

Early commercial experience from transcatheter aortic valve implantation using the Portico™ bioprosthetic valve: 30-day outcomes in the multicentre PORTICO-1 study



Francesco Maisano^{1*}, MD, FESC; Stephen Worthley², MD; Josep Rodés-Cabau³, MD; Axel Hans-Peter Linke⁴, MD; Stephan Fichtlscherer⁵, MD; Ulrich Schäfer⁶, MD; Raj Makkar⁷, MD; Gregory Fontana⁸, MD; Federico M. Asch⁹, MD; Lars Søndergaard¹⁰, MD

1. Clinic for Heart and Vascular Surgery, University Hospital Zurich, Zurich, Switzerland; 2. Royal Adelaide Hospital, Adelaide, Australia; 3. Quebec Heart and Lung Institute, Laval University, Quebec, Canada; 4. Technical University Dresden, Heart Center Dresden, Dresden, Germany; 5. Klinikum der Johann Wolfgang Goethe-Universität Frankfurt, Frankfurt, Germany; 6. UKE Hamburg (Universitätsklinikum Eppendorf), Hamburg, Germany; 7. Cedars Sinai Medical Center, Los Angeles, CA, USA; 8. Los Robles Regional Medical Center, Thousand Oaks, CA, and Hospital Corporation of America, Nashville, TN, USA; 9. Cardiovascular Core Laboratories, MedStar Health Research Institute at Washington Hospital Center, Washington, DC, USA; 10. Department of Cardiology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

KEYWORDS

- aortic stenosis
- clinical research
- degenerative valve
- TAVI

Abstract

Aims: The aim of this study was to investigate the procedural and short-term outcomes of transcatheter aortic valve implantation (TAVI) with the Portico™ self-expanding, resheathable TAVI system from an ongoing long-term multicentre study.

Methods and results: A total of 941 patients (82.4±5.9 years, 65.7% female, STS score 5.8±4.9%) with severe symptomatic aortic stenosis underwent TAVI using the Portico bioprosthesis. Patients were clinically and echocardiographically assessed at implantation, discharge and 30 days post TAVI. An independent CEC and core laboratory adjudicated adverse events (according to VARC-2) and follow-up echocardiograms, respectively. Implantation was successful in 96.0% of patients. Thirty-day all-cause, cardiovascular mortality and disabling stroke rates were 2.7%, 2.4% and 1.6%, respectively. Major vascular complications and life-threatening bleeding occurred in 5.5% and 3.1% of patients, respectively. A new pacemaker was implanted in 18.7% of patients. Aortic valve area (0.70±0.33 cm² vs. 1.79±0.48 cm²) and transvalvular gradient (49.7±15.3 mmHg vs. 8.6±3.9 mmHg) improved significantly. The 30-day rate of moderate or higher paravalvular leak (PVL) was 3.9%.

Conclusions: The Portico TAVI system allows safe and effective treatment of aortic stenosis in patients at increased surgical risk. At 30 days, mortality was low, and good haemodynamic performance was indicated by low transvalvular gradient and a low rate of moderate or higher PVL.

*Corresponding author: Clinic for Heart and Vascular Surgery, University Hospital Zurich, Raemistrasse 100, 8091 Zurich, Switzerland. E-mail: Francesco.Maisano@usz.ch

Abbreviations

AKI	acute kidney injury
AS	aortic stenosis
AVA	aortic valve area
CEC	clinical events committee
CT	computed tomography
NOAF	new-onset atrial fibrillation
PVL	paravalvular leak
TAVI	transcatheter aortic valve implantation
VARC	Valve Academic Research Consortium

Introduction

Transcatheter aortic valve implantation (TAVI) is a recommended treatment for patients with symptomatic aortic valve stenosis (AS) who are at increased surgical risk^{1,2}, taking into account other factors such as patient frailty, comorbidities and patient preferences. Several randomised controlled trials have shown favourable results with TAVI when compared with surgical valve replacement in high-risk and intermediate-risk patients³⁻⁶. Various outcomes, such as the occurrence of paravalvular leak (PVL) and the risk of conduction disturbances requiring implantation of a permanent new pacemaker, depend on optimal positioning of the bioprosthesis. The self-expanding Portico™ transcatheter bioprosthetic aortic valve (St. Jude Medical [now Abbott], St. Paul, MN, USA) has resheathing capabilities allowing valve repositioning during the implantation procedure⁷. This study reports on the procedural and 30-day outcomes of an ongoing multicentre evaluation, assessing the long-term (five-year) clinical outcomes of this device.

Methods

STUDY DESIGN

The ongoing, international, multicentre PORTICO-1 study is a prospective, single-arm, non-randomised clinical investigation (ClinicalTrials.gov: NCT01802788). The objective of the study is to assess long-term clinical outcomes of the Portico valve for treatment of severe, symptomatic AS. The study includes 61 centres in Europe (n=43), Canada (n=8) and Australia (n=10). Study centres functioned in compliance with the Declaration of Helsinki and approvals from ethics committees and local authorities were obtained. All patients provided written informed consent prior to participation. Abbott (formerly St. Jude Medical) sponsored the study. The initial experience of the participating centres with the Portico TAVI system at 30 days post TAVI, including evaluation of echocardiograms and adverse events, is presented here.

PATIENTS AND RISK ASSESSMENT

Patients with echocardiographically confirmed severe AS were eligible for participation. Echocardiographic criteria included an aortic valve area (AVA) ≤ 1.0 cm² or indexed effective orifice area ≤ 0.6 cm²/m² AND a mean aortic gradient >40 mmHg or jet velocity >4.0 m/s or Doppler velocity index <0.25 . Patients were referred by the local Heart Teams based on their high risk for surgery as demonstrated by the Society of Thoracic Surgeons Predicted Risk of

Operative Mortality (STS-PROM) and logistic European System for Cardiac Operative Risk Evaluation scores. A clinical judgement of the Heart Team, based on the individual risk profile (e.g., frailty and comorbidities not captured by STS score), was also accepted. Key exclusion criteria included a non-tricuspid aortic valve, the presence of a prosthetic aortic valve (valve-in-valve procedures), or the need for concomitant structural heart procedure. All inclusion/exclusion criteria are shown in **Table 1**.

VALVE IMPLANTATION AND FOLLOW-UP

All patients underwent transfemoral TAVI using the Portico TAVI system (available in sizes 23, 25, 27 and 29 mm), which has been described in detail elsewhere⁷. Key characteristics include a large-cell, self-expanding nitinol frame, bovine pericardial leaflets functioning at the annular level, resheathing and repositioning capabilities, and a transfemoral delivery system compatible with expandable sheaths such as the Portico Solo™ device (St. Jude Medical [now Abbott]) for an ultra-low insertion profile (11 Fr). Sheathless implantation occurred in some cases.

Table 1. Study inclusion and exclusion criteria.

Inclusion criteria
1. Patient has signed the patient informed consent prior to participating in the clinical investigation.
2. Patient has been referred for a Portico valve implant as per Heart Team decision.
3. Patient has senile degenerative aortic valve stenosis confirmed by echocardiographically derived criteria: <ul style="list-style-type: none"> – An initial aortic valve area (AVA) of less than or equal to (\leq) 1.0 cm² (or indexed EOA less than or equal to (\leq) 0.6 cm²/m²) AND – A mean gradient greater than ($>$) 40 mmHg or jet velocity greater than ($>$) 4.0 m/s or Doppler velocity index less than ($<$) 0.25. If the mean gradient is <40 mmHg and left ventricular ejection fraction (LVEF) $<55\%$, then the site may as well perform a dobutamine stress echo to see if the mean gradient increases to >40 mmHg. (Baseline measurement taken by echo within 6 months of index procedure).
4. Patient has a life expectancy of more than ($>$) 12 months.
Additional criteria for patients enrolled at a French site:
5. Patient is at high risk for surgery as demonstrated by a logistic EuroSCORE equal to or more than (\geq) 20 and/or a Society of Thoracic Surgeons (STS) mortality risk score of more than ($>$) 10% and/or by clinical judgement of the Heart Team based on the individual risk profile (comorbidities).
Exclusion criteria
1. Any case in which the Portico valve would not be indicated for the patient as per current IFU (i.e., any “off-label” use).
2. Patient has a non-tricuspid aortic valve.
3. Patient has a prosthetic valve or ring in the aortic position.
4. Patient needs a concomitant structural heart procedure.
5. Patient is unwilling or unable to comply with all clinical investigation-required follow-up evaluations.
6. Patient is pregnant.

Implanting physicians were trained according to the sponsor. Based on early physician feedback, and data analysis of initial studies with the Portico valve, the training programme was updated to include a greater emphasis on using computed tomography (CT) for sizing, the value of balloon predilatation, the importance of targeting an implant depth of 3-4 mm, and guidelines for post-dilatation. As a result, valve sizing was preferably based on preprocedural imaging with multislice CT. Balloon predilatation and valve positioning without rapid pacing were recommended. Valve resheathing and repositioning was performed if indicated. The valve was released after angiographic confirmation of the appropriate implant position. Post-dilatation was performed at the discretion of the operator to improve sealing and full device expansion at the annulus if aortic insufficiency or valve underexpansion was present. Post-dilatation was performed under rapid pacing to prevent valve dislocation.

Post-procedural antithrombotic therapy was at the physician's discretion.

Patients are followed at 30 days, one year and annually up to five years post implant. Patients without an implant attempt (i.e., delivery system not introduced into the body) were followed until 30 days after the procedure but are not included in this report. Echocardiographic evaluations are performed at baseline, implantation, pre-discharge, 30 days, one year and annually up to five years post implant.

STUDY ENDPOINTS, ASSESSMENTS AND DEFINITIONS

The primary endpoint of this study is all-cause mortality at one year. Secondary clinical endpoints include cardiovascular mortality, myocardial infarction, stroke, acute kidney injury (AKI), access-related complications and bleeding at 30 days. Additional 30-day outcomes include new or worsened conduction disturbances and cardiac arrhythmias, the need for new pacemaker implantation, new-onset atrial fibrillation (NOAF) and NYHA functional classification. An independent clinical events committee (CEC) adjudicated all safety endpoints according to VARC-2 guidelines⁸.

Implant success was defined as successful vascular access, delivery and deployment, a single functioning valve in the proper position and successful retrieval of the delivery system. Total procedure time was defined as access to closure of the vascular access site.

Thirty-day echocardiographic assessments were evaluated by an independent echocardiographic core laboratory (MedStar Health Research Institute, Washington DC, USA). Total aortic regurgitation (AR) severity with paravalvular and transvalvular components was classified into four classes (none/trace, mild, moderate, severe) following VARC-2 and American Society of Echocardiography criteria⁹. Prosthetic valve haemodynamics were analysed according to American Society of Echocardiography guidelines¹⁰. Implantation depth was measured angiographically and was site-reported.

STATISTICAL ANALYSIS

Continuous variables were summarised by mean±standard deviation (SD). Categorical variables were summarised using frequencies

and percentages. Paired Student's t-tests (echocardiographic data, 6-min walk test) and the Wilcoxon signed-rank test (NYHA functional class) were used to compare outcomes at 30 days relative to baseline. Evaluation of all adverse events was based on CEC-adjudicated outcomes. Comparisons of adverse event and PVL rates across valve sizes were performed using Fisher's exact test. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using SAS v9.4 (SAS Institute, Cary, NC, USA).

Results

PATIENTS

Between April 2013 and June 2017, implantation of a Portico bio-prosthetic aortic valve was attempted in 941 patients (Table 2).

Table 2. Demographic and baseline data (n=941).

Age (years)	82.4±5.9	
Female gender	65.7	
Coronary artery disease	50.3	
Previous CABG	9.9	
Previous PCI	22.5	
History of myocardial infarction	11.8	
Prior atrial fibrillation	17.2	
Left bundle branch block	5.0	
Right bundle branch block	3.6	
Heart failure	13.2	
NYHA Class III/IV	64.0	
Diabetes	29.6	
Hypertension	80.7	
Prior stroke	6.1	
Prior TIA	6.4	
Peripheral artery disease	6.2	
Permanent pacemaker	8.5	
Moderate/severe mitral regurgitation	25.2	
Haematologic disorders	10.6	
Liver disease/cirrhosis	2.9	
Chronic kidney disease	30.1	
Chronic lung disease	14.8	
Anticoagulant use	28.7	
Logistic EuroSCORE I (%)	15.7±11.3	
STS score (%)	5.8±4.9	
Frailty indices	5-metre walking time (sec)	8.1±7.6
	Grip strength (kg)	24.15±13.66
	Serum albumin (g/dL)	4.00±2.39
	Mini mental status score	26.9±3.4
	Unintentional weight loss >5 kg within the last year	10.6
Left ventricular systolic dysfunction	20.5	
Left ventricular ejection fraction	57.4±11.55	
Mean aortic valve gradient (mmHg)	49.74±15.32	
Aortic valve area (cm ²)	0.70±0.33	
Data shown in percentages or mean±standard deviation. CABG: coronary artery bypass surgery; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; STS: Society of Thoracic Surgeons; TIA: transient ischaemic attack		

The patients' mean age was 82.4±5.9 years, 65.7% were female and 64% were severely symptomatic (NYHA Class III/IV). Mean STS score was 5.8±4.9% (median: 4.3%). Coronary artery disease was present in 50.3% of the patients, atrial fibrillation in 17.2%, and moderate/severe mitral regurgitation in 25.2%.

PROCEDURAL OUTCOMES

Procedural characteristics and outcomes are provided in **Table 3**. Predilatation and resheathing/repositioning were performed in 88.9% and 41.4% of patients, respectively.

Table 3. Procedural data (n=941).

Portico implant success		98.0
Single successful Portico valve		96.0
Anaesthesia	Conscious sedation/local	75.5
	General	24.5
Valve size	23 mm	5.4
	25 mm	29.0
	27 mm	34.4
	29 mm	31.2
Need for second Portico valve		2.0
Procedural mortality		0.3
Conversion to AVR		0.4
Other TAVR valve		1.2
Predilatation		88.9
Post-dilatation		43.2
Valve resheathed		41.4
Total procedure time (min)		76.5±35.0
Fluoroscopy time (min)		20.4±10.0
Contrast volume (mL)		167.1±163.0
Data in percentages of all patients or mean±standard deviation. AVR: aortic valve replacement; TAVR: transcatheter aortic valve replacement		

In total, 922/941 TAVI procedures were completed with a functioning valve (98%), including 903 (96%) single valve implants and 19 cases (2%) utilising two Portico valves. Nineteen unsuccessful implantations were related to procedural mortality (n=3, 0.3%), conversion to AVR (n=4, 0.4%) and implantation of an alternative commercial TAVR device due to annulus size, Portico migration upon release, or TAV-in-TAV placement to reduce PVL (n=12, 1.2%). Procedural deaths were due to dissection of the right coronary artery ostium, aortic dissection and aortic perforation (one case [0.1% occurrence] of each).

30-DAY OUTCOMES

Thirty-day visits were recorded from 828 patients. Of the 110 patients with no documented 30-day visit, 22 died after the procedure, 24 were withdrawn and 64 missed the 30-day visit. However, 52 had a subsequent visit or were followed for a reported adverse event.

Thirty-day post-TAVI outcomes are summarised in **Table 4**. Thirty-day all-cause mortality was 2.7% (25 patients), including three procedural deaths, 16 post-procedural in-hospital deaths and six deaths after discharge. Cardiovascular mortality at 30 days was 2.4%, and most frequently related to post-procedural complications, cardiac or aortic perforation, coronary obstruction or occlusion and sudden death of unknown cause.

Table 4. 30-day outcomes.

All-cause mortality	2.7
Cardiovascular mortality	2.4
All stroke	2.6
Disabling stroke	1.6
TIA	0.4
Myocardial infarction	1.6
Acute kidney injury	3.4
Stage 2 or 3	3.0
Life-threatening bleeding	3.1
Major bleeding	8.5
Major vascular complications	5.5
New-onset atrial fibrillation	3.7
Overall pacemaker implantation*	17.1
New pacemaker implantation [†]	18.7
Data shown in percentages. *among patients regardless of pacemaker at baseline. [†] among patients without a pacemaker at baseline. TIA: transient ischaemic attack	

Disabling stroke occurred in 15 patients (1.6%) and 32 patients (3.4%) had acute kidney injury (AKI), requiring interim haemodialysis in 10 cases (1.1%). As adjudicated, 29 patients (3.1%) had life-threatening bleeding. Major vascular complications occurred in 5.5% of the patients and were mostly access-related. Transfusion was required in 24 cases (2.6%).

A permanent pacemaker was implanted in 161 patients, representing 17.1% of all patients regardless of pacemaker status at baseline and 18.7% of patients with no prior pacemaker. Pacemaker implantation was associated with greater implant depth (depth relative to the annulus: 6.2±2.7 mm vs. 5.2±2.5 mm, p<0.0001) and higher prevalence of conduction disorder at baseline (21.7% vs. 11.1%, p=0.0003). Regarding predilatation or post-dilatation, the balloon-to-annulus ratio and the balloon-to-left ventricular outflow tract ratio were not significantly different between the two groups.

The AVA increased from 0.70±0.33 cm² at baseline to 1.79±0.50 cm² at 30 days (p<0.0001) (**Figure 1**). At 30 days post TAVI, the mean aortic transvalvular gradient was reduced to 8.6±3.9 mmHg, compared with 49.7±15.3 mmHg at baseline (p<0.0001). At 30 days post TAVI, moderate or higher PVL was observed in 3.9% of the patients (all moderate; no cases of severe PVL were observed). Moderate or higher PVL, compared to mild or lower PVL, was associated with a deeper implant (site-reported angiographic measurement) and more frequent post-dilatation, while the rate of predilatation was the same in

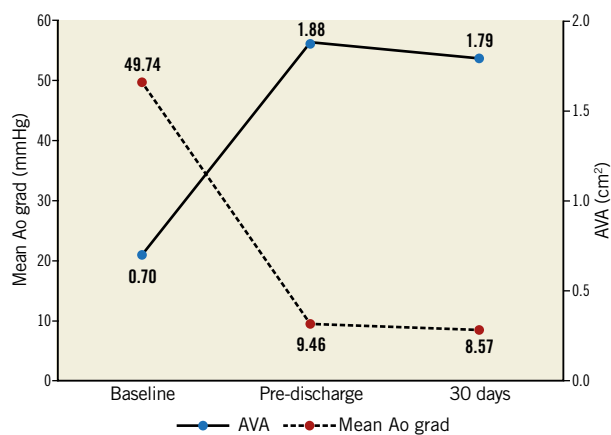


Figure 1. Aortic valve area (AVA) and mean aortic valve gradient.

both groups. The lowest and highest rates of moderate or higher PVL were observed with 27 mm valves (1.7% of valves) and 25 mm valves (6.5%), respectively. Sites performing >15 procedures achieved a lower rate of moderate or higher PVL than sites with fewer procedures (2.6% versus 7.1%, $p=0.0085$). This was driven by a substantial reduction in the rate of moderate or higher PVL from 5.9% in the first 15 procedures to 2.1% in the remaining, later cases.

TAVI was associated with improvement in NYHA functional class ($p<0.0001$), with 13.1% of patients in NYHA Class III/IV at 30 days, versus 64% at baseline (Figure 2).

No significant differences were found among valve sizes with regard to adjudicated adverse events and the rate of pacemaker implantation.

Discussion

This study reports 30-day outcomes of a large, multicentre real-world cohort of patients with severe, symptomatic AS undergoing TAVI with the Portico bioprosthetic aortic valve. While TAVI was initially introduced as a less invasive alternative to surgical valve replacement for patients with high surgical risk, lower-risk

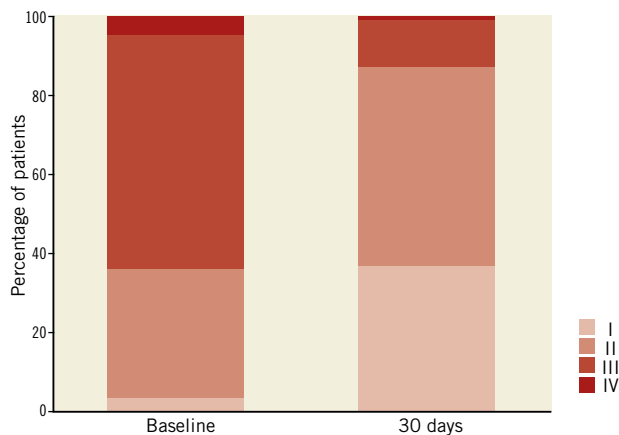


Figure 2. NYHA class at baseline and at 30 days post TAVI.

patients are increasingly considered for TAVI. With a mean STS score of 5.8%, the present study follows this trend. However, other factors not included in the STS assessment may have contributed to a higher surgical risk. Most importantly, frailty and comorbidities were accounted for by the local Heart Teams in assessing the individual surgical risk profile of patients considered for aortic valve replacement. Furthermore, the proportion of subjects with a logistic EuroSCORE I >10% was 62%.

A single Portico valve was successfully implanted in 96.0% of patients. This outcome compares well with results reported from other studies^{11,12} using this device, considering it was achieved by 61 centres worldwide with variable experience and patient load. Immediate, procedural mortality (0.3%) as well as all-cause mortality at 30 days post TAVI (2.7%) were relatively low and comparable with outcomes reported from other TAVI studies with either the Portico or other transcatheter bioprosthetic aortic valves^{5,11-14}. Specifically, 30-day mortality in this study was similar to other studies in populations of similar risk^{6,11,15-18}. Nevertheless, direct comparison between cohorts, even with similar STS score, remains difficult, given other risk factors and conditions that are not captured by the STS score. Within the 30-day post-TAVI period, disabling stroke occurred at a rate of 1.6%, which is within the range of disabling stroke rates reported by other studies on the Portico device^{11,12} and from other devices^{13,14}.

Relatively low rates of permanent pacemaker implantation have been reported from other series with the Portico valve^{11,12}. In this large cohort, a new permanent pacemaker was implanted in 18.7% of patients without prior pacemaker, which is slightly more than in earlier, smaller series with this device^{11,12}. This may be partially due to the conduction disorders at baseline, which were significantly more frequent in patients who received a new pacemaker compared to those without. Nevertheless, the achieved rate of pacemaker implantation in patients at risk is similar to other self-expanding and balloon-expandable prosthetic valves^{19,20} (CoreValve® [Medtronic, Minneapolis, MN, USA]: 28.7%²¹, Evolut™ R [Medtronic]: 19.3%¹⁴, SAPIEN 3 [Edwards Lifesciences, Irvine, CA, USA]: 19.7%³).

In this study, an independent core laboratory provided consistent and unbiased evaluation of echocardiograms. Thirty-day assessment showed significant and clinically relevant improvements from baseline in AVA and aortic transvalvular gradient. During the first part of this study, only the two smaller size Portico valves were available. Therefore, an even larger mean AVA may be expected in a contemporary setting with access to all valve sizes. At 30 days, PVL was moderate in 3.9% of patients and no severe PVL was observed. This outcome is comparable to outcomes reported from other contemporary self-expanding aortic valves, such as the CoreValve (11.4%)²¹, Evolut R (5.3%)¹⁴, 1.9% at discharge¹⁶, or the ACURATE neo™ (Boston Scientific, Marlborough, MA, USA) (4.8%)²² or from balloon-expandable bioprostheses, such as the SAPIEN 3 (3.4%)¹³ or the LOTUS™ valve (Boston Scientific) (0.5%)¹⁸. In 60 patients implanted with the Evolut™ PRO device (Medtronic), no moderate or higher

PVL was seen²³. Results from this study suggest a learning curve effect with respect to PVL. Sites that enrolled >15 patients achieved improved outcomes regarding PVL at 30 days post TAVI. Moreover, the low rate of moderate or higher PVL was associated with frequent predilatation (88.9%) and post-dilatation in 43.2% of the procedures. While predilatation may be less common in current TAVI practices with other valves, these results suggest that it may play an important role in avoiding PVL after implantation of the Portico valve. Given the conformability of large-cell self-expanding and resheathable stents, predilatation facilitates a more gradual and uniform stent deployment. As this may allow better accommodation of the stent within the aortic annulus and of calcific nodules within the stent cells, predilatation was recommended as part of the training programme for this study. In addition, valve resheathing and repositioning, applied in 41.3% of the procedures, may have facilitated a more optimal valve placement and prevention of PVL. Overall, applying predilatation and gradual valve deployment appear to be important aspects of the learning curve for operators gaining experience with the Portico TAVI system. The lack of difference found in the use of predilatation between patients with and without more-than-moderate PVL was most likely due to the frequent use of predilatation in this study (88.9%).

No significant differences in rates of adverse events and pacemaker implantation were found between the valve sizes.

Recently, a multicentre study including 222 patients implanted with the Portico bioprosthesis reported low one-year mortality and stroke rates²⁴. Ongoing follow-up of the present study will show whether these results can be confirmed by data obtained from a larger population. Longer-term follow-up will also assess the benefits of the large cell dimensions of the stent frame of this device regarding coronary access for percutaneous interventions after TAVI.

Limitations

This study involved non-random selection of patients to be treated with the Portico TAVI system. The study enrolment occurred over an extended four-year period, beginning in 2013 after CE mark of the Portico 23 mm valve. Naturally, enrolment was slow until the full family of valve sizes was commercially available in September 2015. Once all sizes were available, 61 sites were activated and the remaining population (85%) was promptly enrolled. Data were obtained from centres with variable experience and patient load, providing a cross-section of centres performing TAVI, and included the initial learning curve in most institutions.

Conclusions

The Portico TAVI system allows safe aortic valve implantation in patients with severe, symptomatic AS. Short-term clinical outcomes are characterised by low all-cause and cardiovascular mortality and good haemodynamic performance, including low transvalvular gradients and a low incidence of moderate or higher PVL.

Impact on daily practice

Procedural and 30-day outcomes show that the Portico TAVI system is safe to implant and provides acceptable haemodynamic performance in the short term, including low transvalvular gradients and low rates of moderate or higher paravalvular leak.

Funding

This study was funded by Abbott.

Conflict of interest statement

L. Søndergaard has received consultant fees and an institutional research grant from Abbott (formerly SJM). U. Schäfer, S. Fichtlscherer and F. Maisano are proctors for Abbott Vascular and have received travel/speaker's honoraria and grant support. J. Rodés-Cabau has received institutional research grants from Abbott. A. Linke and G. Fontana have received speaker honoraria as consultants and grant support from Abbott. R. Makkar and S. Worthley have received consultancy fees from Abbott. F. Asch is Director of MedStar Health with institutional contracts from Abbott.

References

1. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Rodriguez Muñoz D, Rosenhek R, Sjögren J, Tornos Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL; ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2017;38:2739-91.
2. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, Jneid H, Mack MJ, McLeod CJ, O'Gara PT, Rigolin VH, Sundt TM 3rd, Thompson A. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2017;135:e1159-95.
3. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med*. 2011;364:2187-98.
4. Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, Gleason TG, Buchbinder M, Hermiller J Jr, Kleiman NS, Chetcuti S, Heiser J, Merhi W, Zorn G, Tadros P, Robinson N, Petrossian G, Hughes GC, Harrison JK, Conte J, Maini B, Mumtaz M, Chenoweth S, Oh JK; U.S. CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med*. 2014;370:1790-8.
5. 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 PW, Kappetein AP; SURTAVI Investigators. Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med*. 2017;376:1321-31.

6. 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, Babaliarios 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; PARTNER 2 Investigators. Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med*. 2016;374:1609-20.

7. Manoharan G, Spence MS, Rodés-Cabau J, Webb JG. St Jude Medical Portico valve. *EuroIntervention*. 2012;8:Q97-101.

8. Kappetein AP, Head SJ, Généreux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, 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. *Eur Heart J*. 2012;24:2403-18.

9. Zoghbi WA, Adams D, Bonow RO, Enriquez-Sarano M, Foster E, Grayburn PA, Hahn RT, Han Y, Hung J, Lang RM, Little SH, Shah DJ, Shernan S, Thavendiranathan P, Thomas JD, Weissman NJ. Recommendations for Noninvasive Evaluation of Native Valvular Regurgitation. A report from the American Society of Echocardiography in Collaboration with the Society of Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr*. 2017;30:303-71.

10. Zoghbi WA, Chambers JB, Dumesnil JG, Foster E, Gottdiener JS, Grayburn PA, Khandheria BK, Levine RA, Marx GR, Miller FA Jr, Nakatani S, Quiñones MA, Rakowski H, Rodriguez LL, Swaminathan M, Waggoner AD, Weissman NJ, Zabalgoitia M; American Society of Echocardiography's Guidelines and Standards Committee; Task Force on Prosthetic Valves; American College of Cardiology Cardiovascular Imaging Committee; Cardiac Imaging Committee of the American Heart Association; European Association of Echocardiography; European Society of Cardiology; Japanese Society of Echocardiography; Canadian Society of Echocardiography; American College of Cardiology Foundation; American Heart Association; European Association of Echocardiography; European Society of Cardiology; Japanese Society of Echocardiography; Canadian Society of Echocardiography. Recommendations for evaluation of prosthetic valves with echocardiography and doppler ultrasound: a report From the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee, Cardiac Imaging Committee of the

American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography, endorsed by the American College of Cardiology Foundation, American Heart Association, European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography, and Canadian Society of Echocardiography. *J Am Soc Echocardiogr*. 2009;22:975-1014.

11. Möllmann H, Linke A, Holzhey DM, Walther T, Manoharan G, Schäfer U, Heinz-Kuck K, Van Boven AJ, Redwood SR, Kovac J, Butter C, Søndergaard L, Lauten A, Schymik G, Worthley SG. Implantation and 30-Day Follow-Up on All 4 Valve Sizes Within the Portico Transcatheter Aortic Bioprosthetic Family. *JACC Cardiovasc Interv*. 2017;10:1538-47.

12. Perlman GY, Cheung A, Dumont E, Stub D, Dvir D, Del Trigo M, Pelletier M, Alnasser S, Ye J, Wood D, Thompson C, Blanke P, Leipsic J, Seidman MA, LeBlanc H, Buller CE, Rodés-Cabau J, Webb JG. Transcatheter aortic valve replacement with the Portico valve: one-year results of the early Canadian experience. *EuroIntervention*. 2017;12:1653-9.

13. Kodali S, Thourani VH, White J, Malaisrie SC, Lim S, Greason KL, Williams M, Guerrero M, Eisenhauer AC, Kapadia S, Kereiakes DJ, Herrmann HC, Babaliarios V, Szeto WY, Hahn RT, Pibarot P, Weissman NJ, Leipsic J, Blanke P, Whisenant BK, Suri RM, Makkar RR, Ayele GM, Svensson LG, Webb JG, Mack MJ, Smith CR, Leon MB. 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.

14. Popma JJ, Reardon MJ, Khabbaz K, Harrison JK, Hughes GC, Kodali S, George I, Deeb GM, Chetcuti S, Kipperman R, Brown J, Qiao H, Slater J, Williams MR. Early Clinical Outcomes After Transcatheter Aortic Valve Replacement Using a Novel Self-Expanding Bioprosthesis in Patients with Severe Aortic Stenosis Who Are Suboptimal for Surgery: Results of the Evolut R U.S. Study. *JACC Cardiovasc Interv*. 2017;10:268-75.

15. Mas-Peiro S, Vasa-Nicotera M, Weiler H, Papadopoulos N, De Rosa R, Zeiher AM, Fichtlscherer S. Thirty-Day Outcomes in 100 Consecutive Patients Undergoing Transfemoral Aortic Valve Replacement with the Portico Valve on an All-Comer Basis. *J Invasive Cardiol*. 2017;29:431-6.

16. Grube E, Van Mieghem N, Bleiziffer S, Modine T, Bosmans J, Manoharan G, Linke A, Scholtz W, Tchétché D, Finkelstein A, Trillo R, Fiorina C, Walton A, Malkin C, Oh JK, Qiao H, Windecker S; FORWARD Study Investigators. Clinical Outcomes with a Repositionable Self-Expanding Transcatheter Aortic Valve Prosthesis: The International FORWARD Study. *J Am Coll Cardiol*. 2017;70:845-53.

17. Wendler O, Schymik G, Treede H, Baumgartner H, Dumonteil N, Ihlberg L, Neumann FJ, Tarantini G, Zammarano JL, Vahanian A. SOURCE 3 Registry: Design and 30-Day Results of the European Post Approval Registry of the Latest Generation of

the SAPIEN 3 Transcatheter Heart Valve. *Circulation*. 2017;135:1123-32.

18. Falk V, Wöhrle J, Hildick-Smith D, Bleiziffer S, Blackman DJ, Abdel-Wahab M, Gerckens U, Linke A, Ince H, Wenaweser P, Allocco DJ, Dawkins KD, Van Mieghem NM. Safety and efficacy of a repositionable and fully retrievable aortic valve used in routine clinical practice: the RESPOND Study. *Eur Heart J*. 2017;38:3359-66.

19. Marzahn C, Koban C, Seifert M, Isotani A, Neuß M, Hölschermann F, Butter C. Conduction recovery and avoidance of permanent pacing after transcatheter aortic valve implantation. *J Cardiol*. 2018;71:101-8.

20. Auffret V, Puri R, Urena M, Chamandi C, Rodriguez-Gabella T, Philippon F, Rodés-Cabau J. Conduction Disturbances After Transcatheter Aortic Valve Replacement: Current Status and Future Perspectives. *Circulation*. 2017;136:1049-69.

21. Popma JJ, Adams DH, Reardon MJ, Yakubov SJ, Kleiman NS, Heimansohn D, Hermler J Jr, Hughes GC, Harrison JK, Coselli J, Diez J, Kafi A, Schreiber T, Gleason TG, Conte J, Buchbinder M, Deeb GM, Carabello B, Serruys PW, Chenoweth S, Oh JK; CoreValve United States Clinical Investigators. Transcatheter aortic valve replacement using a self-expanding bioprosthesis in

patients with severe aortic stenosis at extreme risk for surgery. *J Am Coll Cardiol*. 2014;63:1972-81.

22. Husser O, Kim W, Pellegrini C, Holzamer A, Walther T, Mayr PN, Joner M, Kasel AM, Trenkwalder T, Michel J, Rheude T, Kastrati A, Schunkert H, Burgdorf C, Hilker M, Möllmann H, Hengstenberg C. Multicenter Comparison of Novel Self-Expanding Versus Balloon-Expandable Transcatheter Heart Valves. *JACC Cardiovasc Interv*. 2017;10:2078-87.

23. Forrest J, Mangi A, Popma J, Khabbaz K, Reardon MJ, Kleiman NS, Yakubov SJ, Watson D, Kodali S, George I, Tadros P, Zorn GL 3rd, Brown J, Kipperman R, Saul S, Qiao H, Oh JK, Williams MR. Early Outcomes With the Evolut PRO Repositionable Self-Expanding Transcatheter Aortic Valve With Pericardial Wrap. *JACC Cardiovasc Interv*. 2018;11:160-8.

24. Linke A, Holzhey D, Möllmann H, Manoharan G, Schäfer U, Frerker C, Worthley SG, van Boven AJ, Redwood S, Kovac J, Butter C, Søndergaard L, Lauten A, Schymik G, Walther T. Treatment of Aortic Stenosis with a Self-Expanding, Resheathable Transcatheter Valve: One-Year Results of the International Multicenter Portico Transcatheter Aortic Valve Implantation System Study. *Circ Cardiovasc Interv*. 2018;11:e005206.