Catheterization and Cardiovascular Interventions 85:E153–E162 (2015)

Outcomes and Predictors of Mortality After Transcatheter Aortic Valve Implantation: Results of the Brazilian Registry

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Objective: The study sought to evaluate outcomes and predictors of mortality after transcatheter aortic valve implantation (TAVI). **Background:** TAVI registries can reliably address outcomes and issues that adversely affect results in real-life. **Methods:** All endpoints and complications were analyzed according to Valve Academic Research Consortium-2 criteria. **Results:** Between January 2008 and January 2013, 418 patients underwent TAVI in 18 centers and were included in the Brazilian registry. The transfemoral approach was used in 96.2% of the procedures. The CoreValve and Sapien XT prosthesis were used in 360 (86.1%) and 58 (13.9%) cases, respectively. All-cause mortality at 30 days and 1 year were 9.1 and 21.5%. Chronic obstructive pulmonary disease (COPD) (HR: 3.50), acute kidney injury (AKI) (HR: 3.07), stroke (HR: 2.71) and moderate/severe paravalvular regurgitation (PVR) (HR: 2.76) emerged as independent predictors of overall mortality. COPD (OR: 3.00), major vascular complications (OR: 7.99) and device malpositioning (OR: 6.97) were predictors of early ($\leq$30 days) mortality, while COPD (HR: 2.68), NYHA class III/IV (HR: 3.04), stroke (HR: 4.15), AKI (HR: 2.44) and moderate/severe PVR (HR: 3.20) impacted late (>30 days) mortality. The use of transesophageal echocardiogram (TEE) to monitor the procedure was found to be a protective factor against overall (HR: 0.57) and late (HR: 0.47) mortality. **Conclusion:** This multicenter registry reflected a real-life national TAVI experience. Comorbidities, periprocedural complications and moderate/severe PVR were associated with increased mortality and the use of TEE to monitor the procedure acted as a protective factor.

Key words: transcatheter valve implantation; aortic valve disease; percutaneous intervention; aortic valve disease; percutaneous valve therapy

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Conflict of interest: F.S.B.J, D.S.: Honoraria for speeches/proctoring from Edwards LifeSciences and Medtronic. L.A.C., R.S.L., J.A.M., P.L., E.G., M.P.: Honoraria for speeches/proctoring from Medtronic. The other authors have no conflicts of interest.

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Additional Supporting Information may be found in the online version of this article.

This article was published online on 13 January 2015. An error was subsequently identified. This notice is included in the online and print versions to indicate that both have been corrected [16 January 2015].

Received 12 August 2014; Revision accepted 6 December 2014

DOI: 10.1002/ccd.25778
Published online 15 December 2014 in Wiley Online Library (wileyonlinelibrary.com)

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) is now a well-established procedure for the treatment of inoperable and high surgical risk patients with severe aortic stenosis. Diverse national registries have been conducted to evaluate real world results of this new treatment modality [1–8] These registries also include patients who are not eligible for randomized clinical trials and provide important information for postmarketing surveillance. Additionally, procedures performed in centers with diverse degrees of experience and specialization can be assessed and, therefore, prediction of outcomes derived from these registries may be more realistic than that from randomized trials. The Brazilian TAVI registry now reflects the 5-year experience of TAVI in Brazil. The aim of the present study was to evaluate clinical outcomes and predictors of mortality from this real-life national registry.

METHODS

The multicenter Brazilian TAVI registry is conducted by the Brazilian Society of Interventional Cardiology. All centers with $\geq$3 valve implantations were invited to participate. Consecutive patients were included prospectively and retrospectively since the first implantation performed in the country. The registry was approved by the Ethics Committee of all institutions and patients included prospectively provided written informed consent.

Patient Selection and Indication for TAVI

TAVI indication was restricted to a selected group of inoperable or high surgical risk patients with severe symptomatic aortic stenosis or degenerated bioprosthetic surgical valves. Operative mortality risk was estimated using the EuroScore and STS risk scores.

Study Prosthesis and Procedure

The self-expandable CoreValve prosthesis (Medtronic, Minneapolis, MN) and the balloon-expandable Sapien XT prosthesis (Edwards Lifesciences, Irvine, CA) were used. The CoreValve prosthesis was available since 2008. The Sapien XT was only approved for use later, in September 2011.

TAVI procedures were performed according to standard techniques. Aspirin (100 mg day^{-1}) and clopidogrel (300 mg loading dose and 75 mg day^{-1}) were administered to patients for a minimum of 1 month. The decision to use general anesthesia and transesophageal echocardiogram (TEE) to monitor the procedure was left to the discretion of the operators.

The transfemoral vascular access was the first choice approach. Alternative transarterial approaches (transubclavian, direct transaortic and transcarotid) were used when the transfemoral access was not feasible.

Complications and End-points

All complications and study end-points were reported according to the Valve Academic Research Consortium-2 (VARC-2) criteria [9].

The primary end-point was all-cause mortality at 1 and 12 months.

A safety composite end-point at 30 days (all-cause mortality, all stroke, life-threatening bleeding, major vascular complication, acute kidney injury (AKI) stages 2 or 3, coronary obstruction requiring intervention and valve dysfunction requiring repeat procedure) and a clinical efficacy composite end-point after 30 days [all-cause mortality, all stroke, hospitalization for valve-related symptoms, New York Heart Association (NYHA) functional class III or IV symptoms or prosthesis dysfunction] were the secondary end-points.

Data Management, Monitoring, and Adjudication

Case report forms were sent to a central database via internet. Remote electronic data monitoring was performed in 100% of cases, to correct for missing and inconsistent information. On-site source documents verification was randomly performed in 20% of all included cases.

All complications and adverse events were adjudicated by an independent committee composed of five cardiologists and one neurologist.

Statistical Analysis

Continuous variables were presented as mean $\pm$ standard deviation (SD) and compared using Student's *t*, Mann–Whitney or Kruskal–Wallis tests, as applicable. Variables not following a normal distribution were expressed as median and interquartile range (IQR). Repeated measures variance analysis or was used for comparisons of variables measured repeatedly at different time points. Categorical variables were presented as frequencies and compared using the chi-square or Fisher exact tests.

The cumulative incidences of clinical events at follow-up were assessed with the Kaplan–Meier

TABLE I. Baseline Characteristics

Variable	$n = 418$
Age (years), mean/median	81.5 ± 7.7/82.5 (77.8–87)
Male gender	200/418 (47.8)
Body mass index (kg m^{-2})	26.1 ± 4.5
NYHA class III/IV	348/418 (83.3)
Hypertension	307/418 (73.4)
Diabetes	133/418 (31.8)
Glomerular filtration rate <60 ml min^{-1}	313/401 (78.1)
Coronary artery disease	242/418 (57.9)
Previous percutaneous coronary intervention	142/418 (34.0)
Previous coronary bypass grafting	72/418 (17.2)
Previous myocardial infarction	62/418 (14.8)
Previous stroke	31/418 (7.4)
Previous balloon valvuloplasty	33/418 (7.9)
Previous aortic valve replacement	13/418 (3.1)
Porcelain aorta	31/418 (7.4)
Pulmonary hypertension	94/418 (22.5)
Peripheral vascular disease	65/418 (15.6)
COPD	73/418 (17.5)
Prior pacemaker	43/418 (10.3)
Atrial fibrillation/flutter	52/418 (12.5)
Logistic EuroScore (%), mean/median	20.2 ± 13.8/16.7 (10.1–27.6)
STS score (%), mean/median	14.2 ± 11.5/10.8 (5.0–19.7)
Mean transaortic gradient (mm Hg)	51.0 ± 16.4
Aortic valve area (cm^2)	0.64 ± 0.18
Moderate/severe mitral regurgitation	76/410 (12.5)
LVEF (%)	57.8 ± 15.2
LVEF <50%	118/413 (28.6)

Values are *n/N* (%), mean ± 1 SD, or median (IQR: interquartile range). COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

method. The log-rank test was used for comparisons of event curves between subgroups.

A stepwise logistic regression analysis was used to identify independent predictors of early (≤30 days) mortality. A Cox multivariate regression analysis was used to determine independent predictors of overall and late (>30 days) mortality. Variables with probability value <0.10 in the univariate analysis and with clinical relevance were selected for the models.

All probability values reported are two-sided, and a probability value ≤0.05 was considered significant.

The statistical software SPSS version 15.0 was used for the analysis.

RESULTS

In Brazil, between January 2008 and January 2013, 597 patients underwent TAVI with the CoreValve or Sapien XT prosthesis in 64 centers. Among them, 418 patients treated in 18 centers were included in the Brazilian TAVI Registry, representing 70% of all TAVI experience in the country with these two devices. The inclusion was prospective in 68.2% (285/418) of the cases. The number of cases included per year increased progressively from 11 in 2008 to 151 in 2012. The median of implantations per participant center was 9 (IQR, 5 to 42), ranging from 3 to 84.

Patients

Among the 418 patients included in the registry, 405 (96.9%) underwent TAVI for the treatment of severe aortic stenosis and 13 (3.1%) for degenerated bioprosthetic surgical valves. Baseline characteristics of the patients are summarized in Table I. The median age was 82.5 years (IQR, 77.8–87), with 83.3% in NYHA functional class III/IV. The median logistic EuroScore and STS score were 16.7% (IQR, 10.1–27.6) and 10.8% (IQR, 5.0–19.7), respectively, without significant changes over the 5 years of the study (EuroScore: $P = 0.336$; STS score: $P = 0.134$). Mean aortic valve area was 0.64 ± 0.18 cm^2 with a mean transvalvular gradient of 51.0 ± 16.4 mm Hg.

Procedure

The majority of implantations were performed in a regular catheterization laboratory (83.5%), using general anesthesia (84%) and monitored by TEE (70.6%). The patients submitted to TAVI under local anesthesia with conscious sedation and without TEE monitoring were generally at higher risk as assessed by the STS score [14.4% (IQR, 6.4–22.9) vs. 9.2% (IQR, 4.8–18.9); $P = 0.006$], although there was no difference in the risk profile assessed using the logistic EuroScore [17.5% (IQR, 10.5–27.9) vs. 16.2% (IQR, 10–27.4); $P = 0.464$]. Proctored procedures were 212 (50.7%). The transfemoral access was used in 402 (96.2%) cases, with a percutaneous approach accomplished with hemostatic devices in 182 (45.3%). Other transarterial routes were used in 3.8% of the valve implantations, always in patients with peripheral vascular disease. Balloon aortic valvuloplasty for predilatation was performed in 255 (61%) cases. The CoreValve prosthesis was used in 86.1%, whereas the Sapien XT prosthesis was used in the remaining cases. Postdilatation was necessary in 39.4% due to paravalvular regurgitation (PVR) or device underexpansion.

Strictly according to the VARC criteria, device success was achieved in 319 patients (76.3%). Moderate or severe PVR was present in 9.2%, whereas a final mean gradient ≥20 mm Hg was observed in 16 (4.4%) patients, 5 (31.3%) of them occurring in valve-in-valve procedures. Malpositioning of the valve (too high or too low in relation to the aortic annulus) occurred in 26 (6.2%) cases, 17 (65.4%) of them resulting in device embolization and 23 (88.5%) requiring the implantation of multiple (≥2) prosthesis. The procedural

TABLE II. Procedural Characteristics and Complications

Variable	$n = 418$
Hybrid operating room	69/418 (16.5)
Proctored procedure	212/418 (50.7)
General Anesthesia	351/418 (84)
TEE guidance	295/418 (70.6)
Approach	
Transfemoral	402/418 (96.2)
Percutaneous	182/402 (45.3)
Surgical	220/402 (54.7)
Subclavian	09/418 (2.2)
Transaortic	06/418 (1.2)
Transcarotid	01/418 (0.2)
Valve-in-valve	13/418 (3.1)
Valvuloplasty	255/418 (61)
Prosthesis	
CoreValve	360/418 (86.1)
Sapien XT	58/418 (13.9)
Postdilatation	146/418 (39.4)
Device success	319/418 (76.3)
Mean gradient (mm Hg)	10.0 ± 5.5
Mean gradient $\geq$20 mm Hg	16/366 (4.4)
Any PVR	289/379 (76.3)
Moderate/severe PVR	35/379 (9.2)
Coronary obstruction	3/418 (0.7)
Valve malpositioning	26/418 (6.2)
Valve embolization	17/418 (4.1)
Multiple valves implanted	23/418 (5.5)
Mitral valve damage/dysfunction	2/418 (0.5)
Annulus rupture	2/418 (0.5)
Tamponade	17/418 (4.0)
Left ventricular perforation	8/418 (1.9)
Conversion to open surgery	4/418 (1.0)

Values are *n/N* (%). PVR: paravalvular regurgitation; TEE: transesophageal echocardiogram

details, the reasons for unsuccessful implantations and intraprocedural complications are presented in Table II.

The median length of stay in hospital was 7 days (IQR, 6–11).

Outcomes and Complications

All-cause mortality at 30 days and 1 year (primary end-point) by Kaplan–Meier analysis were 9.1 and 21.5%, respectively. In the first year, the cause of death was cardiovascular in 72.5% (58/80) of the cases, but after this point in time, cardiovascular deaths corresponded to only 31.8% (7/22). Table III depicts actuarial rates of complications at 30 days and 1 year. Figure 1 illustrates Kaplan-Meier curves of all-cause death, all-cause death or stroke, cardiovascular and non-cardiovascular death.

Peri-procedural myocardial infarction ($\leq$72 hr following TAVI) occurred in three patients (0.7%), two (66.6%) of them due to ostial coronary obstruction. At 30 days and 1 year, the cumulative incidence of myocardial infarction (periprocedural and spontaneous) was 0.7 and 1.8%, respectively.

The rates of stroke or transient ischemic attack (TIA) at 30 days and 1 year were 3.5 and 6.9%, respectively. Disabling strokes were the majority and occurred in 2.2% at 30 days and 3.8% at 1 year. Among 14 patients presenting a stroke or TIA in the first 30 days, the diagnosis was made within the first 24 hr in 8 (57.1%). Two patients experienced a recurrent stroke, both after the first year of TAVI. Strokes were classified as ischemic in 92.9% (13/14) of the cases in the first 30 days, and in 72.7% (08/11) after this period.

Vascular complications and bleeding were frequent after TAVI (13.8 and 18.5% at 30 days and 14.1% and 20.7% at 1 year, respectively) and occurred mainly related to the vascular access and to procedural complications.

AKI was also frequently observed after TAVI (20%). Most of the AKIs were stage I and the frequency of stage II/III was 7.8%.

A new permanent pacemaker was required in 24.4% in the first 30 days and in 27.7% in the first year and was more common after CoreValve implantations (30.3% versus 14.0% at 1 year; $P = 0.014$).

Endocardites was diagnosed in two patients during all study period and both cases were successfully treated with antibiotics.

The composite endpoints of safety at 30 days and efficacy at 1 year occurred in 22.7 and 19.0%, respectively (Table III). The Kaplan–Meier curve of the composite endpoint of clinical efficacy is illustrated in Figure 2.

Predictors of Mortality

Univariate and multivariate predictors of overall, early ($\leq$30 days) and late ($>$30 days) mortality are shown in Supporting Information Table I. In the multivariate analysis (Table IV), COPD (HR: 3.50), stroke (HR: 2.71), AKI (HR: 3.07) and moderate or severe PVR versus none or mild PVR (HR: 2.76) were identified as independent predictors of all-cause mortality throughout the study period. Mild PVR was not associated with a significantly increased risk of death ($P = 0.475$ versus no PVR). Figure 3 illustrates Kaplan–Meier mortality curves stratified by predictors of overall all-cause mortality. The independent predictors of early mortality were COPD (OR: 3.00), major vascular complications (OR: 7.99) and device malpositioning (OR: 6.97), while COPD (HR: 2.68), NYHA functional class III/IV versus class I/II symptoms (HR: 3.04), stroke (HR: 4.15), AKI (HR: 2.44) and moderate or severe PVR (HR: 3.20) were associated with an

TABLE III. 30-day and 1-year Outcomes

Adverse events	Probability at 30 days (%)	CI (95%) Lower	CI (95%) Upper	Probability at 1 year (%)	CI (95%) Lower	CI (95%) Upper
All-cause mortality	9.1	6.4	11.8	21.5	17.2	25.8
Cardiovascular mortality	7.9	5.4	10.4	15.1	11.4	18.8
Myocardial Infarction	0.7	0.0	1.5	1.8	0.2	3.4
All Stroke/TIA	3.5	1.7	5.3	6.9	4.2	9.6
Stroke	3.3	1.5	5.1	5.5	3.0	8.0
Disabling stroke	2.2	0.8	3.6	3.8	1.6	6.0
Vascular complication	13.8	10.5	17.1	14.1	10.8	17.4
Major	8.5	5.8	11.2	8.9	6.2	11.6
Minor	5.6	3.2	8.0	5.6	3.2	8.0
Bleeding	18.5	14.8	22.2	20.7	16.6	24.8
Life-threatening	7.6	5.1	10.1	9.4	6.3	12.5
Major	7.3	4.8	9.8	8.0	5.3	10.7
Minor	4.6	2.4	6.8	4.6	2.4	6.8
Acute kidney injury	20.0	16.1	23.9	–	–	–
Stage 1	13.0	9.7	16.3	–	–	–
Stage 2	2.2	0.6	3.8	–	–	–
Stage 3	5.6	3.2	8.0	–	–	–
Endocardites	0.3	0.0	0.9	0.7	0.0	1.7
Permanent pacemaker	24.4	19.9	28.9	27.7	23.0	32.4
Corevalve	27.0	22.1	31.9	30.3	25.0	35.6
Sapien XT	9.5	1.7	17.3	14.0	2.6	25.4
Safety endpoint (30 days)	22.7	21.0	24.4	–	–	–
Efficacy endpoint (>30 days)	–	–	–	19.0	14.5	23.5

TIA: transient ischemic attack.

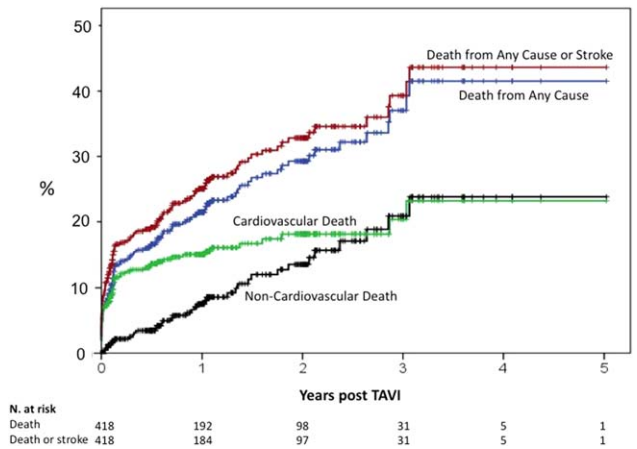

Fig. 1. Kaplan–Meier curves of all-cause death, all-cause death or stroke, cardiovascular death and non-cardiovascular death throughout the study period.

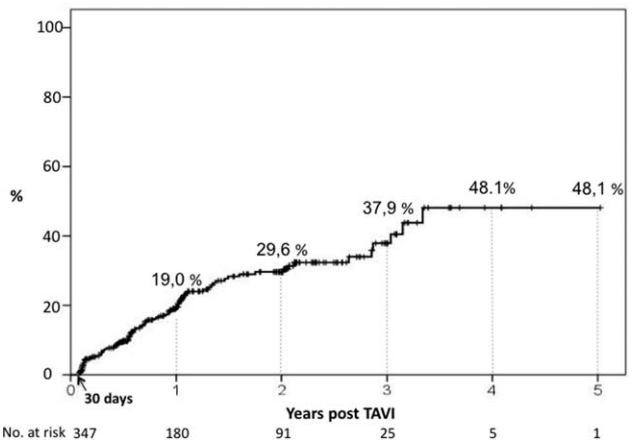

Fig. 2. Kaplan–Meier curve of the composite end-point of clinical efficacy (>30 days) throughout the study period.

increased risk of late mortality. The use of TEE to monitor the implantation procedure was found to be protective against overall (HR: 0.57) and late (HR: 0.47) mortality in the multivariate model (Fig. 4).

The program volume was significantly associated with outcomes, with cumulative all-cause mortality of 36% in centers in the lowest tertile of inclusion in the registry (≤5 cases) and 24.7% in the highest tertile (≥20 cases) (HR: 2.15; 95% CI: 1.07–4.3; $P = 0.031$). There was no difference in the rates of all-cause mortality when comparing the use of the Sapien XT and the CoreValve prosthesis (HR: 1.11; 95% CI: 0.59–2.10; $P = 0.737$).

Clinical and Ecocardiographic Follow-up Data

Complete clinical follow-up was obtained from 416 (99.5%) patients. A substantial improvement in the NYHA functional class was observed at 30 days and at a median time of clinical follow-up of 343.5 days

TABLE IV. Multivariate Analysis: Predictors of All-cause Mortality

Overall mortality	HR	CI (95%) Upper	CI (95%) Lower	*P*
COPD	3.50	5.73	2.14	<0.001
TEE guidance	0.57	0.91	0.36	0.018
Moderate/severe PVR	2.76	5.04	1.51	0.001
Stroke	2.71	5.66	1.30	0.008
Acute kidney injury	3.07	4.98	1.89	<0.001

Early (≤30 days) mortality	OR	CI (95%) Upper	CI (95%) Lower	*P*
COPD	3.00	6.58	1.37	0.006
Valve malpositioning	6.97	18.34	2.65	<0.001
Major vascular complication	7.99	18.52	3.44	<0.001

Late (>30 days) mortality	HR	CI (95%) Upper	CI (95%) Lower	*P*
COPD	2.68	4.82	1.49	0.001
NYHA class III/IV	3.04	8.46	1.09	0.033
TEE guidance	0.47	0.78	0.28	0.004
Moderate/severe PVR	3.20	6.19	1.65	0.001
Stroke	4.15	8.83	1.96	<0.001
Acute kidney injury	2.44	4.25	1.40	0.002

COPD: chronic obstructive pulmonary disease; NYHA: New York Heart Association; PVR: paravalvular regurgitation; TEE: transesophageal echocardiogram.

(IQR, 74.3–721.5), with 345/418 (82.5%) and 304/418 (72.7%) of the patients in NYHA class I/II at each time point, respectively (Fig. 5).

Complete ecocardiographic follow-up data was available from a smaller cohort of 213 (51%) patients. After TAVI, mean transaortic gradient decreased from 51.0 ± 16.2 to 10.0 ± 5.7 mm Hg ($P < 0.001$). A significant improvement in LVEF from $57.9\% \pm 15.3\%$ to $60.9\% \pm 13.1\%$ ($P < 0.001$) was also observed. These acute benefits were maintained after a median time of ecocardiographic follow-up of 258 days (IQR: 90.3–454.5), with a mean gradient of 9.7 ± 5.7 mm Hg and a LVEF of $61.3\% \pm 13.3\%$ ($P = 0.704$ and $P > 0.999$ versus post-TAVI, respectively). Over time, no prosthetic structural deterioration was observed and a single case of thrombosis of a Sapien XT prosthesis was diagnosed and resolved with anticoagulation.

DISCUSSION

The principal findings of this real-world national registry were: (1) the rates of mortality and procedure-related complications were acceptable and comparable to other published experiences, despite the fact that the registry captured the learning curve of all centers, demonstrating the effectiveness of the training program and proctoring provided to centers; (2) baseline clinical factors (COPD and NYHA class III/IV), device malpositioning, major periprocedural complications (major vascular complications, stroke and AKI) and significant PVR impacted mortality; (3) procedural monitoring with TEE protected against mortality.

The all-comers patient cohort of the Brazilian registry was, in general, at similar clinical risk profile when compared to those enrolled in other national registries, with the mean age >80 years and mean logistic EuroScore consistently >20% [1–3,6–8].

In the current registry, the device success rate (76.3%) was lower than reported in previous studies, in general exceeding 90% [1,2,4–7,10]. This difference may be mostly explained by the rigorous adoption of the VARC definitions in the present investigation. Using the same criteria, another study reported similar success rates, around 80% [11]. Despite the lower success rate, all-cause mortality at 30 days and 1 year were 9.1 and 21.5%, respectively, rates that are similar to those reported by other national registries, ranging from 5.4 to 12.7% at 30 days and from 15 to 24% at 1 year [1–7]. Importantly, the great majority of deaths occurring during the first year were of cardiovascular origin, while, after this period, non-cardiovascular deaths were predominant. This finding is in agreement with the results of other TAVI registries [1,5,6].

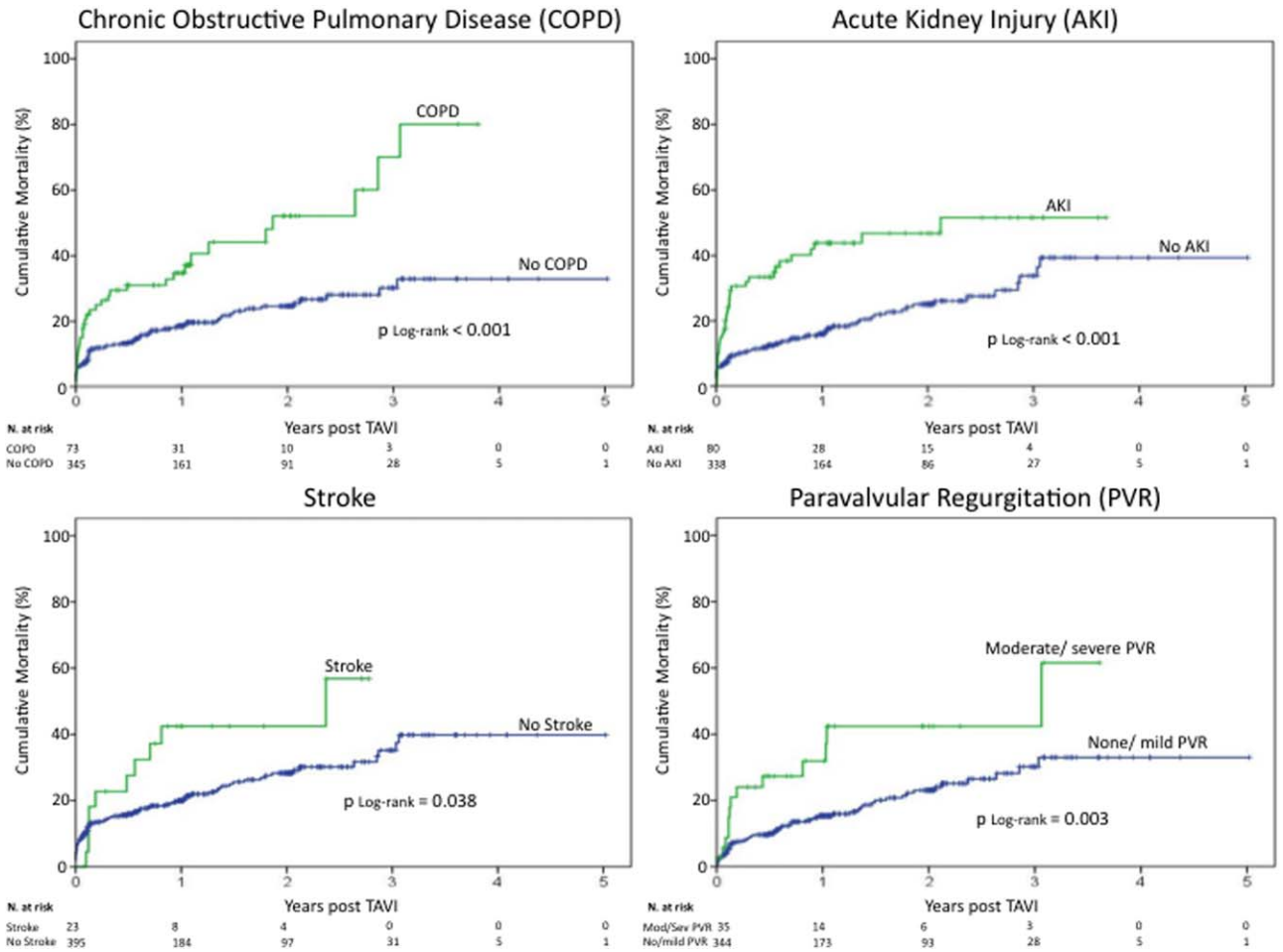

Fig. 3. Kaplan–Meier cumulative mortality curves stratified by presence/absence of independent predictors of overall all-cause mortality.

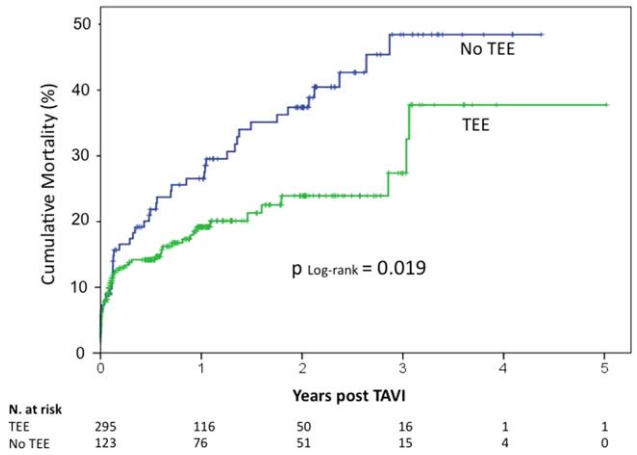

Fig. 4. Kaplan–Meier cumulative all-cause mortality curves for TEE guided and non-TEE guided procedures.

Overall, we also could confirm that the mortality was impacted by the program volume, with the risk of death being 2.15-fold higher in low volume centers, regardless of the presence of a proctor during the implantation procedure.

In the present study, COPD and NYHA class III/IV were the baseline factors identified as predictors of mortality. COPD was an independent predictor of overall, early and late mortality, increasing the risk of death approximately 3-fold. COPD is a frequent comorbidity and patients have increased susceptibility to lung infections, which may contribute to their higher mortality risk found in the present and in previous studies [3,5,12,13]. A detailed analysis of the pulmonary function and a more rigorous clinical follow-up are, therefore, crucial for these patients. NYHA functional class III/IV at baseline was found to be a predictor of late mortality in the current study and was also associated with 1-year mortality in the FRANCE-2 registry [2].

Mortality was also strongly impacted by procedural factors and complications. The occurrence of a major vascular complication (8.5% at 30 days) was the most powerful predictor of early mortality in our study,

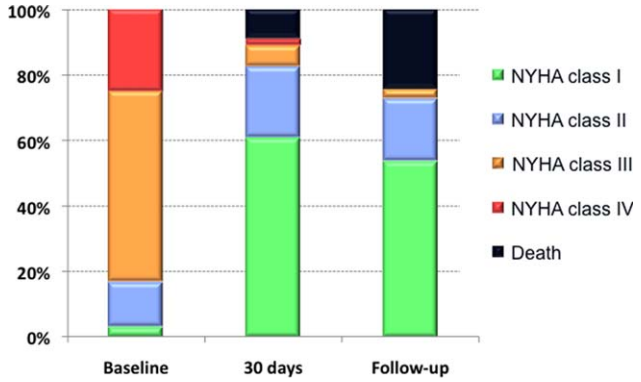

Fig. 5. Proportion of patients in each NYHA functional class at baseline, 30 days and follow-up (343.5 days, IQR 74.3–721.5).

increasing the risk of death approximately 8-fold. This observation is in agreement with the results of the PARTNER trial and indicate that a meticulous selection of the access route and a careful manipulation of vascular sheaths, wires and catheters during TAVI are mandatory and may positively impact outcomes [14,15]. Moreover, the upcoming new generation of aortic valve prosthesis with lower profile delivery systems will certainly add to the safety of the procedure.

Malpositioning of the valve also impacted early mortality, increasing the chance of death approximately 7-fold. This technical issue occurred in 6.2% in our registry and at a pooled estimate rate of 3.5% in a meta-analysis of TAVI studies [10]. When such problem takes place, embolization of the device is frequent and implantation of multiple valves is often needed. Severe PVR or mitral insufficiency may be the consequence of a valve extending excessively into the ventricle. Manipulation of a malpositioned or embolized prosthesis may cause atheroembolism, aortic injury and ostial coronary or bypass graft occlusion. Additionally, conversion to open-heart surgery might occasionally be necessary to treat such problem. This finding highlights the need for new generation transcatether heart valves, with improved delivery systems that allow full repositioning of the prosthesis during implantation.

The development of AKI after TAVI occurred in 20% of our cases, with 7.8% classified as stage II or III, rates that are very similar to those observed in a meta-analysis of TAVI studies using the VARC definitions [10]. This complication was found to impact overall and late all-cause mortality, increasing the risk of death 3.1-fold and 2.4-fold, respectively. Previous studies have reported the same observation [16,17], stressing the need to adopt measures that may prevent this complication in a high risk population of elderly patients with a high prevalence of diabetes and chronic renal failure. Limiting the volume of contrast, cautious hydration and avoiding hypotension and bleeding during the procedure is, therefore, of key importance during TAVI.

In the present study, stroke was found to be an independent predictor of overall and late mortality, increasing the risk of death ~2.7 and 4.1-fold, respectively. The frequency of stroke or TIA (3.5% at 30 days and 6.8% at 1 year) in the Brazilian registry was similar to what was found in a large meta-analysis of published TAVI literature, with the majority of strokes classified as disabling [18]. The risk was not restricted to the periprocedural period, with events occurring during the follow-up. This finding is important when considering that embolic protection devices have the potential to prevent strokes occurring during the procedure but not the late events.

Several studies have shown that PVR is associated with increased mortality after TAVI [2–4,6,13,14,19]. In the Partner trial, even mild PVR impacted long-term mortality [14]. In our study, PVR was observed in three-fourths of the patients, but only the presence of moderate or severe PVR, occurring in 9.2%, emerged as an independent predictor of overall and late mortality after TAVI, increasing the risk of death ~2.8-fold and 3.2-fold, respectively. This finding reinforces the importance of PVR as a major target for improving TAVI outcomes. Interestingly, the multivariate analysis revealed that TEE monitoring during the procedure protected against overall and late all-cause mortality, reducing the risk of death 43 and 53%, respectively. This original observation may be explained by several reasons. Firstly, TEE may contribute to valve sizing, avoiding PVR and annulus rupture. Also, TEE may be of critical relevance to the early recognition and treatment of complications occurring during the procedure. Finally, TEE evaluation after the implantation of the transcatheter valve may be especially important to identify a significant residual transvalvular pressure gradient or PVR, conditions that impact clinical outcomes and that can be resolved with postdilatation with slightly larger balloons. Therefore, this important finding of the Brazilian registry does not support the strategy of using a minimalist approach for TAVI, with conscious sedation and exclusively fluoroscopic guidance, without TEE. TEE guidance maybe imperative for low-volume centers and during the learning phase of the procedure. Nevertheless, the protection observed with TEE guidance deserves confirmation by a randomized study, since the decision to use TEE was non-randomized and patients at higher risk were selected for the minimalist approach in the present investigation.

In the current study, the need for a permanent pacemaker was a frequent complication after TAVI,

occurring in 24.4% of the cases within the first 30 days. The higher rate of pacemaker requirement with the CoreValve (27%) in comparison with the Sapien XT prosthesis (9.5%) is in perfect agreement with previous studies [10,20].

The durable efficacy of TAVI up to 1 year has been demonstrated in the current registry. The 1-year clinical efficacy composite endpoint rate occurred in 19.0% of our patients. This composite endpoint proposed by the VARC document has been rarely reported in previous studies [10,21]. However, several studies have shown improvement in functional class and stability of valve function during the follow-up, which is in accordance with our results [11–14,21].

Important limitations of the present study should be acknowledged. The data was self-reported and almost one-third of the cases were retrospectively entered in the registry. Therefore, complications might have been under-reported. However, on-site source documents verification was randomly performed in 20% of all cases, remote electronic data monitoring was carried out in 100% and all complications were independently adjudicated, which may have attenuated this limitation. Moreover, the primary endpoint of the study was all-cause mortality and as complete clinical follow-up was obtained from 99.5% of the patients, data on survival is extremely robust. The lack of a central echocardiographic core laboratory and the fact that only 51% of the patients had complete serial echocardiographic follow-up limit the interpretation of data regarding changes in valve hemodynamics and structural deterioration over time.

CONCLUSION

In this multicenter real-life registry, outcomes after TAVI were encouraging, despite the fact that the majority of centers were in the learning phase of the procedure. Patients with COPD or functional class III/IV symptoms at baseline were at higher risk of death, as well as those who presented device malpositioning, major periprocedural complications or significant PVR. Procedural monitoring with TEE protected against mortality, suggesting that a minimalist approach for TAVI should not be implemented, at least in low-volume centers and during the learning phase. These findings may assist physicians to obtain the best possible results with this revolutionary technique.

ACKNOWLEDGMENT

The authors acknowledge the expert work of Flavio Tarasoutchi, MD, Auristela Ramos, MD, Adriano Caixeta, MD, Marcelo Katz, MD, Antonio Bacelar, MD, and Fernando Morgadinho, MD, in the Independent Adjudication Committee. They also acknowledge the work of Teresa Cristina Nascimento, RN, as the study coordinator.

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