Long Term Outcomes of Patients Treated With Transcatheter Aortic Valve Implantation

Nili Schamroth Pravda, MD[a,#,*], Pablo Codner, MD[a,#], Hana Vaknin Assa, MD[a], Guy Witberg, MD[a], Abid Assali, MD[b], Katia Orvin, MD[a], Ashraf Hamdan, MD[a], Yichayaou Belosesky, MD[c], Alon Barsheshet, MD[a], Ram Sharoni, MD[d], Omri Soudry, BMedLabSc[e], Leor Perl, MD[a], Yaron Shapira, MD[a], Alik Sagie, MD[a], and Ran Kornowski, MD[a]

Transcatheter aortic-valve implantation (TAVI) is an established treatment option in patients with severe symptomatic aortic stenosis. Intermediate and long-term follow up data of these patients is limited. Data was taken from a large all-comer single center prospective registry (2008 to 2019). The primary end point was all-cause mortality. The secondary endpoints were long-term valve hemodynamic performance; paravalvular leak (PVL) at 5-year follow-up. We also report on temporal trends in this cohort. Our cohort included 998 patients with a mean age of 82.3 ± 7.2 years and 52.2% females. TAVI was performed via the transfemoral, trans-apical, subclavian and other access routes in 93.9%, 3.6%, 2.5%, and 0.6% of patients, respectively. A self-expandable device was used in 69.4% of cases, balloon expandable device in 28.1% and in 2.5% other devices. The cumulative risk for all-cause mortality at 5 years was 43.4% (95% CI 39.1 to 47.7). The immediate and long-term valve gradients were low and maintained. On durability analysis at 5 years, severe structural valve deterioration was present in 1.6% of cases. At 5-year follow-up, PVL was moderate in 3.3% and no patients has severe PVL. On temporal trends analysis, we found that the procedural aspects of TAVI improved over time with lower rates of significant PVL and significantly lower procedural mortality. In conclusion, TAVI patients have a favorable long-term outcome, with excellent valve hemodynamic parameters and good clinical outcomes. Over time and with increasing experience, procedural and patient outcomes have improved. **(Am J Cardiol 2021;141:72−78)**

Transcatheter aortic-valve implantation (TAVI) is an evolving therapeutic technique geared towards patients with severe symptomatic aortic stenosis (AS) at high, intermediate and low risk for surgical valve replacement. TAVI has been based and established upon an increasing body of robust supporting evidence.[1] The intermediate and long-term follow-up data of these patients is however, quite limited. There have been ongoing improvements in TAVI. These include the addition of newer devices, more operator experience and improvements in delivery systems which have led to better patients outcomes and fewer procedural complications.[2,3] Moreover, there is accumulating data regarding the durability of these devices over time.[3−5] With the inclusion of younger and lower risk patient populations, the reliability and hemodynamic functioning of these valves over time is of extreme importance. We report herein on our clinical experience of treating patients with TAVI in our institution, aiming to provide insights into the clinical outcomes in a real-word cohort of all-comers patients. Our aims included exploring the longitudinal changes of the TAVI procedure and clinical results at our center as well as long term durability of transcatheter heart valves among our cohort.

Methods

We included consecutive patients undergoing TAVI for severe symptomatic AS at Rabin Medical Center, a public, academic, tertiary medical center, which is a referral center for both surgical aortic valve replacement and TAVI. The period covered was from November 2008 to December 2019. Patients undergoing valve-in-valve TAVI or transcatheter mitral interventions were excluded. The selection and assessment process of these patients in our institution has previously been described.[6] While patients largely underwent TAVI for significant AS, aortic regurgitation was the predominant pathology in 15 (1.5%) of the cohort. The baseline, procedural and peri-procedural findings are described.

TAVI is routinely done at our center with the assistance of an anesthesiologist. Hemodynamic assessment of the implanted valve is routinely performed immediately after

[a]Department of Cardiology, Rabin Medical Center, Petach Tikva, Israel; affiliated to Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [b]Department of Cardiology, Meir Medical Center, Kfar Saba, Israel; affiliated to Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [c]Department of Geriatrics, Rabin Medical Center, Petach Tikva, Israel; affiliated to Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [d]Cardio-thoracic Surgery department, Rabin Medical Center, Petach Tikva, Israel; affiliated to the Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; and [e]Tel Aviv University, Tel Aviv, Israel. Manuscript received September 27, 2020; revised manuscript received and accepted November 3, 2020.

[#]Equal contribution.See page 77 for disclosure information.

*Corresponding author: Tel: +(972) 54-447-6243; Fax: + 97239249850.

E-mail address: drnscham@gmail.com (N. Schamroth Pravda).

0002-9149/
https://doi.org/10.1016/j.amjcard.2020.11.007

valve deployment in the catheterization suite in a multimodality approach including aortogram, echocardiography, and direct pressure gradient measurements. Clinical events were defined according to the Valve Academic Research Consortium 2 criteria.[7] Structural valve deterioration (SVD) was defined as per consensus statement from the European Society of Cardiology of percutaneous cardiovascular interventions 2017.[8] The prospective data collection was approved by the institutional review board. The primary endpoint was all-cause mortality. Data on mortality was based on mortality files derived from the notification of death form legally required by the Ministry of the Interior. The secondary endpoints were the in hospital and long-term valve hemodynamic competence of the implanted valves. We performed a sub-group analysis of patients who survived for 5 years or more, in which the endpoints evaluated were the presence of residual aortic paravalvular leak (PVL) and SVD. Furthermore, we divided our cohort into 3 longitudinal categories according to the years of treatment: period 1 was from 2008 to 2013, period 2 from 2014 to 2016, and period 3 from 2017 to 2019. We report on longitudinal practice changes in patient characteristics, procedural aspects and outcomes over this 11-year period. Baseline characteristics of the patients are presented as mean and standard deviation for continuous variables and count (%) for categorical variables. Continuous variables were compared using the Student's *t* test and/or Mann Whitney U test, categorical variables were compared using the chi-square and/or Fisher's exact test, as appropriate. All tests were 2 tailed, and a p value <0.05 was considered significant. Periprocedural outcomes were compared using the chi-square test (unadjusted analysis) and adjusted odds ratios were calculated using logistic regression models. All-cause mortality was graphically plotted using Kaplan-Meier curves and compared between groups using the log rank test (unadjusted analysis), Multivariate adjusted hazard ratios were calculated using Cox proportional hazards models. All TAVI-related data was registered in an electronic file and analysed using the SPSS, version 25.0, software (SPSS, Chicago, Illinois).

Results

From November 2008 to December 2019, 998 patients underwent TAVI in our institution for native valve severe AS. Baseline demographic and clinical characteristics are presented in Table 1. The mean age of patients was 82.3 ± 7.2 years (70% of patient ≥80 years old), and 52.2% were female. Baseline echocardiographic data at baseline is shown in Supplementary Table 1. The mean aortic valve mean gradient was 49.3 ± 15.3 mm Hg and mean aortic valve area 0.7 ± 0.2cm.[2] A preprocedural cardiac computer tomography (CCT) was performed in 766 patients (76.7% of the cohort). The average calcium score in these patients was 2340 ± 1396. Procedural characteristics are listed in Table 2. TAVI was performed via the transfemoral, trans-apical, subclavian and other access routes in 93.9%, 3.6%, 2.5%, and 0.6% of patients, respectively. A self-expandable device was used in 69.4% of cases, balloon expandable device in 28.1% and in 2.5% other devices.

Table 1
Baseline characteristics

Variable	(n = 998)
Men	477 (47.8%)
Age (Years)	82.3+-7.2
BMI (kg/m2)	27.9+-5.1
Coronary Artery Disease	387 (38.8%)
Prior Myocardial Infarction	102 (12.6%)
Prior Coronary Artery Bypass Grafting	157 (19.4%)
Prior Cerebral Vascular Accident	168 (17.1%)
Peripheral Vascular Disease	115 (11.7%)
Diabetes Mellitus	377 (38.4%)
Hypertension	914 (93.4%)
Chronic Dialysis	9 (3.2%)
Chronic Obstructive Pulmonary Disease	162 (16.5%)
Atrial Fibrillation	287 (29.2%)
Permanent pacemaker/Defibrillator	79 (8.0%)
Porcelain aorta	39 (4.0%)
Advanced Liver Disease	4 (0.4%)
Frailty	141 (14.4%)
NYHA Class I	12 (1.3%)
NYHA Class II	215 (22.7%)
NYHA Class III	542 (57.3%)
NYHA Class IV	177 (18.7%)
STS score	5.1+-3.9
EuroSCORE 2	4.6+-4.1
Medications (%)	
Aspirin	621 (63.1%)
Clopidogrel	18 (1.8%)
Ticagrelor	2 (0.2%)
Prasugrel	2 (0.2%)
Warfarin	173 (17.6%)
Dabigatran	11 (1.1%)
Apixaban	66 (6.7%)
Rivaroxaban	14 (1.4%)
Low Molecular weight heparin/ unfractionated heparin	3 (1.1%)
Angiotensin-converting enzyme inhibitor (ACE-I) or Angiotensin II receptor blocker (ARB)	585 (59.7%)
Beta Blocker	567 (57.7%)
Furosemide	528 (53.5%)
Statin	806 (81.9%)
Insulin	40 (14.4%)
Oral-antidiabetic agents	79 (28.1%)
Baseline ECG	
Atrial fibrillation / flutter	164 (19.6%)
Sinus Rhythm	673 (80.4%)
Complete Left Bundle Branch Block (LBBB)	101 (10.1%)
Complete Right Bundle Branch Block (RBBB)	87 (8.7%)
Baseline Blood Results	
Hemoglobin (g/dL)	11.9+-1.6
Creatinine (mg/dL)	1.2+-0.8
Mean Glomerular filtration (GFR) (according to MDRD formula)	61.4+-23.0
GFR > 90 ml/min/1.73 m2	113 (11.6%)
GFR 60-89	366 (37.5%)
GFR 30-59	424 (43.4%)
GFR 15-29	49 (5.0%)
GFR <15	24 (2.5%)
Albumin (g/dL)	4.1+-0.4

Table 2
Procedural characteristics

Procedure urgency	
Elective	931 (93.3%)
Urgent	67 (6.7%)
Anaesthesia method	
Conscious sedation	710 (71.4%)
General anaesthesia	122 (12.3%)
Local anaesthesia	163 (16.3%)
Vascular access	
Femoral artery	931 (93.9%)
Axillary Artery	25 (2.5%)
Apical	36 (3.6%)
Other	6 (0.6%)
Bail-out surgical	2 (0.2%)
Concomitant PCI	134 (13.4%)
Peripheral artery stent	5 (0.5%)
Embolic protection device	19 (1.9%)
Balloon pre-dilatation	336 (34.4%)
Valve type	
Medtronic Corevalve	259 (25.9%)
Medtronic Evolute R	268 (26.8%)
Medtronic Evolute PRO	156 (15.6%)
Edwards SAPIEN 3	184 (18.4%)
Edwards SAPIEN / XT	96 (9.6%)
Boston Scientific/Symethis ACURATE neo	10 (1.0%)
Boston Scientific Lotus	25 (2.5%)
Balloon post-dilatation	237 (24.76%)
Fluoroscopy time (min)	20.9+12.1
Contrast volume (ml)	155.6+-65.6
TAVR device success	926 (94.0%)

Table 3
Complications (periprocedural)

Angiographic perivalvular leak - None	546 (55.71%)
Angiographic perivalvular leak - Minimal	206 (21.02%)
Angiographic perivalvular leak – Mild	218 (22.24%)
Angiographic perivalvular leak - Moderate or severe	10 (1.02%)
Need for a second valve	28 (2.86%)
Coronary obstruction	3 (0.30%)
Ventricular septal perforation	1 (0.10%)
Cardiac tamponade	10 (1.02%)
Annular rupture	0 (0.00%)
Valve malpositioning	2 (0.20%)
Valve migration or embolization	19 (1.93%)
Peri-procedural MI (< 72 h after the index procedure)	4 (0.40%)
In-hospital stroke	33 (3.35%)
In hospital Transient Ischemic Attack	2 (0.20%)
Minor bleeding event	31 (3.17%)
Major bleeding event	17 (1.74%)
Acute kidney injury – Stage 1	28 (2.95%)
Acute kidney injury - Stage 2	9 (0.95%)
Acute kidney injury - Stage 3	3 (0.32%)
Need for post procedure hemodialysis	2 (0.20%)
Minor Vascular Complication	150 (15.23%)
Major Vascular Complications	31 (3.15%)
Complete Atrioventricular Block	28 (9.9%)
New Left Bundle Branch Block	222 (29.9%)
New Right Bundle Branch Block	82 (11.1%)
New permanent pacemaker implantation	134 (13.6%)
Procedural Mortality	19 (1.9%)
In hospital Mortality	25 (2.5%)
Mean Follow up (years after procedure)	2.9+-2.3
Overall mortality	336 (33.7%)
Kaplan Meier 5-year mortality	43.4 (CI 39.1 -47.7)

Peri-procedural complications are listed in Table 3. Vascular complications were common and occurred in 18.3% of the cohort, of which most (80.3%) were regarded as minor. These included 57 case of unplanned use of endovascular stent, 48 femoral artery pseudoaneurysms that were treated either conservatively or with the use of intravascular thombin, 4 arteriovenous fistulas and 37 other miscellaneous minor vascular complications. Approximately 13.6% of patients required a permanent pacemaker (PPM) post-TAVI. Of those who required a PPM, 82.2% had been treated with a self-expandable valve device. Postprocedural trans-aortic valve peak and mean gradients were: 14.9 ± 9.5 and 8.3 ± 5.9 mm Hg, respectively. Favorable valve hemodynamic performance was maintained on average at 5-year follow up. (Figure 1). Cumulative 5-year mortality risk was 43.4% (95% CI 39.1 to 47.7). STS score was the only significant independent predictor of 3-year and 5-year mortality (Supplementary Table 2 and Figure 2). One hundred and seventy-seven patients survived and had available clinical and echocardiographic data at 5 years follow up. The average age of those at 5 year follow up was 88.2 ± 6.0 years. Most of these patients were in NYHA functional class I/II (26.6% in NYHA class I, 64.2% in NYHA class II, 7.6% in NYHA class III, and 1.6% in NYHA class IV). In these patients, PVL was moderate or more in 3.3%. There were no patients with severe PVL. Overall, 27.1% and 1.6% met the definition for moderate and severe SVD respectively.

Result of the subanalysis of temporal trends in our cohort as shown in Table 4. We found that patients treated in the later period were significantly younger and had a lower STS score compared to the earlier periods. Over time, procedural time, length of hospital stay and the amount of contrast volume used were significantly reduced. The transaortic valve gradients post TAVI were low over all the time periods. Rates of moderate or more PVL and procedural mortality were significantly decreased over the periods.

Discussion

Over the years, TAVI has evolved as a refined treatment for patients with severe AS. However, coupled with this advancement, data from real-word registries on long-term patient outcomes and/or valve durability are fundamental to improve results further. Herewith we describe clinical outcomes of a large prospectively collected data cohort of patients over an 11-year period who had severe symptomatic AS and underwent TAVI in our institution. Our main findings are as follows: First, the primary end-point of all-cause mortality at median follow up time of 5 years was 43.4% (95% CI 39.1 to 47.7). Secondly, the immediate achieved valve gradients were favorable and maintained over the duration of the follow-up period. For patients who survived to 5 year follow up, the prevalence of severe SVD was low. Thirdly, in our temporal trends analysis, we found that over the years since TAVI was first performed in 2008 at our department, treated patients became relatively

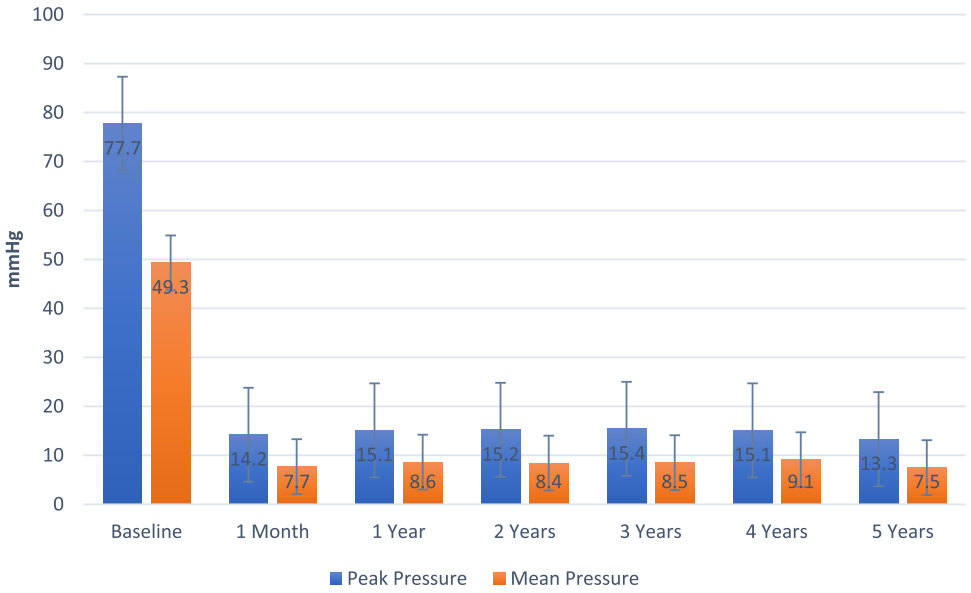

Figure 1. Aortic valve gradients over time.

younger with lesser co-morbidities as reflected by lower STS scores. Procedures were done quicker, with less contrast use and shorter hospital stays. This was also associated with lower procedural mortality and lower rates of PVL.

Our primary endpoint of all-cause mortality at 5 years follow up was 43.4% (95% CI 39.1 to 47.7). The mean STS score in our cohort was 5.1 ± 3.9 corresponding to intermediate risk. Our all-cause mortality is consistent and slightly lower than that reported in other TAVI registries of intermediate risk patients. In the PARTNER 2 trial, the all-cause mortality of patients in the TAVI arm at 5 years follow up was 46.0%.[9] In a large propensity matched analysis of TAVI patients at intermediate risk treated between 2010 and 2012, Barbanti et al. reported all-cause mortality rates of 48.3%.[10] The slightly lower mortality rates found in our cohort is possibly due to our registry extending up to 2019 with an increasing number of younger patients at intermediate and low surgical risks. This could also be indicative of increasing expertise, as our center has a growing annualized volume of TAVI procedures. Higher procedure volume correlates with lower mortality rates. [11] Patient selection for TAVI at our institution is performed in the setting of an experienced and multi-disciplinary "Heart Team." Selected patients undergo a comprehensive pre-procedural medical evaluation in a dedicated cardiac or geriatric unit. This approach may optimize patients' assessment and procedural preparation.

Importantly, our cohort showed that the immediate and long-term valve hemodynamic following TAVI were decent and maintained during follow up. An increasing body of evidence is accumulating showing the adequate hemodynamic valve performance of TAVI over time.[4,5] In

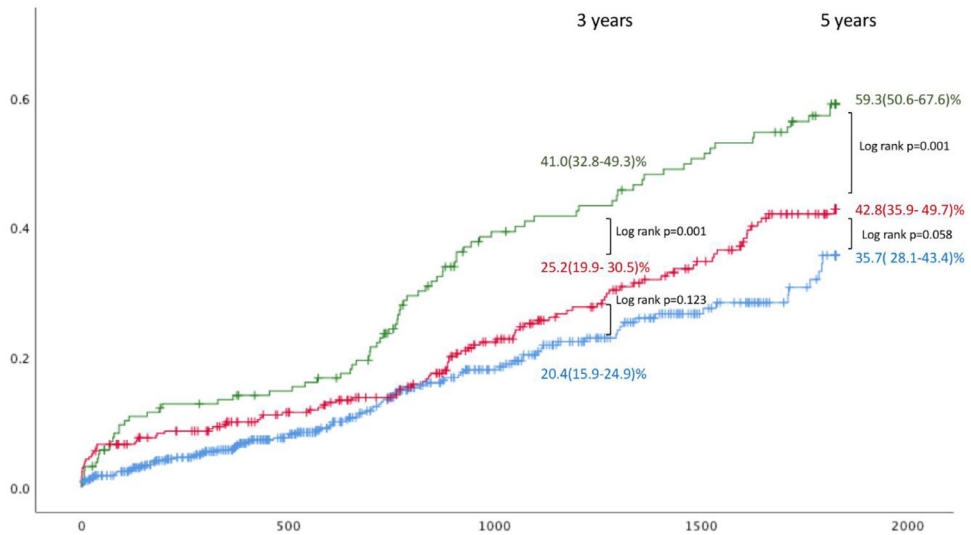

Figure 2. Mortality according to STS stratification (blue – low risk, red – intermediate risk, green – high and extremely high risk). (Color version of figure is available online)

Table 4
Temporal trends

	Period 1 (2008-2013)	Period 2 (2014-2016)	Period 3 (2017-2019)	*P* value
Number of Patients	246	298	451	
Age (years)	83.5+-6.3	83.5+-6.9	80.8+-7.5	<0.001
STS score	7.6+-4.7	5.0+-3.3	3.7+-2.8	<0.001
Patients with NYHA at baseline III/IV	239 (96.8%)	234 (78.0%)	285 (65.1%)	<0.001
Fluoroscopy Time (minutes)	22.7+-7.5	20.7+-15.3	20.9+-12.1	0.351
Contrast Volume (ml)	192.8+-70.6	156.0+-52.9	129.7+-50.9	<0.001
Length of Hospital Stay (days)	6.4+-4.6	5.0+-2.7	4.4+-2.8	<0.001
Women (% of total number of patients)	149 (60.3%)	157 (52.3%)	213 (47.4%)	0.005
Patients with Bicuspid Valve	2 (0.8%)	10 (3.4%)	20 (4.6%)	0.028
Vascular Access − Femoral	202 (81.8%)	286 (95.3%)	443 (98.2%)	<0.001
Vascular Access − Non-femoral	45 (18.2%)	14 (4.7%)	8 (1.8%)	<0.001
Balloon Pre-dilatation	219 (65.2%)	63 (18.8%)	54 (16.1%)	<0.001
Balloon Post-dilatation	28 (11.7%)	74 (30.8%)	138 (57.5%)	<0.001
Perivalvular Leak − moderate or more	107 (43.5%)	68 (22.9%)	53 (12.1%)	<0.001
Post TAVI Peak Aortic Valve gradient (mm Hg)	15.1+-7.9	14.7+-11.1	15.1+-9.2	0.877
Post TAVI mean Aortic Valve Gradient (mm Hg)	8.2+-4.9	8.5+-7.5	8.3+-4.4	0.788
In hospital CVA	10 (4.0%)	9 (3.0%)	14 (3.2%)	0.558
Minor Vascular Complications	48 (19.5%)	46 (15.3%)	56 (12.8%)	0.065
Major Vascular Complications	6 (2.4%)	6 (2.0%)	19 (4.3%)	
New Permanent Pacemaker Inserted	41 (16.6%)	44 (14.8%)	49 (11.2%)	0.108
1 Year Kaplan Meier Mortality Rate (95% Confidence Interval)	11.1 (7.4-14.8)	9.0 (5.6-12.3)	6.9 (4.4-9.4)	0.297
3 Year Kaplan Meier Mortality Rate (95% CI)	30.0 (24.3-35.7)	24.7 (19.8-29.6)	22.6 (15.4-29.8)	0.209
Procedural Mortality	10 (4.1%)	8 (2.7%)	1 (0.2%)	0.001

our subanalysis at 5 year follow up, the prevalence of moderate PVL was low, with no patients with severe PVL. This is most probably related to transition to newer devices with outer skirting and repositionable features, increased use of post dilation, as seen in our temporal trends analysis, and improve CCT based procedural planning. Post TAVI deployment analysis is routinely performed at our center with a multi-modality approach guiding decision making regarding the need for balloon post-dilation to reduce PVL.

The temporal trends we report herein are in correlation with an increasing body of evidence showing an increasing TAVI use in lower risk and relatively younger patients.[12] Temporal trends analysis has shown that our team has become more skilled as manifested by shortened procedural time and reduced hospital stay post TAVI. Alkhalil et al. found that a short hospital stay in selected patients is safe and has the potential to minimize functional decline and offer early rehabilitation to patient after TAVI.[13] This could be extremely beneficially in the elderly patients who constitute the majority of patients undergoing TAVI. We also found that over time the procedure was performed with significantly less contrast medium volume utilization. This is specifically important in preventing acute kidney injury and consequent poor outcomes, especially in octogenarians.[14] However vascular complications, although mostly minor, remained burdensome. Rates of major vascular complications were relatively low in comparison to other series.[15,16] Our rates of conduction abnormalities following TAVI are similar to previous reported data.[17] These were mostly seen in those in whom a self-expandable valve device was used, which is the majority of the devices used in our cohort. The need for new PPM was similar to the rates of implantation seen in other registries with a trend towards a lower number of patients needing a new PPM over time. [3,9,10]. This could be due to a preference of using balloon expandable valves for patients with baseline conduction abnormalities and anatomically guided minimizing implantation depth according to the CT-based membranous septum length.[18] At present, monitoring of conduction abnormalities is still one of the main issues delaying patient discharge. The incidence of in-hospital cerebrovascular accidents was similar over the 3 time periods. We assume that this rate could be diminished with the increasing use and availability of cerebral embolic protection devices which became available to us only in the very last period of our treated cohort.[19] The present study is a single-center analysis, and clinical and echocardiographic outcomes were self- reported with inherent limitations. However, the data was prospectively collected in a dedicated database and outcomes were rigorously assessed and reported based on the Valve Academic Research Consortium 2 criteria definitions. We did not have data on the different causes of mortality to differentiate between causes of death which were cardiovascular-related or non-cardiovascular related. We did not have CCT data for our entire cohort as our TAVI program started in 2008, but CCT for pre-TAVI procedural planning only became routine in the year 2015. Long-term echocardiographic data was not available for all our patients who were followed up for 5 years or more.

In conclusion, patients undergoing TAVI in our all-comer registry had encouraging intermediate and long-term clinical outcomes. Valve hemodynamic was maintained with a low rate of SVD. There have been many advances in the procedural aspects of TAVI in the past decade and these developments were adopted at our center causing improved procedural aspects and broadened patient population throughout the analysis.

Authors' Contributions

Nili Schamroth Pravda: Investigation, Writing - Original Draft, Methodology, Data Curation; Pablo Codner: Investigation, Writing - Original Draft, Conceptualization, Methodology, Formal analysis; Hana Vaknin Assa: Investigation, Resources, Writing - Review & Editing; Guy Witberg Formal analysis, Writing - Review & Editing, Methodology, Visualization; Abid Assali: Investigation, Resources, Writing - Review & Editing; Katia Orvin: Investigation, Resources, Writing - Review & Editing; Ashraf Hamdan: Investigation, Resources, Writing - Review & Editing; Yichayaou Belosesky: Investigation, Resources, Writing - Review & Editing; Alon Barsheshet: Investigation, Resources, Writing - Review & Editing; Ram Sharoni: Investigation, Resources, Writing - Review & Editing; Omri Soudry: Data Curation, Investigation, Writing - Review & Editing; Leor Perl: Investigation, Resources, Writing - Review & Editing; Yaron Shapira: Investigation, Resources, Writing - Review & Editing; Alik Sagie: Investigation, Resources, Writing - Review & Editing; Ran Kornowski: Conceptualization, Methodology, Writing - Review & Editing, Supervision.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2020.11.007.

1. Siontis GCM, Overtchouk P, Cahill TJ, Modine T, Prendergast B, Praz F, Pilgrim T, Petrinic T, Nikolakopoulou A, Salanti G, Søndergaard L, Verma S, Jüni P, Windecker S. Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of symptomatic severe aortic stenosis: an updated meta-analysis. *Eur Heart J* 2019;40:3143–3153.
2. Mentias A, Saad M, Desai MY, Horwitz PA, Rossen JD, Panaich S, Elbadawi A, Qazi A, Sorajja P, Jneid H, Kapadia S, London B, Vaughan Sarrazin MS. Temporal trends and clinical outcomes of transcatheter aortic valve replacement in nonagenarians. *J Am Heart Assoc* 2019;8:e013685.
3. Auffret V, Lefevre T, Van Belle E, Eltchaninoff H, Iung B, Koning R, Motreff P, Leprince P, Verhoye JP, Manigold T, Souteyrand G, Boulmier D, Joly P, Pinaud F, Himbert D, Collet JP, Rioufol G, Ghostine S, Bar O, Dibie A, Champagnac D, Leroux L, Collet F, Teiger E, Darremont O, Folliguet T, Leclercq F, Lhermusier T, Olhmann P, Huret B, Lorgis L, Drogoul L, Bertrand B, Spaulding C, Quilliet L, Cuisset T, Delomez M, Beygui F, Claudel JP, Hepp A, Jegou A, Gommeaux A, Mirode A, Christiaens L, Christophe C, Cassat C, Metz D, Mangin L, Isaaz K, Jacquemin L, Guyon P, Pouillot C, Makowski S, Bataille V, Rodés-Cabau J, Gilard M, Le Breton H, FRANCE TAVI Investigators. Temporal trends in transcatheter aortic valve replacement in France: FRANCE 2 to FRANCE TAVI. *J Am Coll Cardiol* 2017;70:42–55.
4. Blackman DJ, Saraf S, MacCarthy PA, Myat A, Anderson SG, Malkin CJ, Cunnington MS, Somers K, Brennan P, Manoharan G, Parker J, Aldalati O, Brecker SJ, Dowling C, Hoole SP, Dorman S, Mullen M, Kennon S, Jerrum M, Chandrala P, Roberts DH, Tay J, Doshi SN, Ludman PF, Fairbairn TA, Crowe J, Levy RD, Banning AP, Ruparelia N, Spence MS, Hildick-Smith D. Long-term durability of transcatheter aortic valve prostheses. *J Am Coll Cardiol* 2019;73:537–545.
5. Søndergaard L, Ihlemann N, Capodanno D, Jørgensen TH, Nissen H, Kjeldsen BJ, Chang Y, Steinbrüchel DA, Olsen PS, Petronio AS, Thyregod HGH. Durability of Transcatheter and surgical bioprosthetic aortic valves in patients at lower surgical risk. *J Am Coll Cardiol* 2019;73:546–553.
6. Codner P, Orvin K, Assali A, Sharony R, Vaknin-Assa H, Shapira Y, Schwartzenberg S, Bental T, Sagie A, Kornowski R. Long-term outcomes for patients with severe symptomatic aortic stenosis treated with transcatheter aortic valve implantation. *Am J Cardiol* 2015;116:1391–1398.
7. Kappetein AP, Head SJ, Généreux P, Piazza N, Mieghem NM Van, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, Es GA Van, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodés-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB. 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.
8. Capodanno D, Petronio AS, Prendergast B, Eltchaninoff H, Vahanian A, Modine T, Lancellotti P, Sondergaard L, Ludman PF, Tamburino C, Piazza N, Hancock J, Mehilli J, Byrne RA, Baumbach A, Kappetein AP, Windecker S, Bax J, Haude M. 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 for Cardio-Thoracic Surgery (EACTS). *Eur J Cardio Thorac Surg* 2017;52:408–417.
9. Makkar RR, Thourani VH, Mack MJ, Kodali SK, Kapadia S, Webb JG, Yoon SH, Trento A, Svensson LG, Herrmann HC, Szeto WY, Miller DC, Satler L, Cohen DJ, Dewey TM, Babaliaros V, Williams MR, Kereiakes DJ, Zajarias A, Greason KL, Whisenant BK, Hodson RW, Brown DL, Fearon WF, Russo MJ, Pibarot P, Hahn RT, Jaber WA, Rogers E, Xu K, Wheeler J, Alu MC, Smith CR, Leon MB, PARTNER 2 Investigators. Five-year outcomes of transcatheter or surgical aortic-valve replacement. *N Engl J Med* 2020;382:799–809.
10. Barbanti M, Tamburino C, D'Errigo P, Biancari F, Ranucci M, Rosato S, Santoro G, Fusco D, Seccareccia F. Five-year outcomes of transfemoral transcatheter aortic valve replacement or surgical aortic valve replacement in a real world population: final results from the OBSERVANT study. *Circ Cardiovasc Interv* 2019;12:e007825.
11. Vemulapalli S, Carroll JD, Mack MJ, Li Z, Dai D, Kosinski AS, Kumbhani DJ, Ruiz CE, Thourani VH, Hanzel G, Gleason TG, Herrmann HC, Brindis RG, Bavaria JE. Procedural volume and outcomes for transcatheter aortic-valve replacement. *N Engl J Med* 2019;380:2541–2550.
12. Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M, Kapadia SR, Chris Malaisrie S, Cohen DJ, Pibarot P, Leipsic J, Hahn RT, Blanke P, Williams MR, McCabe JM, Brown DL, Babaliaros V, Goldman S, Szeto WY, Genereux P, Pershad A, Pocock SJ, Alu MC, Webb JG, Smith CR. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med* 2019;380:1695–1705.
13. Alkhalil A, Lamba H, Deo S, Bezerra HG, Patel SM, Markowitz A, Simon DI, Costa MA, Davis AC, Attizzani GF. Safety of shorter length of hospital stay for patients undergoing minimalist transcatheter aortic valve replacement. *Catheter Cardiovasc Interv* 2018;91:345–353.
14. Cheungpasitporn W, Thongprayoon C, Kashani K. Transcatheter aortic valve replacement; a kidney's perspective. *J Ren Inj Prev* 2016;5:1–7.
15. Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, Thourani VH, Tuzcu EM, Miller DC, Herrmann HC, Doshi D, Cohen DJ, Pichard AD, Kapadia S, Dewey T, Babaliaros V, Szeto WY, Williams MR, Kereiakes D, Zajarias A, Greason KL, Whisenant BK, Hodson RW, Moses JW, Trento A, Brown DL, Fearon WF, Pibarot P, Hahn RT, Jaber WA, Anderson WN, Alu MC, Webb JG. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2016;374:1609–1620.
16. Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Søndergaard L, Mumtaz M, Adams DH, Deeb GM, Maini B, Gada H, Chetcuti S, Gleason T, Heiser J, Lange R, Merhi W, Oh JK, Olsen PS, Piazza N, Williams M, Windecker S, Yakubov SJ, Grube E, Makkar R, Lee JS, Conte J, Vang E, Nguyen H, Chang Y, Mugglin AS, Serruys PWJC, Kappetein AP. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2017;376:1321–1331.
17. Boon RMA van der, Houthuizen P, Urena M, Poels TT, Mieghem NM van, Brueren GRG, Altintas S, Nuis RJ, Serruys PW, Garsse LAFM

van, Domburg RT van, Cabau JR, Jaegere PPT de, Prinzen FW. Trends in the occurrence of new conduction abnormalities after transcatheter aortic valve implantation. *Catheter Cardiovasc Interv* 2015;85:E144–E152.

18. Hamdan A, Guetta V, Klempfner R, Konen E, Raanani E, Glikson M, Goitein O, Segev A, Barbash I, Fefer P, Spiegelstein D, Goldenberg I, Schwammenthal E. Inverse relationship between membranous septal length and the risk of atrioventricular block in patients undergoing transcatheter aortic valve implantation. *JACC Cardiovasc Interv* 2015;8:1218–1228.
19. Seeger J, Gonska B, Otto M, Rottbauer W, Wöhrle J. Cerebral embolic protection during transcatheter aortic valve replacement significantly reduces death and stroke compared with unprotected procedures. *JACC Cardiovasc Interv* 2017;10:2297–2303.