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ORIGINAL ARTICLE

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European multicentre experience with the sutureless Perceval valve: clinical and haemodynamic outcomes up to 5 years in over 700 patients[†]

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Abstract

OBJECTIVES: This report summarizes the 5-year clinical and haemodynamic data from three prospective, European multicentre trials with the Perceval sutureless aortic valve.

METHODS: From April 2007 to August 2012, 731 consecutive patients (mean age: 78.5 years; 68.1% females; mean logistic EuroSCORE 10.9%) underwent AVR with the Perceval valve in 25 European centres. Isolated AVR was performed in 498 (68.1%) patients. A minimally invasive approach was performed in 189 (25.9%) cases. The cumulative follow-up was 729 patients-years.

RESULTS: In isolated AVR, mean cross-clamp and cardiopulmonary bypass times were 30.8 and 50.8 min in full sternotomy, and 37.6 and 64.4 min in the minimally invasive approach, respectively. Early cardiac-related deaths occurred in 1.9%. Overall survival rates at 1 and 5 years were 92.1 and 74.7%, respectively. Major paravalvular leak occurred in 1.4% and 1% at early and late follow-up, respectively. Significant improvement in clinical status was observed postoperatively in the majority of patients. Mean and peak gradients decreased from 42.9 and 74.0 mmHg preoperatively, to 7.8 and 16 mmHg at the 3-year follow-up. LV mass decreased from 254.5 to 177.4 g at 3 years.

CONCLUSIONS: This European multicentre experience, with the largest cohort of patients with sutureless valves to date, shows excellent clinical and haemodynamic results that remain stable even up to the 5-year follow-up. Even in this elderly patient cohort with 40% octogenarians, both early and late mortality rates were very low. There were no valve migrations, structural valve degeneration or valve thrombosis in the follow-up. The sutureless technique is a promising alternative to biological aortic valve replacement.

Keywords: Aortic valve replacement • Sutureless heart valve prosthesis • Prospective study

INTRODUCTION

Aortic valve replacement (AVR) is the accepted 'gold standard' for the treatment of severe or symptomatic aortic valve stenosis. Owing to increasing age of the patient population (reflecting the demographic changes) in the Western world, the use of biological valves has increased over the past years. At the same time, a large proportion of these patients require concomitant surgical procedures in addition to AVR [1].

Although transapical or trans-femoral aortic valve implantations (TAVIs) have been introduced for high-risk patients, they are limited to patients with an isolated aortic valve pathology [2].

Three consecutive European, multicentre, prospective, non-randomized clinical trials (Pilot, Pivotal and CAVALIER) were designed to evaluate the sutureless Perceval aortic valve prosthesis in elderly patients. The Perceval valve (Sorin Group, Saluggia, Italy) is a bioprosthetic heart valve made of bovine pericardium allowing for a fast implantation through a sutureless

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technique. We describe the combined results of these three consecutive trials.

MATERIALS AND METHODS

Study design

This series comprises the cumulative results of patients undergoing aortic valve replacement with or without concomitant procedures from three consecutive European prospective multicentre trials (Perceval Pilot, Perceval Pivotal and CAVALIER), between 2007 and 2012.

Twenty-five centres in eight European countries took part in these three studies. Approval for these studies was granted by the ethical committees of the hospitals involved and each patient gave their signed informed consent before being enrolled in the trials.

Perceval Pilot trial

The objective of the Pilot trial was to assess the safety of aortic valve replacement with the sutureless Perceval valve in 30 symptomatic patients, aged 75 and older. The primary end point was the assessment of the safety of the Perceval prosthesis in terms of mortality and morbidity at 30 days, correlated to prosthetic valve performance. Secondary end points were the evaluation of mortality and morbidity, the evaluation of the clinical status on the basis of the New York Heart Association (NYHA) functional classification, and the evaluation of the haemodynamic performance at 1, 3, 6 and 12 months from implantation, respectively. A total of 30 patients were enrolled in this trial and follow-up at 5 years has been completed.

Perceval Pivotal trial

The primary objective of the Pivotal study was to assess the performance of the Perceval valve at 3–6 months after implantation in 150 symptomatic patients aged ≥75 years, requiring surgical intervention to replace the aortic valve. The primary end point was the assessment of the Perceval prosthesis safety and performance at 3–6 months after surgery. Secondary end points included the evaluation of the Perceval valve in terms of improvement of clinical status, haemodynamic performance by echocardiography, and assessment of mortality and morbidity rates at discharge and 12 months after implant, respectively.

These two Perceval trials aimed at obtaining initial European Conformity (CE) mark approval, even though only two prosthesis sizes (Size S and Size M) were available. The outcomes showed adequate safety and performance, and allowed the Perceval to obtain CE mark in January 2011 (for Sizes S and M) under limited indications.

CAVALIER trial

The CAVALIER trial was designed to assess the safety and effectiveness of the Perceval valve at 12 months after implantation when used to replace a diseased or dysfunctional aortic valve or aortic valve prosthesis in symptomatic patients older than 65 years. The primary end point was the evaluation of the safety (assessed in terms of mortality and morbidity) and effectiveness (assessed in terms of improvement of clinical status as well as haemodynamic performance) of the Perceval valve at 12 months after the implants. The secondary end points of the clinical investigation were the assessment of safety and effectiveness at discharge and 3–6 months after surgery and yearly thereafter. Besides lowering the age limit to younger patients (65 years or older), this study included two additional prosthesis sizes: Size L (from February 2010) and Size XL (from July 2012).

Annex B of the Supplementary material shows the inclusion and exclusion criteria.

Perceval sutureless valve

The Perceval valve is a surgical bioprosthetic heart valve comprising a biological component of bovine pericardium and an elastic Ni-Ti alloy stent made of two rings and nine vertical struts covered by a thin coating of Carbofilm™ that improves biocompatibility (Fig. 1). The stent has the dual task of supporting the valve and holding it in place without any permanent suture. Owing to its elastic properties, the stent adapts to the anatomy of the aorta and follows its movements, relieving the stress on the leaflets. The valve is collapsed with atraumatic device compression, assuring that the valve leaflets are not affected.

Surgical procedure

The patients were operated either through a standard median sternotomy or upper ministernotomy. Anaesthetic and surgical techniques were standardized according to the preferences of each centre. A transverse aortotomy was performed ∼0.5 cm distal to the sinotubular junction in order to leave a free edge for closure of the aortotomy after implantation of the device.

The native calcified aortic valve was excised and the aortic annulus decalcified. A regular annular profile was beneficial to ensure optimal sealing and preventing the risk of paraprosthetic leak. The sizing of the annulus was done with dedicated sizers.

For this series, the study valve was available in three sizes: Size S, to be implanted in annular sizes from 19 to 21 mm, Size M

Figure 1: The Perceval valve.

to be implanted in annular sizes from 21 to 23 mm and Size L for patients with an annular size from 23 to 25 mm.

The implantation technique included several steps as already described elsewhere [3–5].

Concomitant coronary artery bypass graft (CABG) procedures were additionally performed in patients with coronary artery disease. This was usually done during the time when the study valve was being collapsed to keep the aortic cross-clamp time as short as possible.

After closure of the aortotomy in the usual fashion, release of the aortic cross-clamp and thorough de-airing, valve functioning was investigated by transoesophageal echocardiography in all patients.

Following the procedure, the patients received anticoagulation treatment according to the standard protocol in use at each centre for bioprostheses.

Patients

From April 2007 to August 2012, a total of 765 patients were enrolled in these three Perceval studies (30 Pilot, 150 Pivotal and 585 CAVALIER subjects). Out of 765 patients included in the study, the Perceval valve was implanted in 731 patients (95.6%), while in 34 cases (4.4%), conversion to commercially available valves was required.

The enrolment was carried out in a sequential, prospective manner such that all patients identified as candidates for standard aortic valve replacement with a bioprosthesis (according to the practice of each centre) were offered the option of participating in the assessment if they fulfilled the selection criteria defined in each protocol (Supplementary material, Annex B).

Follow-up

According to the study protocol, clinical evaluation, electrocardiogram (ECG), blood examination and transthoracic echocardiographic examination were performed at discharge (or 30 days), at 3–6 months, at 12 months and then annually up to 5 years.

An echo core laboratory performed a full analysis of the images and relevant calculations and an independent Clinical Events Committee reviewed and adjudicated the complications.

Adverse events were reported according to current guidelines [6]. The Kaplan–Meier survival curve is shown in Fig. 2.

Statistical analysis

Statistical analyses were performed on all patients successfully implanted with a Perceval valve. Categorical variables are reported as absolute and relative frequencies. For continuous data, means and standard deviations were calculated. Cumulative survival and freedom from events were estimated using the Kaplan–Meier method, with 95% confidence intervals (95% CIs). Statistical analyses were performed using the SAS software (Release 9.2, by SAS Institute, Inc., Cary, NC, USA). A *P*-value of <0.05 was considered to be statistically significant.

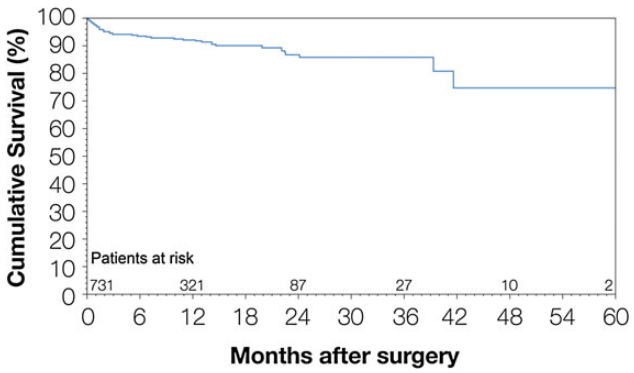

Figure 2: Kaplan–Meier survival curve.

RESULTS

Patient demographics and procedural outcomes

The mean age of the 731 patients was 78.5 ± 5.3 years (range, 62–92 years); 43.1% of patients were ≥80 years old. The preoperative data are reported in Table 1. The majority of patients presented with valve stenosis (509/69.6%) due to degenerative disease. Out of 731 patients, 542 patients (74.1%) underwent surgery via median sternotomy, whereas the remaining 189 patients (25.9%) underwent a minimally invasive surgical approach. Two hundred and forty (32.8%) patients had concomitant procedures. In 192 (26.3%) patients, coronary artery bypass grafting was performed. Operative data are summarized in Table 2.

Table 1: Preoperative characteristics and risk factors (mean ± SD)

Patients	*n* = 731	%
Sex		
F	498	68.1
M	233	31.9
Mean age ± SD (range)	78.5 ± 5.3 (62.0–92.0)	
Patients ≥80 years	315	43.1
Mean height ± SD (range) (cm)	162.9 ± 7.9 (140.0–186.0)	
Mean weight ± SD (range) (kg)	72.4 ± 13.4 (38.0–112.0)	
Mean BSA ± SD (range)	1.8 ± 0.2 (1.3–2.4)	
Risk factors[a]		
Systemic hypertension	589	80.6
Diabetes	203	27.8
Smokers	155	21.2
Extracardiac arteriopathy	117	16.0
Renal insufficiency	108	14.8
Cerebrovascular disease	75	10.3
Previous cardiovascular surgery[b]		
CABG	14	1.9
Previous valve surgery	7	1.0
CABG + previous valve surgery	1	0.4
NYHA		
I	19	2.6
II	163	22.3
III	488	66.8
IV	42	5.7
Not available	19	2.6
Type of valve lesion		
Stenosis	509	69.6
Stenoinsufficiency	221	30.2
Insufficiency	1	0.1
Mean EuroSCORE ± SD (range)	10.9 ± 8.2 (1.2–75.3)	
Mean STS score ± SD (range)	8.5 ± 8.6 (0.8–67.5)	
Rhythm disorders		
Previous atrial fibrillation/flutter	88	12.0
Previous heart block	52	7.1

[a]Patients can have more than one risk factor.
[b]Patient can have more than one previous surgery.

Table 2: Operative data

Patients	*n* = 731	%
Surgical approach		
Median sternotomy	542	74.1
Minimally invasive approach	189	25.9
Aortic valve condition		
Tricuspid	714	97.7
Bicuspid	8	1.1
Other (7 previous bioprostheses, 1 pseudo-bicuspid, 1 monocuspid)	9	1.2
Valve size		
S/21	122	16.7
M/23	383	52.4
L/25	226	30.9
Concomitant procedures[a]		
None	491	67.2
Concomitant procedures	240	32.8
CABGs	192	26.3
Septal myectomy	27	3.7
Other cardiac concomitant procedures	27	3.7
Other non-cardiac concomitant procedures	11	1.5

[a]Patients can have more than one procedure.

Table 3: Procedure timings

	Isolated AVR (*n* = 498) Mean (SD)	Concomitant cardiac procedure (*n* = 233) Mean (SD)	Overall (*n* = 731) Mean (SD)
Median sternotomy			
CPB time	50.8 (19.5)	79.5 (33.3)	62.4 (29.5)
Cross-clamp time	30.8 (10.8)	51.5 (23.6)	39.2 (19.9)
Minimally invasive			
CPB time	64.4 (19.2)	68.5 (23.1)	64.7 (19.5)
Cross-clamp time	37.6 (12.0)	42.6 (13.7)	37.9 (12.1)
Overall			
CPB time	55.8 (20.5)	78.9 (32.9)	63.0 (27.2)
Cross-clamp time	33.3 (11.7)	51.0 (23.2)	38.8 (18.2)

The mean aortic cross-clamp time and the cardiopulmonary bypass (CPB) time were 30.8 and 50.8 min, respectively, for isolated aortic valve replacement via median sternotomy and 37.6 and 64.4 min for a minimally invasive approach (Table 3).

Early and late mortality, morbidity and functional status

Early (≤30-day) all-cause and cardiac early mortality rates were 3.4% (25/731) and 1.9% (14/731), respectively (Table 4). Among the early cardiac deaths, 3 occurred in the operating theatre. One of these occurred during surgery in a patient with a very critical preoperative status; the patient underwent successful implant of the device that was then removed due to the presence of a previous endocarditic lesion and the patient did not survive the surgery due to myocardial failure. In the second case, death was caused by an acute myocardial dysfunction. The third case was due to annulus rupture during traditional valve implantation following aortic regurgitation with the Perceval valve.

Early complications accounted for 29 thromboembolic events (4.0%), which include 12 strokes (1.6%); 15 non-structural dysfunctions (2%), of which 10 were classified as major paravalvular leaks (1.4%), 2 cases of endocarditis (0.3%) and 10 explants (1 due to perioperative bleeding from a tear below the right coronary ostium during extensive decalcification of the annulus, 3 to mis-sizing, 5 to mis-positioning and 1 to endocarditis).

Late (>30-day) all-cause and and cardiac mortality rates were 7.0% (51/729 patient/year) and 1.4% (10/729 patient/year), respectively. The causes of both early and late mortality are summarized in Table 4.

Late thromboembolic events were reported as 2.3% (*n* = 17) per late patient-year (6 events led to stroke), and late major paravalvular leak (PVL) events were reported as 1.0% (*n* = 7). Forty-four patients (6.0%) with no prior history of cardiac rhythm disorders experienced early AV block III. Valve explants occurred in 11 patients (1.5% per late patient-year). Eight explants were due to endocarditis, 1 was related to a left-shunt between the aorta and the right ventricle, 1 to fibrous pannus overgrowth and 1 to a pseudo-aneurysm of the non-coronary sinus resulting in paravalvular regurgitation.

No cases of valve thrombosis, structural valve deterioration or valve migration or dislodgement after surgery were reported.

Table 5 reports the early and late complications

The functional status significantly improved along with haemodynamic performance in the majority of the population. A marked decrease in NYHA stage was observed in the majority of patients, such that 89.1 and 91.0% of patients with available information fell in classes I–II at 12 months and at 2 years, respectively.

Haemodynamic outcomes

The mean gradient was 10.3 mmHg at discharge/1 month, 8.9 mmHg at 3–6 months and 12 months, 8.8 mmHg at 2 years, and 7.7and 7.8 mmHg at 3 and 4 years, respectively. At the 5-year follow-up, the few data available at the time of the data analysis (6 echo exams) showed a mean gradient of 7.8 mmHg. This gradient reduction was correlated to an increase in the effective orifice area from 0.75 cm^2 preoperatively to 1.49 cm^2 at discharge/1 month, 1.51 cm^2 at 3–6 months, 1.55 cm^2 at 12 months, up to 1.80 cm^2 at 5 years, and to a LV mass regression, which went from 254.5 g to 177.4 g at 3 years. Haemodynamic results are reported by valve size in Table 6.

In the non-structural valve deterioration (SVD) group, only one case of severe intra- and paraprosthetic leak was assessed by the Core lab at the 2-year follow-up. This patient was explanted due to a pseudo-aneurysm of the non-coronary sinus, resulting in the need of replacing the valve along with the ascending aorta.

DISCUSSION

Aortic valve replacement has been widely accepted as the gold standard for the treatment of patients with aortic valve stenosis [7]. The mean age of the patients referred for AVR has been

Table 4: Specific causes of early (≤30 days) and late (>30 days) deaths

	Early, *n* = 25	Late, *n* = 51
Cardiac	*n* = 14 (days postoperative)	*n* = 10 (days postoperative)
In operative room	3	
Heart failure	2 (1, 4)	6 (40, 85, 105, 302, 395, 902)
Rhythm troubles	5 (0, 4, 6, 16, 23)	
Endocarditis	1 (13)	1 (264)
Multiorgan failure	1 (11)	1 (191)
Cardiac insufficiency	2 (19, 24)	
Sepsis		1 (685)
Stroke		1 (58)
Non-cardiac	*n* = 8 (days post-op)	*n* = 30
Multiorgan failure	4 (7, 14, 29, 29)	4 (40, 45, 55, 101)
Liver insufficiency	1 (4)	
Gastrointestinal bleeding	1 (18)	
Neurological vascular accident	1 (30)	
Sepsis leading to respiratory insufficiency and coma	1 (30)	
Sepsis		2 (33, 43)
Infections		7 (33, 41, 55, 67, 154, 682, 733)
Renal failure		5 (181, 311, 329, 361, 432)
Diarrhoea and dehydration		1 (60)
Respiratory insufficiency		2 (37, 40)
Neoplastic pathology		4 (49, 84, 220, 297)
Autoimmune thrombocytopenia		1 (71)
Accident		1 (76)
Cerebral bleeding		1 (670)
Cerebral haematoma due to fall		1 (204)
Worsening of chronic obstructive pulmonary disease		1 (170)
Sudden, unexpected, unexplained	*n* = 3 (13, 24, 28)	*n* = 11 (34, 76, 82, 88, 152, 165, 376, 443, 602, 1196, 1267)

increasing along with demographic changes. Therefore, concepts of aortic valve replacement to avoid long ischaemia times, as well as long periods of extracorporeal circulation (ECC) should be welcomed among the surgical community.

In the present study cohort >40% of the patients were 80 years or older. The 5-year outcomes from patients undergoing AVR with the Perceval valve demonstrate that the device is safe and performs well, even in an elderly population with comorbidities.

Previous studies demonstrated that the duration of aortic cross-clamping and CPB are independent predictors of survival after either aortic valve replacement or combined valve operations with CABG. Ranucci *et al.* [8] reported that the aortic cross-clamp time is an independent predictor of severe cardiovascular morbidity, with an increased risk of 1.4% per 1 min increase [8, 9]. Therefore, a new technology for shortening the aortic cross-clamp time and, consequently, CPB time is mandatory to further reduce mortality after AVR surgery, especially in geriatric patients.

The Perceval valve features a fairly high adaptability to different surgical approaches as shown by this study. The implantations were performed either via full sternotomy or minimally invasive approach (ministernotomy or right anterior minithoracotomy) [10, 11].

Previous experiences showed that the use of less-invasive AVR was associated with excellent outcomes in terms of postoperative complications and hospital stay [12, 13]. However, the reduced working space for the exposure and implantation of the prosthetic valves (especially in small or calcified aortic annuli) caused the drawback of the increasing surgical times. In such cases the adoption of sutureless technology may facilitate the less-invasive AVR approach. In this study the low cross-clamp times that were achieved with both surgical approaches demonstrate the ease of implantation of the Perceval valve.

The possibility of performing simultaneous procedures, in particular CABG, with this device represents an advantage when compared with other interventional techniques, such as transcatheter aortic valve implantations (TAVIs). This is important as, according to the society of thoracic surgeons (STS) database, the proportion of candidates requiring concomitant CABG has risen from 5 to 25% over the past 20 years. Previous experience already demonstrated the safety and efficacy of the Perceval valve even in cases of concomitant cardiac procedures [14].

In patients requiring aortic valve replacement along with concomitant procedures, shortening the aortic cross-clamp and CPB time may help reduce the mortality and morbidity. Therefore, the use of sutureless valves may help reduce the procedural times owing to the absence of the need for sutures.

The clinical results up to the 5-year follow-up reported in this large cohort of patients confirm the safety and efficacy of the Perceval sutureless aortic valve. Rates of early and late mortality and complications such as stroke and PVL are comparable with reported rates for traditional AVR [15, 16]. Even in cases requiring explantation of the Perceval, the procedure was easy and the Perceval valve was removed without technical issues, as previously described [17].

New occurrences of early AV block III leading to pacemaker implant in patients with no prior history of cardiac rhythm disorders was 6.0%, which is within the ranges reported in the literature for traditional AVR [18]. This rate could also be related to the initial learning curve effect. Additionally, the large number of centres in this cohort and variability of operators and protocols of rhythm disorders management could be considered as an additional potential contributing factor, considering that in one of the biggest cohorts in experienced centres the rate was lower (4.2%) [19].

Table 5: Observed postoperative adverse events rates. All patients, *n* = 731. Cumulative follow-up = 729 paientts-year

	Total		Early events (≤30 days)		Late events (>30 days)			
	n	%	*n*	%	*n*	%	%/pts-yr	
Deaths	76	10.4	25	3.4	51	7.0	7.0	(5.4–8.6)
Cardiac	24	2.1	14	1.9	10	1.4	1.4	(1.2–1.6)
Non-cardiac	38	5.2	8	1.1	30	4.1	4.1	(2.9–5.3)
Sudden, unexpected, unexplained death/unknown	14	1.9	3	0.4	11	1.5	1.5	(0.8–2.2)
Explants	21	2.9	10	1.4	11	1.5	1.5	(0.8–2.2)
Thromboembolism	46	6.3	29	4.0	17	2.3	2.3	(1.4–3.2)
Stroke	18	2.5	12	1.6	6	0.8	0.8	(0.3–1.3)
Non-structural valve dysfunction	26	3.6	15	2.0	11	1.5	1.5	(0.8–2.2)
Intraprosthetic regurgitation	5	0.7	4	0.6	1	0.1	0.1	(0.0–0.3)
Minor	2	0.3	2	0.3	0	0.0	0.0	-
Major	3	0.4	2	0.3	1	0.1	0.1	(0.0–0.3)
Paravalvular leak	19	2.6	10	1.4	9	1.2	1.2	(0.6–1.9)
Minor	2	0.3	0	0.0	2	0.3	0.3	(0.0–0.6)
Major	17	2.3	10	1.4	7	1.0	1.0	(0.4–1.6))
Secondary paravalvular leak	2	0.3	1	0.1	1	0.1	0.1	(0.0–0.3)
Endocarditis	14	1.9	2	0.3	12	1.6	1.7	(0.9–2.4)
Valve thrombosis	0	0.0	0	0.0	0	0.0	0.0	–
Structural valve deterioration	0	0.0	0	0.0	0	0.0	0.0	–
Haemolysis	8	1.1	4	0.6	4	0.6	0.6	–
Other								
AV block III in patients without preoperative cardiac rhythm abnormalities	54	7.4	44	6.0	1.4	1.4	1.4	(1.2–1.6)

Table 6: Haemodynamic performance as evaluated by transthoracic echocardiography (Mean ± SD)

	Preoperative	Discharge/1 month	3–6 months	12 months	2 years	3 years	4 years	5 years
LVEF (%)	60.1 ± 11.6	58.4 ± 11.2	60.7 ± 9.9	61.4 ± 9.9	67.0 ± 8.5	67.0 ± 9.0	66.1 ± 9.1	65.8 ± 7.7
size 21	63.8 ± 12.9	62.1 ± 10.0	62.7 ± 9.9	64.9 ± 8.9	65.5 ± 11.1	68.1 ± 5.8	64.3 ± 5.1	64.0 ± 4.2
size 23	61.9 ± 11.1	60.6 ± 10.7	62.7 ± 9.6	63.2 ± 8.6	67.9 ± 7.5	66.4 ± 10.8	67.0 ± 10.9	67.0 ± 10.1
size 25	55.1 ± 10.0	52.9 ± 10.4	55.9 ± 8.6	55.5 ± 10.5	56.0	NA	NA	NA
MPG (mmHg)	42.9 ± 16.4	10.3 ± 4.4	8.9 ± 4.3	8.9 ± 4.7	8.8 ± 3.9	7.7 ± 2.8	7.8 ± 3.8	8.8 ± 4.6
size 21	43.4 ± 17.7	10.9 ± 5.1	10.5 ± 6.3	10.2 ± 5.2	8.2 ± 3.4	9.7 ± 3.0	8.7 ± 4.0	10.5 ± 7.8
size 23	41.8 ± 15.9	10.5 ± 4.5	8.9 ± 4.0	8.8 ± 4.9	9.0 ± 4.1	6.8 ± 2.3	7.5 ± 4.0	8.0 ± 3.6
size 25	44.7 ± 16.6	9.5 ± 3.8	8.0 ± 3.2	8.2 ± 3.7	7.8	NA	NA	NA
PPG (mmHg)	74.0 ± 25.6	20.4 ± 8.5	17.8 ± 7.7	17.7 ± 8.0	20.0 ± 7.9	16.0 ± 5.2	17.8 ± 8.1	21.1 ± 9.7
size 21	78.8 ± 27.9	22.6 ± 10.6	21.0 ± 9.0	20.7 ± 9.7	19.4 ± 5.7	19.0 ± 4.5	20.6 ± 9.3	27.0 ± 15.5
size 23	72.5 ± 24.6	21.1 ± 8.4	18.3 ± 7.8	17.6 ± 7.8	20.3 ± 8.5	14.6 ± 5.0	16.7 ± 8.0	18.2 ± 6.4
size 25	73.6 ± 25.7	17.9 ± 6.5	15.1 ± 5.5	15.8 ± 6.3	14.3	NA	NA	NA
EOA (cm^2)	0.75 ± 0.23	1.49 ± 0.39	1.51 ± 0.37	1.55 ± 0.37	1.70 ± 0.46	1.64 ± 0.42	1.68 ± 0.43	1.80 ± 0.30
size 21	0.75 ± 0.27	1.40 ± 0.37	1.40 ± 0.37	1.47 ± 0.37	1.71 ± 0.49	1.44 ± 0.22	1.40 ± 0.30	1.55 ± 0.09
size 23	0.76 ± 0.23	1.52 ± 0.41	1.51 ± 0.38	1.56 ± 0.40	1.71 ± 0.46	1.74 ± 0.46	1.79 ± 0.44	1.92 ± 0.30
size 25	0.73 ± 0.19	1.49 ± 0.35	1.56 ± 0.37	1.57 ± 0.31	1.19	NA	NA	NA
LVMASS (g)	254.5 ± 77.6	238.6 ± 74.3	216.2 ± 66.5	216.6 ± 70.6	188.6 ± 66.1	177.4 ± 46.9	116.0 ± 12.7	227.7 ± 74.3
size 21	224.0 ± 64.4	190.0 ± 63.0	169.9 ± 49.5	180.7 ± 59.6	142.0 ± 80.6	174.2 ± 57.3	107.0	266.5 ± 44.5
size 23	253.7 ± 79.2	233.8 ± 70.8	214.3 ± 65.7	212.8 ± 68.5	185.4 ± 54.3	179.1 ± 43.9	125.0	150.0
size 25	269.5 ± 77.1	262.6 ± 73.7	241.8 ± 62.8	242.5 ± 70.6	316.0	NA	NA	NA

No valve dislodgement or migration, thrombosis or structural valve deterioration was observed even after a follow-up of up to 5 years.

The valve implantation resulted in significant improvement of patients' symptoms. Even though a majority of patients were quite short in stature with a small aortic annulus and received small-sized prostheses, the postoperative transvalvular gradients were low and remained stable over time up to the 5-year follow-up. In patients with a critically small annulus, this valve allows maximization of the bioprosthetic diameter, as previously reported [20]. The haemodynamic data show an improvement of left ventricular function.

CONCLUSIONS

Although numerous publications (usually single-centre reports) on the results of AVR with Perceval sutureless valve have been

published, this is first report with more than 700 patients from multiple centres in Europe.

In summary, this study reports the widest and longest experience with a sutureless valve and highlights its safety and efficacy even in an elderly population. The Perceval valve implantation could be easily performed by offering a significant reduction of cross-clamping and CPB times compared with both the traditional valve prostheses and the other sutureless prostheses available on the market (www.sts.org/documents/pdf/Spring2005STS%20ExecutiveSummary.pdf) [21, 22], even when performed via a minimally invasive approach. Therefore, in patients needing aortic valve replacement with or without concomitant procedures, this device could have an advantage compared with conventional sutured valves. The continuation of the patient follow-up will provide further assessment of long-term valve performance.

LIMITATIONS

The main limitation of the current study is the lack of a control group and a randomization in its design. The lack of a control group did not allow the authors to fully assess the benefits of the Perceval valve compared with the aortic conventional valves, which are still considered the gold standard for patients with symptomatic aortic stenosis. A large prospective randomized controlled trial comparing the sutureless technologies with the traditional standard aortic replacement is mandatory in the near future to confirm the findings from the current study.

The limited follow-up period represents a temporary limitation (median follow-up: 351 days; range: 0–5.1 years), since the patients from both the Pivotal and CAVALIER trials are currently followed up and the 5-year data analysis will be provided in future publications to attest the mid-term valve performance.

Furthermore, EuroSCORE was used for the three studies even though the EuroSCORE may overestimate the risk of mortality.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

Conflict of interest: the participating centres received an unrestricted study grant from Sorin to conduct this study. The following authors are consultants/proctors for Sorin: M. Shrestha, T. Fischlein, B. Meuris, M Misfeld and F. Laborde. The participating study centres and physicians are listed in Annex A of the Supplementary material.

REFERENCES

[1] Beckmann A, Funkat AK, Lewandowski J, Frie M, Schiller W, Hekmat K *et al.* Cardiac Surgery in Germany during 2012: a report on behalf of the German Society for Thoracic and Cardiovascular Surgery. Thorac Cardiovasc Surg 2014;62:5–17.
[2] Cribier A, Eltchaninoff H, Bash A, Borenstein N, Tron C, Bauer F *et al.* Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. Circulation 2002;106:3006–8.
[3] Shrestha M, Folliguet T, Meuris B, Dibie A, Bara C, Herregods MC *et al.* Sutureless Perceval S aortic valve replacement: a multicenter prospective pilot trial. J Heart Valve Dis 2009;18:698–702.
[4] Folliguet TA, Laborde F, Zannis K, Ghorayeb G, Haverich A, Shrestha M. Sutureless perceval aortic valve replacement: results of two European centers. Ann Thorac Surg 2012;93:1483–8.
[5] Flameng W, Herregods MC, Hermans H, Van der Mieren G, Vercalsteren M, Poortmans G *et al.* Effect of sutureless implantation of the Perceval S aortic valve bioprosthesis on intraoperative and early postoperative outcomes. J Thorac Cardiovasc Surg 2011;142:1453–7.
[6] Akins CW, Miller DC, Turina MI, Kouchoukos NT, Blackstone EH, Grunkemeier GL *et al.* STS; AATS; EACTS. Guidelines for reporting mortality and morbidity after cardiac valve interventions. Eur J Cardiothorac Surg 2008;33:523–8.
[7] Schwarz F, Baumann P, Manthey J, Hoffmann M, Schuler G, Mehmel HC *et al.* The effect of aortic valve replacement on survival. Circulation 1982;66:1105–10.
[8] Flameng WJ, Herijgers P, Szecsi J, Sergeant PT, Daenen WJ, Scheys I. Determinants of early and late results of combined valve operations and coronary artery bypass grafting. Ann Thorac Surg 1996;61:621–8.
[9] Ranucci M, Frigiola A, Menicanti L, Castelvecchio A, De Vincentiis C, Pistuddi V *et al.* for the Surgical and Clinical Outcome Research (SCORE) Group. Aortic cross-clamp time, new prostheses, and outcome in aortic valve replacement. J Heart Valve Dis 2012;21:732–9.
[10] Santarpino G, Pfeiffer S, Schmidt J, Concistre G, Fischlein T. Sutureless aortic valve replacement: first-year single-center experience. Ann Thorac Surg 2012;94:504–9.
[11] Gilmanov D, Farneti P, Miceli A, Bevilacqua S, Glauber M. Perceval S sutureless aortic valve prosthesis implantation via right anterior minithoracotomy. Multimed Man Cardiothorac Surg 2013. doi:10.1093/mmcts/mmt012.
[12] Murtuza B, Pepper JR, Stanbridge RD, Jones C, Rao C, Darzi A *et al.* Minimally access aortic valve replacement: is it worth it? Ann Thorac Surg 2008;85:1121–31.
[13] Brown ML, McKellar SH, Sundt TM, Schaff HV. Ministernotomy versus conventional sternotomy for aortic valve replacement: a systematic review and meta-analysis. J Thorac Cardiovasc Surg 2009;137:670–9.
[14] Shrestha M, Folliguet TA, Pfeiffer S, Meuris B, Carrel T, Bechtel M *et al.* Aortic valve replacement and concomitant procedures with the Perceval valve: results of European trials. Ann Thorac Surg 2014;98:1294–300, pii: S0003-4975(14)01085-6.
[15] Hamm CW, Möllman H, Holzhey D, Beckmann A, Veit C, Figulla HR *et al.* The German Aortic Valve Registry (GARY): in-hospital outcome. Eur Heart J 2014;35:1588–98.
[16] Ionescu A, Fraser AG, Butchart EG. Prevalence and clinical significance of incidental paraprosthetic valvular regurgitation. Heart 2003;83:1316–21.
[17] Santarpino G, Pfeiffer S, Concistrè G, Fischlein T. A supra-annular malposition of the Perceval S sutureless aortic valve: the 'χ-movement' removal technique and subsequent reimplantation. Interact CardioVasc Thorac Surg 2012;15:280–1.
[18] Matthews IG, Fazal IA, Bates MGD, Turley A. In patients undergoing aortic valve replacement, what factors predict the requirement for permanent pacemaker implantation? Interact CardioVasc Thorac Surg 2011;12:475–9.
[19] Miceli A, Santarpino G, Pfeiffer S, Murzi M, Gilmanov D *et al.* Minimally invasive aortic valve replacement with Perceval S sutureless valve: Early outcomes and one-year survival from two European centers. J Thorac Cardiovasc Surg 2014;148:2838–43.
[20] Shrestha M, Maeding I, Höffler K, Koigeldiyev N, Marsch G, Siemeni T *et al.* Aortic valve replacement in geriatric patients with small aortic roots: are sutureless valves the future? Interact CardioVasc Thorac Surg 2013;17:778–82.
[21] Kocher AA, Laufer G, Haverich A, Shrestha M, Walther T, Misfeld M *et al.* One-year outcomes of the Surgical Treatment of Aortic Stenosis With a Next Generation Surgical Aortic Valve (TRITON) trial: a prospective multicenter study of rapid-deployment aortic valve replacement with the EDWARDS INTUITY Valve System. J Thorac Cardiovasc Surg 2013;145:110–5; discussion 115–6.
[22] Martens S, Sadowski J, Eckstein FS, Bartus K, Kapelak B, Sievers HH *et al.* Clinical experience with the ATS 3f Enable® Sutureless Bioprosthesis. Eur J Cardiothorac Surg 2011;40:749–55.

APPENDIX. CONFERENCE DISCUSSION

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Dr G. Dellgren *(Gothenburg, Sweden):* Shrestha and co-workers have described the early outcome with new sutureless aortic valve prosthesis. This is a clinical study performed in Europe, and as such, it is of great interest for the European

community. The conceptual design and idea follows that of how new valves are investigated in clinical studies and echocardiography data is included, which nowadays is a prerequisite when reporting the outcome of new valves. Despite the fact that a shorter operation and good haemodynamic outcome with low gradients and regression of left ventricular hypertrophy were achieved in most patients, I have great concerns with how valve complications were reported in this study. In my opinion, the current guidelines have not been followed. The reason for following these guidelines is that it allows comparison with the more traditional technique and older case series, especially when a study like this is designed without a control group. It is extremely important that great innovations are being developed and investigated in Europe; however, I would have much preferred one good study, prospectively randomized preferably, instead of three poor ones piled together by these investigators. If that would have been the case, we would by now have had some answers whether or not this new technique is better than the traditional one. Now we just know that it's feasible and possibly worse than the traditional technique.

My questions are the following: Why did you not report data according to the current guidelines? For instance, both structural valve deterioration and non-structural deterioration includes deterioration of the operated valve and abnormalities not intrinsic to the valve itself, respectively, and should be based on reoperation and autopsy or clinical examination, which is echo. Please outline your thoughts on this.

Secondly, although 731 patients were included, cumulative patient-years were only 729, despite the fact that some reached 5 years of follow-up. Is this correct? If so, why was the follow-up not extended a little bit further, maybe into 2013?

Finally, in general, SVD and non-SVD are close to zero at 5-year follow-up with most valves recognised today. However, in your series, the non-structural dysfunction was close to 6%, 3% being reoperated and another 3% with major paravalvular leaks. So if you would consider this an excellent clinical and haemodynamic outcome, as you mentioned in your manuscript, I would like to have your opinion on that too.

Dr Shrestha: For the first question, these are the results of three pooled studies, and the first study, because of the time frame from 2007 to 2003, there were also gaps between the three studies, so that means that you cannot have a longer median follow-up because we have about one-year gap in between the three studies. So cumulatively, that brings down the follow-up. That's one of the answers.

The second is that this is a multicentre study. We tried to follow all the guidelines, but still, if somebody dies, we couldn't get an autopsy on all the patients, we informed everyone before. When they signed, I included that we would like to have them, but still, sometimes it doesn't happen. If you are not even informed about the autopsies, then you cannot really change anything. Some of these ladies and gentlemen, were living alone at home, and so if somebody dies, then maybe it was not followed.

The third is because this is the first real big study with the sutureless valves. The first pilot trial was only about the feasibility of the trial. That was the main goal of that. So that's the reason. Initially, at least the first one was only for 5 years, but, of course, now, even outside the trial we are following these patients also.

Dr F. Casselman *(Aalst, Belgium):* What are your insights in the positioning of this valve in the market versus TAVI versus surgical valves? If we could replace all surgical valves by a sutureless technology, then I would understand. I mean you have a 92-year-old lady. In our institution, it's hard to sell that to the cardiologists to put in a sutureless valve, as they are going to come with TAVI as a suggestion.

Dr Shrestha: She is 93 now. She was operated 7 years ago. For us, actually, this is a surgical valve, but still, having said that, because it is quicker than a nonsurgical valve, we look for patients, at least now, beyond the study, who are operable, but if we think somebody has a life expectancy of, let's say, more than 2, 3 years, clinically looking at them, then we would go for this valve. Initially, when she came for the first time, she was an 86-year-old lady, but she was living at home, and even after 7 years, she is still living at home. So for me personally, TAVI is for someone who is not operable within the classical sense.