aortic regurgitation or valve-in-valve procedure. All patients gave informed consent for the procedure and for data collection and analysis for scientific purposes; data collection was approved by the local ethics committee. Data was prospectively collected in our TAVI-dedicated database and retrospectively analyzed. Preoperative clinical variables were defined according to the European System for Cardiac Operative Risk Evaluation (EuroSCORE II) definitions.[4] Postoperative outcomes and clinical end points

were reported following the updated Valve Academic Research Consortium (VARC-2) recommendations.[5]

Preoperative Evaluation

All cases were discussed and approved during multidisciplinary Heart Team meetings. Our policy was based on a TF-first approach; therefore, the TA access was chosen when TF was not possible due to severe calcifications, small caliper, and tortuosity of iliac and femoral vessels. Furthermore, the TA access has always been considered as the first alternative access in our institution. ECG-triggered thoraco-abdominal Angio-CT scan was performed in all patients. Preoperative patient's screening was performed according to well established recommendations.[6] The TA access was contraindicated in patients with severe left ventricular (LV) dysfunction (LV ejection fraction <20%), LV apical aneurysms, and apical thrombosis.[7]

Study Devices and Surgical Technique

During the study period, balloon-expandable Sapien (SA), Sapien XT (SXT), Sapien 3 (S3) (Edwards Lifesciences, Irvine, CA), self-expandable ACURATE-TA (AC) (Boston Scientific, Boston, MA) and self-expandable JenaValve (JV) (JenaValve Technology, Inc., Invine, CA) were implanted.

Due to the small number of patients treated with JV and since it has been withdrawn from clinical use, we decided to exclude it from this analysis. Procedures were performed in the standard fashion.[7,8] In particular, Sapien (and its evolutions) was deployed by balloon inflation under rapid ventricular pacing; the AC valve was deployed using 2 steps top-to-down fashion with rapid pacing during the second step; the JV was generally implanted without rapid pacing. All patients received dual antiplatelet therapy for 6 months postoperatively and then aspirin (100 mg/day). In patients with atrial fibrillation or other indications for anticoagulation, warfarin with a target INR 2-3 was added to aspirin alone; in these patients dual antiplatelet therapy was never given.

Follow-Up

Clinical and echocardiographic evaluation was performed at hospital admission, before discharge, 1-3 months postoperatively, and on a yearly basis thereafter in a TAVI-dedicated outpatient clinic. All serial echocardiograms for each patient were included in the analysis. In this setting,

bidimensional and 3D echocardiography was carried out using a iE33 echocardiography system (Philips Healthcare, The Netherlands), following the recommendations from specific guidelines for echocardiography in transcatheter interventions for valvular heart disease.[9] We performed telephone interviews and asked for a copy of the most recent echocardiographic evaluation in patients unable to come to our hospital for follow-up evaluation. Patient-prosthesis mismatch was defined as severe if effective orifice area index (EOAi) was <0.65 cm^2/m^2 and moderate if EOAi was between 0.65 cm^2/m^2 and 0.85 cm^2/m^2. Structural valve deterioration (SVD) was defined according to the most recent EAPCI/ESC/EACTS definitions.[10]

Endpoints

Primary endpoint was overall survival. Secondary endpoints were survival of patients stratified by surgical risk profile according to STS-PROM score (low-risk: STS <4%; intermediate-risk: STS 4%-8%; high-risk: STS >8%), comparison of last generation TA-TAVI devices (S3 and AC). We also aimed at developing a machine-learning technique to identify predictors of survival at follow-up.

Statistical Analysis

Descriptive statistics are reported as I quartile/median/III quartile for continuous variables, and absolute numbers (percentages) for categorical variables. Wilcoxon-Kruskal-Wallis and Pearson chi-squared tests were performed to compare the distribution of continuous and categorical variables, respectively. *P*-values underwent Benjamini-Hochberg correction for the multiplicity of testing. The survival distribution was evaluated using the Kaplan-Meier approach. The distribution of cardiovascular death was evaluated using the Cumulative Incidence Function to account for competing risks. A hybrid approach based on machine learning techniques (MLTs) was employed to predict survival and to identify survival predictors, using a Bagging Decision Tree algorithm and a Random Forest (RF) algorithm for survival data, respectively. MLTs are increasingly used for clinical data since they allow for the detection of complex relationships between the outcomes of interest and the covariates, overcoming the limits of traditional analysis techniques (ie, regression approaches),[11] especially when a high number of predictors is evaluated in front of a low number of events. The performance of the Bagging Decision Tree algorithm was evaluated using an out-of-basket error rate via an

integrated Brier score metric. The strength of the association between predictors and outcome was evaluated using the Minimal Depth ranking for variable selection of the RF algorithm. To understand the role played by the strongest survival predictors identified using the RF, it was graphically represented their impact on survival. Bagging decision tree was also estimated to predict patients' survival. A Shiny web application was developed based on the Bagging decision tree. The tool calculates the survival probabilities at follow-up, according to the patients' characteristics. The analyses were performed using R software (version 3.6.2) with the packages survival, survminer, ipred, randomforestSRC, and rms.

Results

Baseline

Since March 2009 to May 2019, 263 consecutive patients underwent trans-apical valve implantation at our institution. Mitral valve-in-valve or valve-in-ring procedures, aortic valve-in-valve procedures, TAVI for pure aortic regurgitation were performed in 11, 9, and 5 patients, respectively and were excluded from the analysis. We also excluded 4 more patients who received JV for aortic valve stenosis. The remaining 234 patients underwent TA-TAVI for severe native aortic valve stenosis and represent the population of this study. Preoperative patients' data for the overall population and for patients with S3 and AC devices are depicted in Table 1. Median age was 81 years (IQR: 77-84 years), 119 patients (50.8%) were male, and 156 patients (66.7%) were in New York Heart Association functional classification III or IV. Median EuroSCORE II and STS-PROM score were 4.8% (IQR: 3.1-8.1) and 4.6% (IQR: 2.9-8), respectively. S3 and AC patients were similar in terms of baseline characteristics.

Early Results

The first-generation SA was implanted in 39 patients (16.7%) from March 2009 to August 2010; SXT was implanted in 72 patients (30.8%), from September 2010 to January 2017. The last generation valves, S3 and AC were used in 78 (33.3%) and 45 (19.2%) patients, respectively. S3 was introduced in our practice in March 2014, while AC in February 2016. Procedural, early clinical and hemodynamic results of the entire population and of patients with S3 and AC are shown in Table 2. Overall all-cause 30-day VARC-2 mortality was 5.1% (12 patients) and it was

TABLE 1. Clinical and echocardiographic variables at baseline

Variables	Overall (n = 234)	Sapien 3 (n = 78)	Acurate TA (n = 45)	*P*-value
Age, y	81 (77-84)	80 (76-84)	81 (77-84)	0.613
Gender				0.877
Male	119 (50.8)	40 (51.3)	21 (46.7)	
Female	115 (49.1)	38 (48.7)	24 (53.3)	
Height, cm	165 (158.5-170)	164 (156.5-170)	166 (160-170)	0.877
Weight, kg	68 (60-76)	67 (59-76.5)	72 (58-78)	0.811
BSA	1.75 (1.6-1.9)	1.75 (1.6-1.9)	1.8 (1.6-1.9)	0.811
BMI	22.4 (21.4-23.4)	22.25 (21.2-22.9)	22.2 (21.3-22.8)	0.877
Arterial hypertension	213 (91)	69 (88.5)	44 (97.8)	0.613
Diabetes mellitus	76 (32.5)	30 (38.5)	15 (33.3)	0.877
Peripheral vascular disease	129 (55.1)	40 (51.3)	24 (53.3)	0.909
COPD	42 (17.9)	15 (19.2)	6 (13.3)	0.811
Neurologic dysfunction	21 (9.0)	7 (9)	5 (11.1)	0.877
Previous AMI				0.877
Absent	192 (82.1)	54 (69.2)	33 (73.3)	
<90 days	6 (2.6)	4 (5.1)	1 (2)	
>90 days	36 (15.4)	20 (25.6)	11 (24.4)	
History of CAD	123 (52.6)	42 (53.8)	31 (68.9)	0.811
Previous cardiac surgery	54 (23.1)	18 (23.1)	10 (22.2)	0.877
Serum creatinine, mg/dl	1.04 (0.85-1.31)	0.97 (0.82-1.21)	1.08 (0.80-1.29)	0.877
Hemoglobin, g/L	119.5 (110-132)	118 (110.3-131)	115 (106-130)	0.827
NYHA functional class				0.613
I	8 (3.4)	0 (0)	0 (0)	
II	70 (29.9)	24 (30.8)	22 (48.9)	
III	123 (52.6)	42 (53.8)	21 (46.7)	
IV	33 (14.1)	12 (15.4)	2 (4.4)	
Cardiac rhythm				0.613
Sinus rhythm	136 (58.1)	37 (47.4)	30 (66.7)	
Atrial fibrillation	74 (31.6)	32 (41)	11 (24.4)	
Pace-maker	24 (10.3)	9 (11.5)	4 (8.9)	
Critical status	6 (2.6)	2 (2.6)	2 (4.4)	0.877
EuroSCORE I	11.6 (8.2-22.5)	10.6 (7.6-20.9)	8.6 (6.5-10.2)	0.380
EuroSCORE II	4.8 (3.1-8.1)	4 (2.3-5.8)	3 (2.1-3.3)	0.811
STS score	4.6 (2.9-8)	3.3 (2.3-4.8)	3.3 (2.6-4.3)	0.908
Peak aortic gradient, mmHg	70 (55-85)	69 (54.5-85.5)	71 (64.5-85)	0.755
Mean aortic gradient, mmHg	42 (32-52)	41 (32-50)	46 (38.25-51.75)	0.755
iEOA, cm^2/m^2	0.47 (0.38-0.60)	0.44 (0.36-0.58)	0.46 (0.39-0.52)	0.877
Aortic regurgitation				0.755
1+/4	119 (50.9)	42 (53.8)	25 (55.6)	
2+/4	37 (15.8)	8 (10.3)	1 (2)	
3+/4	4 (1.7)	3 (3.8)	0 (0)	
4+/4	0 (0)	0 (0)	0 (0)	
Mitral regurgitation				0.755
1+/4	119 (50.9)	36 (46.1)	25 (55.6)	
2+/4	36 (15.4)	10 (12.8)	3 (6.7)	
3+/4	11 (4.7)	4 (5.1)	0 (0)	
4+/4	0 (0)	0 (0)	0 (0)	

(*continued*)

TABLE 1. (*continued*)

Variables	Overall (n = 234)	Sapien 3 (n = 78)	Acurate TA (n = 45)	*P*-value
Ejection fraction, %	56 (47-64)	58 (47-65)	56 (50-64)	0.980
End-diastolic volume, ml/m^2	62 (49-73)	57 (48-76)	57 (49-65)	0.811
Porcelain aorta	35 (15)	7 (9)	5 (11.1)	1.0

AMI, acute myocardial injury; BMI, body mass index; BSA, body surface area; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; iEOA, indexed effective orifice area; NYHA, New York Heart Association; STS, Society of Thoracic Surgeons.

similar between S3 and AC patients. Overall VARC-2 device success was 95.7% (224 patients) with no differences between S3 and AC. Procedural complications were observed in 20 patients (8.5%) overall, with no differences between groups. The incidence of permanent pace-maker implantation was 6.8% (16 patients); in particular, it was 10.3% (8 patients) and 4.4% (2 patients) in S3 and AC patients respectively, $P = 0.878$. The incidence of major/minor stroke was 1.7% (4 patients). Complications related to the LV apex occurred in 2 patients (0.9%); of these, 1 was managed through the same mini-thoracotomy and 1 required conversion to sternotomy and cardiopulmonary bypass institution. They all survived and were successfully discharged. At discharge, peak gradients were 15 mmHg (IQR:11.3-19) and 15.5 mmHg (IQR: 10.3-21) in S3 and AC, respectively ($P = 1$); mean gradients were 9 mmHg (IQR 6-10) and 10 (IQR 6-12) in S3 and AC, respectively ($P = 0.878$). A total of 68 patients (30.6%) had PVL at discharge, of these mild and moderate PVL were found in 64 (27.4%) and 4 (1.7%) patients, respectively. At discharge, severe PVL was never found. PVL rate was 24.4% (19 patients) and 40% (18 patients) in S3 and AC patients, respectively ($P = 0.878$); of these only 1 PVL was moderate, and it was in the S3 group.

Survival

Median follow-up time was 35.2 months (IQR: 13.4-55.0). Median follow up for S3 and AC patients was 23.7 months (IQR: 12-43) and 20.5 months (IQR: 12-25.3), respectively. Kaplan-Meier overall survival rates at 2, 5, and 8 years were 75% (95% CI: 69-81), 44% (95% CI: 36-53), and 15% (95% CI: 8-26), respectively. Kaplan-Meier survival from cardiovascular mortality at 2, 5 and 8 years was 91.3% (95% CI: 87.6%-95.1%), 82.4% (95% CI: 76.3-88.5%), and 69.7% (95% CI: 60.7%-78.7%).

According to STS surgical risk, survival rates at 2, 5, and 8 years were 72% (95% CI: 62-83), 51% (95% CI: 38-69), and 15% (95% CI: 5-47) in

TABLE 2. Procedural and postoperative outcomes

Variables	Overall (n = 234)	Sapien 3 (n = 78)	Acurate TA (n = 45)	*P*-value
Sapien	39 (16.7)			-
23mm	15 (6.4)			
26mm	24 (10.3)			
Sapien XT	72 (30.8)			
23mm	18 (7.7)			
26mm	36 (15.4)			
29mm	18 (7.7)			
Sapien 3	78 (33.3)	78 (100)		
20mm	1 (0.4)	1 (1.3)		
23mm	24 (10.3)	24 (30.8)		
26mm	36 (15.4)	36 (46.2)		
29mm	15 (2.1)	15 (19.2)		
Acurate TA	45 (19.2)		45 (100)	
S	8 (3.4)		8 (17.8))	
M	15 (6.4)		15 (33.3)	
L	22 (9.4)		22 (48.9)	
Intraprocedural complication	20 (8.5)	5 (6.4)	3 (6.7)	1.0
Prosthesis embolization	2 (0.9)	0	0	
Need for circulatory support	6 (2.6)	0	1 (2.2)	0.878
Conversion to full sternotomy	4 (1.7)	0	0	-
Bleeding/rupture of LV apex	2 (0.9)	0	0	-
Cardiac arrest	4 (1.7)	2 (2.6)	0	0.878
Annular rupture	2 (0.9)	0	0	-
VARC device success	224 (95.7)	73 (93.6)	44 (97.8)	0.878
ICU stay, hours	24 (24-48)	24 (24-48)	24 (24-54)	0.878
Stroke				0.919
TIA	1 (0.4)	0	0	
Minor	1 (0.4)	1 (1.3)	0	
Major	2 (0.9)	0	1 (2.2)	
Life-threating/major bleeding	7 (3)	2 (2.6)	0	1.0
Pace-maker implantation	16 (6.8)	8 (10.3)	2 (4.4)	0.878
Creatinine peak, mg/dl	1.3 (1.06-1.77)	1.29 (1.10-1.62)	1.30 (1.03-1.91)	1.0
CVVH	18 (7.7)	9 (11.5)	3 (6.7)	0.878
Chronic dialysis	1 (0.4)	0	0	-
VARC overall mortality	12 (5.1)	5 (6.4)	2 (4.4)	0.992
VARC cardiovascular mortality	6 (2.6)	3 (3.8)	2 (4.4)	0.992
Transvalvular peak gradient at discharge, mmHg	17 (12-22)	15 (11.25-19)	15.5 (10.25-21)	1.0
Transvalvular mean gradient at discharge, mmHg	9 (7-12)	9 (6-10)	10 (6-12)	0.878
Paravalvular leak	68 (30.6)	19 (24.4)	18 (40)	0.878
Mild	64 (27.4)	18 (23.1)	18 (40)	
Moderate	4(1.7)	1(1.3)	0	
Mitral regurgitation				0.878
1+/4	100 (42.7)	24 (30.8)	15 (33.3)	
2+/4	15 (6.4)	3 (3.8)	5 (11.1)	
3+/4	2 (0.9)	0	0	
4+/4	0	0	0	
Ejection fraction, %	56 (47.5-63)	55.5 (45.75-60.25)	55 (52-62)	0.878

CVVH, continuous veno-venous hemofiltration; ICU, intensive care unit; LV, left ventricle; TIA, transient ischemic attack; VARC, valve academic research consortium.

the low-risk group (STS <4%), respectively; 84% (95% CI: 75-95), 40% (95% CI: 28-58), and 16% (95% CI: 7-36), in the intermediate-risk group (STS 4%-8%), respectively, and 73% (95% CI: 61-88), 45% (95% CI: 31-65), and 14% (95% CI: 5-37), in the high-risk group (STS >8%), respectively ($P = 0.65$). Survival was similar between S3 and AC. In particular, overall survival at 1, 2, and 3 years in the S3 group was: 82% (95% CI: 74%-92%), 70% (95% CI: 60%-82%) and 68% (95% CI: 57%-81%), respectively; in the AC group, it was: 90% (95% CI: 82%-100%), 69% (95% CI: 54%-88%) and 51% (95% CI: 31%-83%), respectively ($P = 0.79$) (Fig 1A-D). Three patients underwent reoperation (1.4%), 2 for severe SVD (one 23 mm SA and one 29 mm SXT, 6 and 4 years after TAVI, respectively) and 1 for valve-thrombosis (26 mm S3, 4 years after TAVI); the firsts underwent surgical aortic valve replacement whereas the latter was treated by a valve-in-valve TF-TAVI. One patient had valve-endocarditis treated by antibiotics with complete recovery. In addition, pseudoaneurysm of the LV apex was found in 1 patient who underwent strict echocardiographic follow-up due to very advanced age and multiple comorbidities.

Hemodynamics at Follow-Up

Hemodynamic data regarding valve function at follow-up are shown in Fig 2. Mean transvalvular gradient at 1, 3, and 5 years for SA was 7 mmHg (IQR: 5-10 mmHg), 4 mmHg (IQR: 2-8 mmHg), and 4 mmHg (IQR: 2-6.5 mmHg), respectively; for SXT it was 9.5 mmHg (IQR: 4.25-12), 8 mmHg (IQR: 6-14 mmHg), and 11.5 mmHg (IQR: 9.5-15 mmHg), respectively; for S3 it was 9 mmHg (IQR: 4-12 mmHg), 8 mmHg (IQR: 4.5-13.5 mmHg), and 19 mmHg (IQR: 15-19.5 mmHg), respectively; and for AC it was 7 mmHg (IQR: 3.25-11.75), and 5.5 mmHg (3.25-7.75 mmHg), respectively (data at 5 years was not available). SVD occurred in 25 patients (11.3%) overall. In patients with SA, SXT, S3, and AC, SVD was found in 5 (13.6%), 11 (10.7%), 8 (11%) (13.4% considering the entire Sapien family) and 1 (2.3%) patient, respectively. Complete hemodynamic data of all devices at all timepoints is shown in the Supplemental Material.

Machine Learning Model for Independent Predictors of Mortality

According to the RF's Minimal Depth ranking for variables selection measure, the strongest survival predictors were age, body mass index,

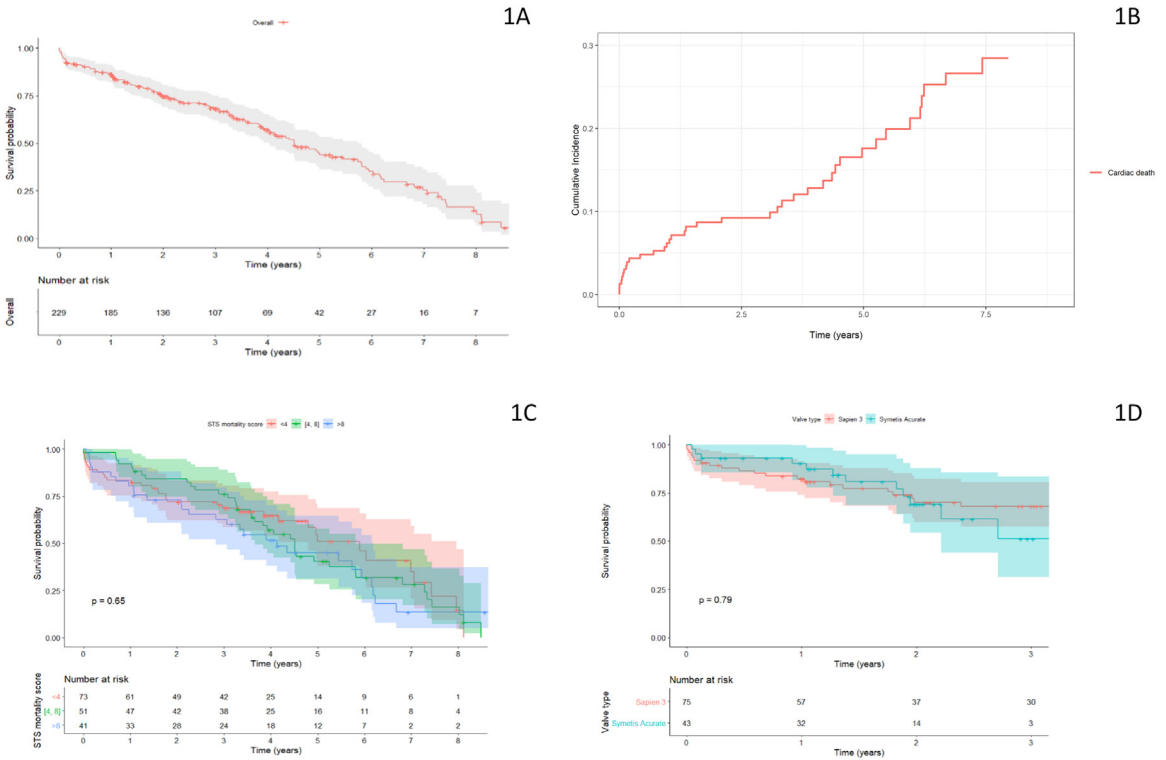

FIG 1. Kaplan-Meier survival estimates and cumulative incidence function for overall survival (1A); cardiovascular mortality at follow-up (1B); survival according to STS score (1C); survival according to Sapien 3 and Acurate-TA (1D). (Color version of figure is available online.)

and ejection fraction (Fig 3). The figure in the Supplement Material presents the impact of survival predictors on survival probability at follow-up. Survival decreases as age increases. For what concerns ejection fraction, survival predictions were better for subjects with an ejection fraction higher than 50%. The performance of the bagging algorithm was very good, with an out-of-basket of 19.4%. Fig 4 shows an example of the on-line tool that has been developed in order to predict survival after TA-TAVI in each single patient.

Discussion

This study reports a comprehensive analysis of 10-year experience with TA-TAVI in a single-center. The main findings of this study can be summarized as follows: 1) patients undergoing TA-TAVI have good post-procedural early and long-term outcomes in terms of survival and valve-related complications; 2) hemodynamic evaluation of all study devices showed good performances at follow-up with no differences between the 2 currently commercially available prostheses, 3) MLTs represent a new interesting tool for risk prediction of survival not only in the early postoperative period but also during follow-up.

TAVI has evolved rapidly in the last decade, from its first appearance in high-risk inoperable patients until its adoption in the low-risk population.[12,13] However, the knowledge about mid- and long-term TAVI results is still poor and difficult due to the low long-term survival expectation of patients operated in the early experience. Survival data reported in our study show good early and mid-term outcomes followed by a decrease at 5- and 8-year follow-up (44% at 5-year follow-up and 15% at 8-year follow-up). These results are similar to those reported in other studies regarding both TA and TF-TAVI.[14] Although many papers show worse survival in TA patients,[15-17] recent risk-adjusted analyses demonstrated that access (TF vs TA) had no impact on long-term survival.[18] A previous paper by our group with mid-term results, showed no differences in survival at follow-up between TF and TA patients.[19] Furthermore, the incidence of access-related complications was extremely low in this series, confirming the safety of the apical access. Nevertheless, previous studies have demonstrated that the TA access does not impact left ventricular function[20] and also that it can be safely performed in patients with low ejection fraction.[21] This aspect is crucial for several reasons: first, TA should still be considered as an excellent alternative access if TF is not indicated; second, there are several procedures that still need

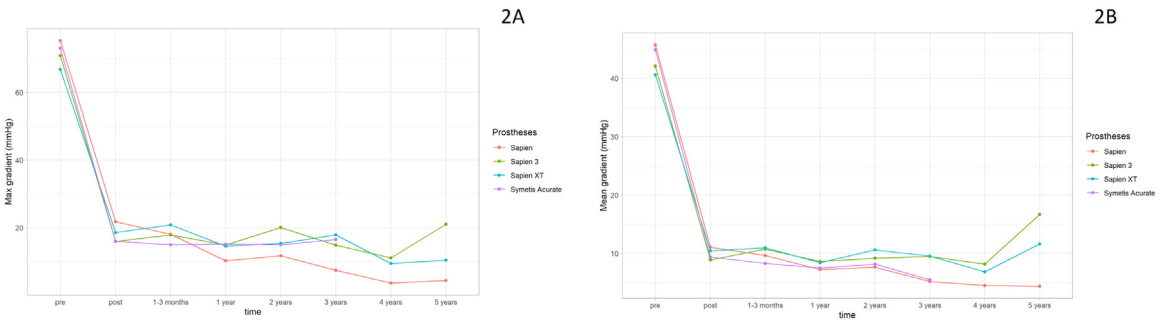

FIG 2. Peak and mean transaortic gradients at baseline, at discharge and at follow-up for each prosthesis. (Color version of figure is available online.)

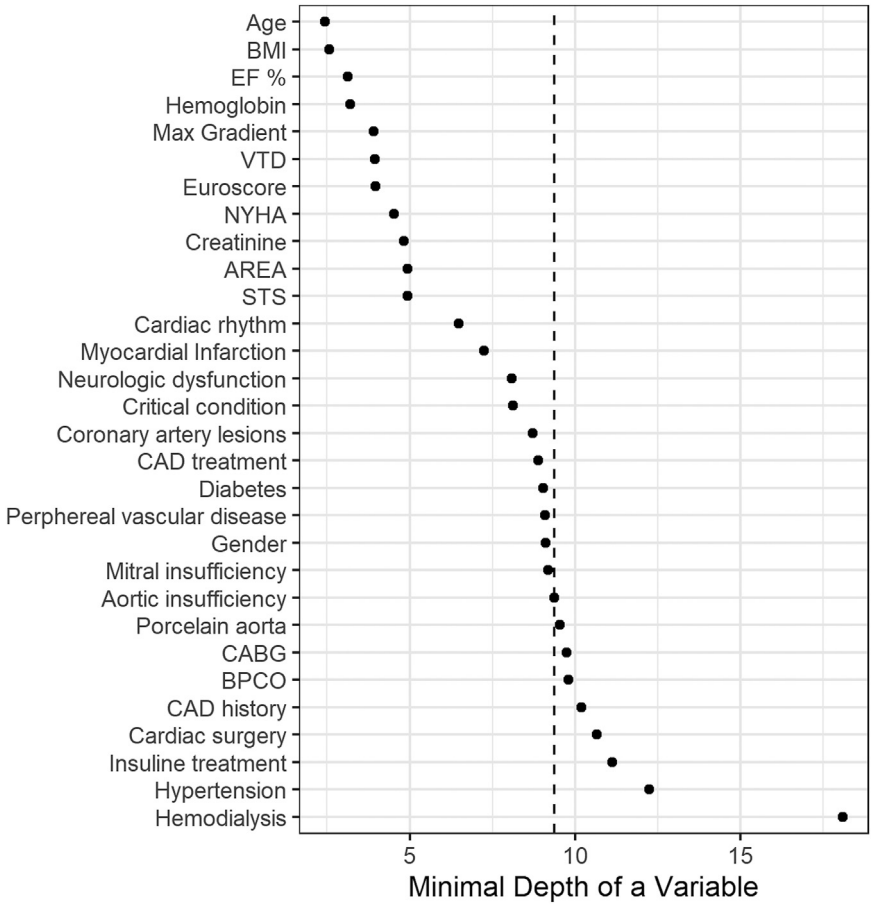

FIG 3. Rank of the survival predictors identified by the RF algorithm according to minimal depth ranking for variable selection.

an apical approach such as on-pump beating heart neochordae implantation and transcatheter mitral valve replacement.

The fact that we did not observe significant differences in mortality among patients with low, intermediate and high-risk profile is not really surprising. In fact, the currently available scoring systems (EuroSCORE, STS score) have shown to be poorly related with long-term outcomes in TAVI patients. Grossi et al.[22] demonstrated that EuroSCORE was not significantly correlated with mortality in a highly selected cohort of aged patients with numerous cardiac and non-cardiac comorbidities. Several TAVI specific models have been developed over time: STS/ACC,[23] FRANCE-2,[24] SURTAVI,[25] etc. All the above-mentioned scores predict

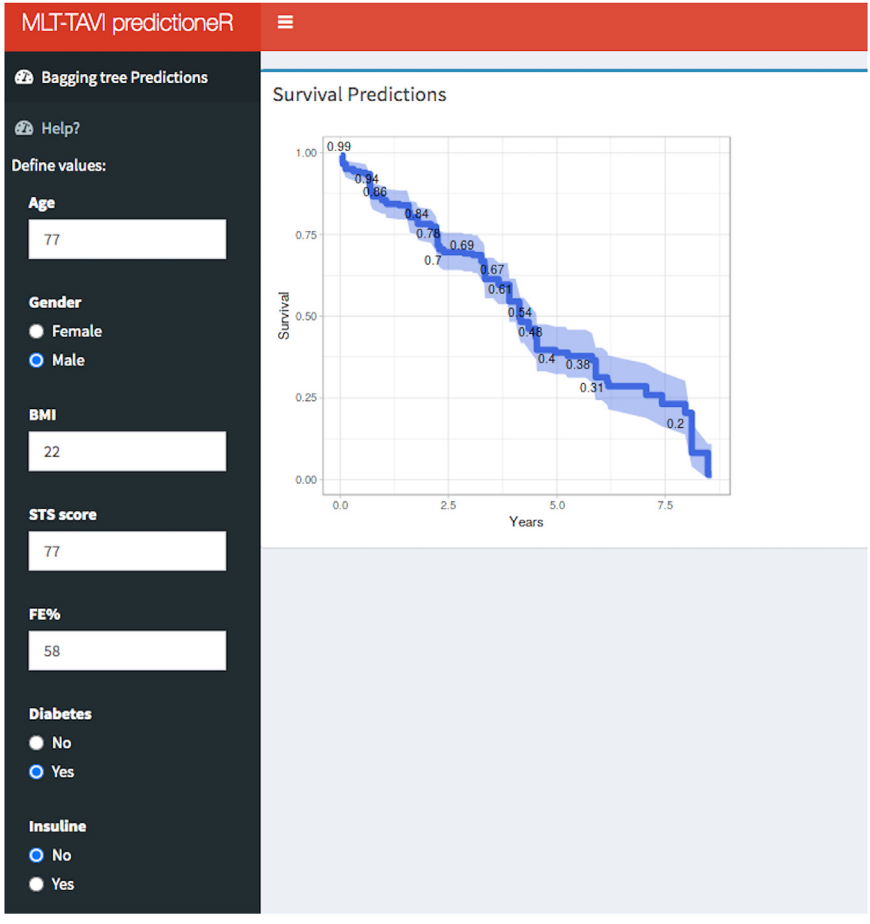

FIG 4. Screenshot of a proof of an on-line tool that enables prediction of patient survival after TA-TAVI through a Machine learning technique model. (Color version of figure is available online.)

early mortality (all 30-day, SURTAVI 1-year, too). In order to identify predictors of mortality at longer follow-up times, we used MLTs with a random forest algorithm and a bagging algorithm. Differently from traditional risk prediction scores, these techniques allow the creation of a predicted survival curve for each single patient, thus giving an idea not only of early results but also of the potential fate of every single patient at follow up. There is also the possibility to generate an app-based tool for immediate and bedside patient evaluation. Further studies on larger populations with long follow-up are definitely needed to validate this model that, so far, should be considered still under development.

The evaluation of valve durability in TAVI studies is always difficult because, due to the rapid evolution of devices and to the initial patient selection (inoperable and high-risk patients), patients with a long follow-up available are few and were treated with first generation devices. Therefore, a reliable evaluation of TAVI-devices durability is still far from what we are used with surgical aortic valve prostheses whose durability is well documented by several real long-term studies.[26] SVD in TAVI devices has been shown to occur in about 0%-15% of patients beyond 5-year follow-up.[27] However, many studies on TAVI valves deterioration include different devices that have different structural characteristics (leaflets, stents, height, etc), different crimping systems and also different anticalcification treatments; all these factors may significantly affect valve durability. Therefore, freedom from SVD analysis should be made for every single device and generation in order to be reliable; this implies large cohorts and long follow-up times. For this reason, we decided to report only the number of patients who developed SVD. We found a reasonably low incidence of SVD, 11.3% in the entire cohort, similar to Durand and coll. who found, in a recently published paper using the new European definitions, a SVD rate of 10.4% 7 years after TAVI.[28] Another finding that confirms the good durability of TAVI valves is that hemodynamic performance of devices included in this study was good and remained stable over time. Looking at the 2 most recent devices (S3 and AC), both prostheses showed good early and mid-term hemodynamic performance. Five-year follow-up from the PARTNER 2A trial demonstrated higher SVD or bioprosthetic valve failure with SXT than surgery (9.5% vs 3.5%, $P = 0.002$).[29] In contrast, the newer generation S3 had a rate of 2.7% at 4 years for SVD or bioprosthetic valve failure, and recent studies on AC suggest a favorable durability at 5-year follow-up.[30]

Conclusion

According to our data, TA-TAVI provides excellent early and long-term outcomes. All TA-TAVI devices and in particular the 2 commercially available at the moment showed similar clinical and hemodynamic outcomes. These data support the choice of TA-TAVI as an optimal alternative access whenever the TF route is not feasible.

Authors' Contribution

Augusto D'Onofrio: conceptualization, data curation, methodology, supervision, visualization, validation, writing—original draft, Chiara Tessari: data curation, investigation, methodology, validation, visualization,

writing—original draft, Giuseppe Tarantini: conceptualization, supervision, validation, Giorgia Cibin: data curation, investigation, Giulia Lorenzoni: formal analysis, investigation, visualization, writing—original draft, Rita Pesce: Data curation, Investigation, Chiara Fraccaro: conceptualization, supervision, validation, Massimo Napodano: conceptualization, supervision, validation, Dario Gregori: Formal analysis, investigation, visualization, validation, Gino Gerosa: conceptualization, supervision, Validation.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cpcardiol.2023.101734.

REFERENCES

1. D'Onofrio A, Salizzoni S, Agrifoglio M, et al. Medium term outcomes of transapical aortic valve implantation: results from the Italian Registry of Trans-Apical Aortic Valve Implantation. *Ann Thorac Surg* 2013;96:830–5.
2. Siontis GC, Praz F, Pilgrim T, et al. Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of severe aortic stenosis: a meta-analysis of randomized trials. *Eur Heart J* 2016;37:3503–12.
3. Nakatsuka D, Tabata M. Transapical approach for transcatheter aortic valve implantation. *Ann Cardiothorac Surg* 2017;6:553–4.
4. Nashef SA, Roques F, Sharples LD, et al. EuroSCORE II. *Eur J Cardiothorac Surg* 2012;41:734–44.
5. Kappatein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the valve academic research consortium-2 consensus document. *J Thorac Cardiovasc Surg* 2013;145:6–23.
6. Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J* 2017;38:2739–91.
7. Webb JG, Altwegg L, Masson JB, et al. A new transcatheter aortic valve and percutaneous valve delivery system. *J Am Coll Cardiol* 2009;53:1855–8.
8. Walther T, Dewey T, Borger MA, et al. Transapical aortic valve implantation: step by step. *Ann Thorac Surg* 2009;87:276–83.
9. Dokainish H, Nguyen JS, Bobek J, et al. Assessment of the American Society of Echocardiography-European Association of Echocardiography guidelines for diastolic function in patients with depressed ejection fraction: an echocardiographic and invasive haemodynamic study. *Eur J Echocardiogr* 2011;12:857–64.
10. Capodanno D, Petronio AS, Prendergast B, et al. Standardized definitions of structural deterioration and valve failure in assessing long-term durability of transcatheter and surgical aortic bioprosthetic valves: a consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) endorsed by the

European Society of Cardiology (ESC) and the European Association of Cardio-Thoracic Surgery (EACTS). *Eur J Cardiothorac Surg* 2017;52:408–17.
11. Couronné R, Probst P, Boulesteix A-L. Random forest versus logistic regression: a large-scale benchmark experiment. *BMC Bioinformatics* 2018;19:270.
12. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Eng J Med* 2019;380:1695–705.
13. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Eng J Med* 2019;380:1706–15.
14. Chakos A, Wilson-Smith A, Arora S, et al. Long term outcomes of transcatheter aortic valve implantation (TAVI); a systematic review of 5-year survival and beyond. *Ann Cardiothorac Surg* 2017;6:432–43.
15. Kodali S, Thourani VH, White J, et al. Early clinical and echocardiographic outcomes after SAPIEN 3 transcatheter aortic valve replacement in inoperable, high-risk and intermediate-risk patients with aortic stenosis. *Eur Heart J* 2016;37:2252–62.
16. Yamamoto M, Mouillet G, Meguro K, et al. Clinical results of transcatheter aortic valve implantation in octogenarians and nonagenarians: insights from the FRANCE-2 registry. *Ann Thorac Surg* 2014;97:29–36.
17. Biancari F, D'Errigo P, Rosato S, et al. Transcatheter aortic valve replacement in nonagenarians: early and intermediate outcome from the OBSERVANT study and meta-analysis of the literature. *Heart Vessels* 2016;1:1–9.
18. Reents W, Barth S, Griese DP, et al. Transfemoral versus transapical transcatheter aortic valve implantation: a single-centre experience. *Eur J Cardiothorac Surg* 2019;55:744–50.
19. D'Onofrio A, Facchin M, Besola L, et al. Intermediate clinical and hemodynamic outcomes after transcatheter aortic valve implantation. *Ann Thorac Surg* 2016;101:881–8.
20. D'Onofrio A, Besola L, Rizzoli G, et al. Impact of changes in left ventricular ejection fraction on survival after transapical aortic valve implantation. *Ann Thorac Surg* 2017;103:559–66.
21. D'Onofrio A, Salizzoni S, Filippini C, et al. Transapical aortic valve replacement is a safe option in patients with poor left ventricular ejection fraction: results from the Italian Transcatheter Balloon-Expandable registry (ITER). *Eur J Cardiothorac Surg* 2017;52:874–80.
22. Grossi EA, Schwartz CF, Yu PJ, et al. High-risk aortic valve replacement: are the outcomes as bad as predicted? *Ann Thorac Surg* 2008;85:102–6.
23. Arsalan M, Weferling M, Hecker F, et al. TAVI risk scoring using established versus neu scoring system: role of the new STS/ACC model. *EuroIntervention* 2018;13:1520–6.
24. Lee ZX, Elangovan S, Anderson R, et al. Short- and medium-term survival after TAVI: clinical predictors and the role of the FRANCE-2 score. *Int J Cardiol Heart Vasc* 2020;31:100657.
25. van Mieghem NM, Head SJ, van der Boon RM, et al. The SURTAVI model: proposal for the pragmatic risk stratification for patients with severe aortic stenosis. *EuroIntervention* 2012;8:258–66.

26. Rahimtoola SH. Choice of prosthetic heart valve in adults: an update. *J Am Coll Cardiol* 2009;55:2413–26.
27. Fauvel C, Capoulade R, Durand E, et al. Durability of transcatheter aortic valve implantation: a translational review. *Arch Cardiovasc Dis* 2020;113:209–21.
28. Durand E, Sokoloff A, Urena-Alcazar M, et al. Assessment of long-term structural deterioration of transcatheter aortic bioprosthetic valves using the new European definition. *Circ Cardiovasc Interv* 2019;12:e007597.
29. Makkar RR, Thourani VH, Mack MJ, et al. Five-year outcomes of transcatheter or surgical aortic-valve replacement. *N Eng J Med* 2020;382:799–809.
30. Pibarot P, Ternacle J, Jaber WA, et al. Structural deterioration of transcatheter versus surgical aortic valve bioprostheses in the PARTNER 2 Trial. *J Am Coll Cardiol* 2020;76:1830–43.