VIA MEDICA

ORIGINAL ARTICLE

Cardiology Journal
2019, Vol. 26, No. 1, 56–65
DOI: 10.5603/CJ.a2018.0098

ISSN 1897–5593

Sutureless aortic valve replacement in high risk patients neutralizes expected worse hospital outcome: A clinical and economic analysis

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Abstract

Background: *Aortic valve replacement (AVR) by sutureless prostheses is changing surgeon options, although which patients benefit most, as well as their possible economic impact is still to be defined.*

Methods: *Perceval-S prosthesis (LivaNova) is reserved, at the documented Institution, for patients at perceived high surgical risk. This retrospective analysis of outcome and resource consumption compared Perceval with other tissue valves. To clarify the comparison, only patients respecting 'instructions-for-use' of Perceval were reviewed. Inclusion criteria: > 65 years, +/– coronary artery bypass grafting, patent foramen ovale closure or myectomy. Exclusion criteria: bicuspid, combined valve or aortic surgery. Costs were calculated per patient on a daily basis including preoperative tests, operating costs (hourly basis), disposables, drugs, blood components and personnel.*

Results: *The sutureless group (SU-AVR) had a higher risk profile than the sutured group (ST-AVR). Cardiopulmonary bypass (CPB) and cross-clamp times were significantly shorter in SU-AVR (isolated AVR: cross-clamp 52.9 ± 12.6 vs. 69 ± 15.3 min, $p < 0.001$; CPB 79.4 ± 20.3 vs. 92.7 ± 18.2 min, $p < 0.001$). Hospital mortality was 0.9% in SU-AVR and nil in ST-AVR, $p = 0.489$; intubation 7 (IQR 5–10.7) and 7 h (IQR 5–9), $p = 0.785$; intensive care unit 1 (IQR 1–1) and 1 day (IQR 1–1), $p = 0.258$; ward stay 5.5 (IQR 4–7) and 5 days (IQR 4–6), $p = 0.002$; pacemaker 5.7% (6/106) and 0.9% (1/109), $p = 0.063$, respectively. Hospital costs (excluding the prosthesis) were $12,825 (IQR 11,733–15,334) for SU-AVR and $12,386 (IQR 11,217–14,230) in ST-AVR, $p = 0.055$.*

Conclusions: *Despite higher operative risks in SU-AVR, hospital mortality, morbidity and resource consumption did not differ. Operative times were shorter with the sutureless device and this improvement, along with more frequent ministernotomy, may have improved many postoperative aims.* (Cardiol J 2019; 26, 1: 56–65)

Key words: sutureless, perceval, aortic valve

Introduction

Despite disparities, life expectancy has improved globally and in some Western and Asian countries, is well beyond 80 years [1]. Consequently, the number of patients with degenerative calcific aortic valve disease is rapidly increasing [2]. As a result, both clinical and economic aspects of their treatment are attracting interest [3].

Despite recent innovations in transcatheter valve technology, surgical aortic valve replacement (AVR) remains a proven therapy. AVR is usually

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Received: 1.02.2018 Accepted: 2.08.2018

Presented at AATS Centennial Congress; April 29-May 03, 2017; Boston, MA, USA.

performed by means of sutured mechanical or tissue valves, but sutureless and rapid-deployment prostheses are changing surgeon options. Their usefulness in various settings has been reported, although data from randomized studies are still scarce [4]. Consequently, which patients benefit most is still unknown, as is the economic impact of sutureless technology. The ACEVAC study (Analisi Clinico Economica Valvole Aortiche Chirurgiche, Clinical and Economic Analysis of Aortic Valve Replacement) has been initiated to investigate these issues.

Perceval-S prosthesis (SorinGroup, Saluggia, Italy; now LivaNova, London, UK) obtained CE marking in 2011 and was chosen by the present study's hospital as the leading sutureless/rapid deployment device. Due to the higher cost of this prosthesis compared to conventionally sutured valves, policy herein assigned sutureless prostheses to high surgical risk patients. Given that more compromised patients require more hospital resources and that cross-clamp time is correlated with negative outcome, a tool that reduces valve implantation time could smoothen the postoperative course with consequent clinical and economic benefits [5, 6]. Thus, this more expensive prosthesis was allocated to more fragile and co-morbid patients. The ACEVAC study was undertaken to verify whether this policy was safe and effective from a clinical and economic point of view. In other words, the aim of this investigation was to compare clinical performance and hospital resource consumption between patients that were allocated to Perceval or to a standard sutured tissue valve according to their clinical risk profile.

Methods

The ACEVAC study was performed in a tertiary care teaching hospital situated in northern Italy. This institution is a private non-profit hospital providing acute care on behalf of the regional health system. Patients accede through the universal national insurance. Although implanting sutureless prostheses since 2011, a renewed internal administrative system for financial control has been available since 2013, and were thus retrospectively collected clinical data and resource consumption of AVR only from that year. This single-center spontaneous investigation was approved by the local ethics committee (ID: NP2116/2015). A specific informed consent was waived due to the retrospective nature of the study.

Considering that implantation of the Perceval valve requires mandatory anatomical characteristics of the aortic root to permit auto-anchorage of the prosthesis (mainly a sinotubular-junction to aortic-annulus-diameter ratio < 1.3), only patients indicated under the conditions required by the instruction for use (IFU) of Perceval were deliberately included. This choice was made to optimize comparison between this group (SU-AVR) and the standard sutured prostheses (ST-AVR) group, in other words, all patients were anatomically eligible for Perceval. Thus, inclusion criteria were as follows: AVR by means of a tissue valve between 1/2013 and 6/2015, age ≥ 65 years, and replacement of a diseased native or a malfunctioning prosthetic aortic valve. Exclusion criteria were as follows: mitral or tricuspid associated repair/replacement (previous or actual), associated ascending aorta replacement, acute aortic dissection, acute infective endocarditis, bicuspid aortic valve (any type of Sievers' classification), hypersensitivity to nickel alloys, and anatomical characteristics outside IFU specifications. Patients who underwent other associated procedures not listed as contra-indications (e.g., coronary artery bypass grafting [CABG], septal myectomy, foramen ovalis closure) were also enrolled. Finally, patients who received other procedures without interference from a hypothetical Perceval implantation (e.g., atrial fibrillation ablation, carotid endoarterectomy) but increasing costs and operation times, were not enrolled.

The decision to implant a sutureless or sutured valve was taken the day before the operation during the final clinical status meeting for each patient. Perceval was reserved for cases judged at being at higher operative risk. Conventional scoring systems were calculated before the operation for informed consent and database filling, but a fixed threshold for assignment to specific treatment was not adopted (i.e., the prosthesis type was not allocated according to any specific EuroSCORE or Society of Thoracic Surgeons [STS] score class). Computed tomography was not routinely performed, so deviation from a strategy was possible only in cases of adverse intraoperative findings or in cases of specific prosthesis size being unavailable.

Operations were performed under general anesthesia. Cardiopulmonary bypass (CPB) was conducted under mild hypothermia (34°C core temperature) and retrograde cold blood cardioplegia was usually administered. For minimally invasive approaches (ministernotomy [MIS]), a reversed-T partial sternotomy was performed. In these cases, central cannulation (distal ascending aorta and right atrium, through the superior vena cava) with anterograde cardioplegia was the preferred strategy.

Usually, available prostheses included Mitroflow, Crown PRT and Perceval-S (Sorin Group), C-E Perimount Magna (Edwards Lifesciencies) and Trifecta (St. Jude). Stented valves were implanted in a supra-annular position using "U" non-everting 2-0 braided sutures with pledgets (except in the commissural position — without pledgets). Respiratory weaning was performed in intensive care unit (ICU) after circulatory stabilization, blood loss control, complete rewarming and awakening. Transferal to a surgical ward was considered feasible usually in the morning after extubation whenever inotropes or renal replacement therapy were absent. Discharge was performed at cardiac rehabilitation services outside the study hospital. Clinical data was collected from prospective registries already active during the study period and by reviewing papers or electronic documents of hospitalization.

Cost data were retrospectively retrieved for each patient in the index hospitalization, defined as the acute hospitalization during which AVR was performed. Examinations, blood samples, radiologic investigations, specialist consultations, and transfusions were calculated for each patient. The skin-to-skin time (plus a constant) was retrieved and multiplied for the hourly cost of two surgeons, one anesthetist and operating room personnel. The cost of procedural packs (sternotomy, AVR, CABG, and others) containing sutures, blades, gauzes, drains, epicardial wires, and other tools were accounted for. The expense for the perfusionist and the material for CPB was calculated as a fixed cost per operation, derived from a contract between the present hospital and an outsourced perfusion service. In cases of complications (pacemaker, hemodialysis, intra-aortic balloon, reoperation, etc.), these costs was added equally. Finally, a daily mean charge for ward stay and ICU (including meals, laundry, sterilization, general logistic, drugs, labor cost and general cost of the facility) was available for each fiscal year and calculated according to the length of stay. The cost of the prosthesis was not included in order to give a neutral evaluation of resource consumption.

All costs were collected in euro, and are herein reported in dollars (€/$ = 1.0672). Considering that inflation rate during the study period was very low (0% to 0.6%), no correction was made for uniform purchasing power [7].

Statistical analysis

Continuous variables are summarized as mean ± standard deviation when normally distributed, or otherwise as median and interquartile range (IQR). Consequently, comparisons were made using the unpaired t test or Mann-Whitney non-parametric test. Categorical variables are summarized by frequencies and percentages; comparisons were made using the χ^2 test or the Fisher exact test when the frequency was less than five. Two-sided p values of less than 0.05 were considered to be statistically significant. All calculations were performed using MedCalc statistical software (v. 16.8; MedCalc Software bvba, Ostend, Belgium).

Results

After considering inclusion/exclusion criteria, 231 consecutive patients were available for analysis. There were 113 patients, who had a sutureless prosthesis as aortic valve substitute (SU-AVR), while 118 patients had aortic valve replacement by means of a standard sutured valve (ST-AVR).

Patient characteristics

Compared with patients undergoing ST-AVR, SU-AVR patients were older and more likely to be female, overweight, diabetic, anemic and frail (Table 1). In addition, they were more likely to have symptomatic heart failure, systemic and pulmonary hypertension, higher trans-valvular gradients and smaller aortic annuli. Operative risk scores differed significantly: median EuroSCORE II and STS score were respectively 3.9% and 3.6% for SU-AVR group and 2.3% and 2.0% for ST-AVR group (IQR and other score systems are reported in Table 1).

Intraoperative results

SU-AVR comprised only Perceval prostheses, while ST-AVR accounted for 42 C-E Perimount Magna, 23 Trifecta, 9 Crown PRT and 44 Mitroflow valves. More than a quarter of the SU-AVR group (27.4%) received an MIS, while only a minority of ST-AVR (5.9%) had an MIS ($p < 0.001$). Mean CPB time, mean cross-clamp time, median skin-to-skin time for isolated AVR (possible myectomy included) and AVR+CABG are reported in Table 2. Shorter times related to the central part of the operation were recorded for SU-AVR cases, but overall operation length did not differ. This was the case both in isolated or non-isolated AVR. Concomitant procedures were performed in 35.9% with a similar incidence for the groups. In CABG cases, a median of one coronary anastomosis was made in both groups. The results of the MIS cohorts are reported in Table 3.

Table 1. Patient demographics.

	SU-AVR (n = 113) Perceval	ST-AVR (n = 118) Sutured	P
Age [years]	80.1 ± 5.5	75.5 ± 5.6	< 0.001
Female	65.5% (74)	32.2% (38)	< 0.001
NYHA IV	8.8% (10)	2.5% (3)	0.038
Hypertension	95.6% (108)	83% (98)	0.002
BMI [kg/m^2]	27.4 ± 5.1	26.7 ± 3.8	0.298
BSA [m^2]	1.78 (IQR 1.63–1.92)	1.85 (IQR 1.74–7.97)	0.003
Diabetes	31% (35)	18.2% (22)	0.033
Creatinine [mg/mL]	0.98 (IQR 0.8–1.19)	0.94 (IQR 0.8–1.14)	0.508
Hemoglobin [g/dL]	12 ± 1.5	12.5 ± 1.5	0.01
Platelets [*10^3/μL]	179 (IQR 153–218.2)	169.5 (IQR 138–206)	0.046
Redo	8.8% (10)	3.3% (4)	0.131
Ejection fraction [%]	60 (IQR 51–65.3)	59 (IQR 53–64)	0.661
Peak aortic gradient [mmHg]	78.7 (IQR 64.5–91.8)	69.1 (IQR 44–81.2)	< 0.001
Aortic valve area [cm^2]	0.7 (IQR 0.6–0.8)	0.8 (IQR 0.64–0.9)	0.019
LV outflow tract [mm]	20 (IQR 19–20)	21 (IQR 20–22)	< 0.001
Mitral regurgitation (> 2)	5.3% (6)	0.8% (1)	0.059
SPAP [mmHg]	30 (IQR 29.5–40)	25 (IQR 25–39)	0.007
EuroSCORE II [%]	3.9 (IQR 2.2–7.1)	2.3 (IQR 1.4–3.6)	< 0.001
STS score [%]	3.55 (IQR 2.02–5.75)	2.21 (1.59–3.21)	< 0.001
EuroSCORE I standard [%]	9 (IQR 7.7–10)	7 (IQR 5–8)	< 0.001
EuroSCORE I logistic [%]	10.2 (IQR 7.5–16.5)	7 (IQR 4–10)	< 0.001
Frailty index (0 min, 6 max)	1 (IQR 1–3)	0 (IQR 0–0)	< 0.001

BSA — body surface area; BMI — body mass index; IQR — interquartile range; LV — left ventricular; NYHA — New York Heart Association; SPAP — systolic pulmonary artery pressure; STS — Society of Thoracic Surgeons

Table 2. Intraoperative results.

	SU-AVR (n = 113) Perceval	ST-AVR (n = 118) Sutured	P
Ministernotomy	27.4% (31)	5.9% (7)	< 0.001
Isolated AVR, CPB time [min]	79.4 ± 20.3	92.7 ± 18. 2	< 0.001
Isolated AVR, cross-clamp [min]	52.9 ± 12.6	69 ± 15.3	< 0.001
Isolated AVR, skin-to-skin [min]	206 (IQR 180–243.3)	215 (IQR 182.8–248.7)	0.537
Concomitant procedures	35.4% (40)	36.4% (43)	0.361
Number of grafts in case of CABG	1 (IQR 1–2)	1.5 (IQR 1–2)	0.208
CABG + AVR, CPB time [min]	110.7 ± 38.6	133.8 ± 31.2	0.006
CABG + AVR, cross-clamp [min]	73.8 ± 23.8	95.8 ± 16.9	< 0.001
CABG + AVR, skin-to-skin [min]	268 (IQR 245.7–321.2)	285 (250–333)	0.301

AVR — aortic valve replacement; CABG — coronary artery bypass grafting; CPB — cardiopulmonary bypass; IQR — interquartile range

Hospital outcome

In-hospital mortality was 0.9% for SU-AVR and nil for ST-AVR (p = 0.489), and in all cases were lower than expected using preoperative scoring systems. Other clinical results are reported in Table 4. Most of the analyzed indicators did not differ between the two groups. The performance of SU-AVR group was similar to ST-AVR in ICU

Table 3. Results in minimally invasive surgery patients.

	SU-AVR (n = 31) Perceval	ST-AVR (n = 7) Sutured	P
CPB time [min]	83.6 ± 16.1	109.4 ± 18.0	< 0.001
Cross-clamp [min]	56.3 ± 11.6	85.7 ± 17.1	< 0.001
Skin-to-skin [min]	220 (IQR 186.2–247.7)	235 (IQR 211.2–254.2)	0.300
Hospital mortality	0% (0)	0% (0)	
Intubation time [h]	6 (IQR 5.0–7.7)	8 (IQR 6.2–11.0)	0.099
ICU stay [day]	1 (IQR 1–1)	1 (IQR 1.0–1.7)	0.492
Serious bleeding	0% (0)	0% (0)	
Postoperative myocardial infarctus	0% (0)	0% (0)	
Postoperative neurological deficit	3.2% (1)	0% (0)	1
Postoperative ultrafiltration	0% (0)	0% (0)	
Transfusion	74.2% (23)	57.1% (4)	0.375
Creatinine peak [mg/dL]	1.05 (IQR 0.89–1.31)	1.07 (IQR 1.01–1.30)	0.585
New atrial fibrillation	62.1% (18/29)	50.0% (2/4)	0.638
Platelets, minimum [$\times 10^3/\mu$L]	87 (IQR 77.2–111.0)	70 (IQR 62.2–99.0)	0.275
New permanent pacemaker	10.0% (3/30)	14.3% (1/7)	1
Ejection fraction discharge [%]	60 (IQR 57.2–64.7)	60 (IQR 52–60)	0.261
Paravalvular leak, grade > 0	6.5% (2)	0% (0)	1
Mitral regurgitation grade > 1	3.2% (1)	14.3% (1)	
Pulmonary hypertension	9.7% (3)	0% (0)	1
Hemoglobin at discharge [g/dL]	10.7 ± 1.1	9.2 ± 0.9	0.001
Postoperative ward stay [day]	6 (IQR 4.2–7.0)	3 (IQR 3.0–7.7)	0.092
Hospital cost ($)	12,768 (IQR 11,530–14,807)	13,543 (IQR 11,036–15,612)	0.836

CPB — cardiopulmonary bypass; ICU — intensive care unit; IQR — interquartile range

transit (median stay 1 day, IQR 1–1), while SU-AVR patients had longer stays in surgical wards after the operation. The postoperative peak of creatinine did not differ and permanent dialysis was not required, although the nadir of platelets was lower for SU--AVR. Although no patients required platelet infusion, except one in SU-AVR (0.9%, p = 0.978), the number of thrombocytes was similar at discharge: 154 ± 73 × $10^3/\mu$L in SU-AVR and 164 ± 65 × 10^3/ /μL in ST-AVR (p = 0.27). Postoperative adverse events occurred in similar frequencies. From an echocardiographic perspective, performances of SU-AVR and ST-AVR at discharge were similar: left ventricular ejection fraction, pulmonary pressures, paravalvular leaks, medium gradients did not differ except for small prostheses, where SU-AVR size S had higher gradients than ST-AVR size 19 and 21.

Hospital costs

Economic endpoints at index hospitalization are shown in Table 5 and did not differ except for costs related to ward stay, reflecting the longer permanence of SU-AVR group in wards waiting for the start of the rehabilitation program: $3,679 (IQR 2,861–4,496) for SU-AVR and $3,064 (IQR 2,861––4,496) for ST-AVR (p = 0.039). Furthermore, radiologic examination and blood product costs were dissimilar, although the absolute differences ($55 between the medians of radiologic charges and $102 between the medians of blood products consumption costs) were low compared to overall hospital costs. Finally, reflecting the fact that other stronger determinants of expenditure were similar, the overall hospital cost of hospitalization between SU-AVR and ST-AVR did not differ, $12,825 (IQR 11,733–15,334) and 12,386 (IQR 11,217–14,230), respectively (p = 0.055).

Discussion

In the current health care environment, it is imperative that any new technology, particularly those that add initial higher costs, undergo rigorous economic evaluation. This is especially true for a condition such as degenerative aortic stenosis that is expected to grow, given worldwide

Table 4. Clinical results.

	SU-AVR (n = 113) Perceval	ST-AVR (n = 118) Sutured	P
Hospital mortality	0.9% (1)	0% (0)	0.489
Intubation time [h]	7 (IQR 5–10.7)	7 (IQR 5–9)	0.785
ICU stay [day]	1 (IQR 1–1)	1 (IQR 1–1)	0.258
Serious bleeding	1.8% (2)	1.7% (2)	1
Postoperative myocardial infarctus	0.9% (1)	0% (0)	0.491
Postoperative neurological deficit	2.7% (3)	0.8% (1)	0.361
Postoperative ultrafiltration	4.4% (5)	2.5% (3)	0.492
Creatinine peak [mg/dL]	1.12 (IQR 0.9–1.47)	1.06 (IQR 0.86–1.39)	0.529
New atrial fibrillation	53.7% (58/108)	42.9% (39/91)	0.131
Platelets, minimum [$\times 10^3/\mu$L]	82 (IQR 64–105)	91 (IQR 70–117)	0.037
New permanent pacemaker	5.7% (6/106)	0.9% (1/109)	0.063
Ejection fraction discharge [%]	60 (IQR 53–62)	60 (IQR 55–60)	0.849
Medium aortic gradient [mmHg]:			
Small prostheses	18 (IQR 14.9–23.3)	9.5 (IQR 6.7–14.5)	0.004
Medium prostheses	14.2 (IQR 10–15.4)	10 (IQR 8.8–12.8)	0.111
Large prostheses	11 (IQR 9.3–12.9)	9.3 (IQR 6.7–13.4)	0.165
Paravalvular leak, grade > 0	3.5% (4)	2.5% (3)	0.717
Mitral regurgitation grade > 1	4.4% (5)	4.2% (5)	1
Pulmonary hypertension	6.2% (7)	1.7% (2)	0.055
Hemoglobin at discharge [g/dL]	10.3 ± 1.1	9.9 ± 1.2	0.013
Postoperative ward stay [day]	5.5 (IQR 4–7)	5 (IQR 4–6)	0.002

ICU — intensive care unit; IQR — interquartile range

Table 5. Hospital costs.

	SU-AVR (n = 113) Perceval	ST-AVR (n = 118) Sutured	P
Operating room ($)	5670 (IQR 5,288–6,160)	5,712 (IQR 5,340–6,271)	0.259
Laboratory ($)	284 (IQR 229–376)	274 (IQR 226–362)	0.541
ICU stay ($)	1,967 (IQR 1,967–1,967)	1,967 (IQR 1,967–1,967)	0.308
Radiology ($)	148 (IQR 93–203)	93 (IQR 93–161)	0.004
Other exams ($)	232 (IQR 179–297)	229 (IQR 179–330)	0.468
Pre-/Postopoperative ward stay ($)	3,679 (IQR 2,861–4,496)	3,064 (IQR 2,861–4,496)	0.039
Blood products ($)	457 (IQR 307–494)	355 (IQR 299–355)	< 0.001
Materials ($)	1,482 (IQR 1,482–1,632)	1,482 (IQR 1,482–1,632)	0.614
Overall ($)	12,825 (IQR 11,733–15,334)	12,386 (IQR 11,217–14,230)	0.055

ICU — intensive care unit; IQR — interquartile range

ageing. Guidelines recommend AVR in severe, symptomatic (and under certain conditions, also asymptomatic) aortic stenosis, with surgical AVR being the standard approach for patients with a low-to-intermediate operative risk. In high risk or inoperable patients, the results of the transcatheter technology revolution are now available, and the cost/effectiveness ratio of transcatheter aortic valve replacement (TAVR) is still under review. Furthermore, the surgical range of aortic valve substitutes has been recently renovated by sutureless/rapid devices, which could accelerate AVR and facilitate MIS. Research is growing but data from large randomized studies comparing conventional

sutured and expensive sutureless devices are still lacking [3, 4]. Consequently, which patients benefit most, as well as the economic impact of this new technology are still to be defined. However, since the Perceval valve has been available, the present hospital has assigned this costly new substitute to patients considered at high surgical risk. This is because more compromised patients require more hospital resources and cross-clamp time is correlated with negative outcome, and so any tool that reduces valve implantation time could improve the postoperative course with clinical and economic benefits from the hospital's perspective.

Before the beginning of this study, only one study was available on this topic: it was retrospective and it included two small propensity matched cohorts of patients, operated with either a Perceval or a stented prosthesis [8]. The sutureless group had a better hospital outcome and was a cost-saving strategy, although Pollari et al. [8] can be criticized mainly given their propensity scoring. Indeed, the intention to define the probability of receiving the Perceval valve was achieved by using a multivariate regression analysis, with only variables related to clinical status but no specific variables allowing for the Perceval implantation (i.e., sinotubular-junction to aortic-annulus-diameter ratio < 1.3, tricuspid aortic valve and other IFU prescriptions). Therefore, while undertaking the ACEVAC study to audit the present policy, only patients in the ST-AVR group that could have received a Perceval in accordance with the IFU were included. Thus, the present cohorts had a similar "technical" propensity to receive sutureless, but different clinical profiles, i.e., high probability of complications and increased resource consumption for SU-AVR and low risk for ST-AVR group.

The present study showed that despite an increased risk in the sutureless group (e.g., age +4.6 years; diabetes 1.8×; contemporaneous risk scores for operative mortality 1.7×), hospital mortality did not differ. Operative times were lower in SU-AVR, with or without CABG and the incidence of MIS was also higher. These two factors may have favorably impacted many of the postoperative end-points.

The role of the length of CPB and cross-clamping in determining postoperative morbidity is supported in the literature, but is also self-evident [5]. It goes without saying that a long non-physiologic state, such as extracorporeal circulation, produces more unwanted consequences than a short CPB. Consequently, Perceval, at the same technical safety and efficacy, is expected to give a smoother postoperative course. Therefore, despite a worst clinical profile of SU-AVR, this cohort had the same outcome as the other one that had better preoperative parameters, i.e. ST-AVR. This was true for mortality, many postoperative events and resource consumption. Hypothetically, if these favorable results were due to the short cross-clamp time, other devices such as automatic knot fasteners, could have produced the same outcome. Until today, a direct comparison between sutureless valves and sutured prosthesis plus knot fastener has not been available, although it seems clear that sutureless devices can be very convenient in sever calcified aortic roots.

It can be argued that operative times were relevant enough to achieve these results as, although CPB time was lower, the skin-to-skin time did not differ. The opinion herein suggests, an alternative interpretation can be found by observing the incidence of MIS. SU-AVR received ministernotomy in more than a quarter (27.4%) of cases, while only a few patients (5.9%) of the ST-AVR had MIS.

Apart from aesthetic benefits, numerous advantages have been advocated for a minimally invasive approach, such as reduced release of inflammatory mediators and circulating micro particles, limited blood loss and early mobilization [9–11]. In the author's experience and as reported by others, rapid deployment devices facilitated adoption of MIS because they provide surgeons with a faster, easier and more reproducible way to perform AVR through minimal incision, while still allowing controlled implantation of the prosthesis under direct visualization [12]. Thus, if favorable results of SU-AVR are from a shorter cardioplegic arrest/extracorporeal circulation time or by a minimally invasive procedure, equally they can be attributed to the use of a sutureless device.

In must be noted however that the present findings were not univocal and favorable for sutureless valves. Some authors have already reported that use of a Perceval prosthesis is an independent predictor of thrombocytopenia, although without any clinical implications for patients [13, 14]. Also recorded was a more marked post-operative drop in the number of platelets for the group receiving a Perceval valve: SU-AVR touched a lower minimum than ST-AVR ($p = 0.037$) despite a higher baseline value ($p = 0.046$). The average fall of platelets is estimated to be 52%, and 44.5% of preoperative value for SU-AVR and ST-AVR, respectively ($p < 0.001$). However, in accordance with other reports that compared Perceval with stented valves, the need for transfusion of platelets did not differ [13–15]. Indeed, Stanger et al. [16] reported

that Perceval was associated with a lower need for platelets despite being a significant predictor for post-operative thrombocytopenia.

The post-operative length of stay in surgery wards was another study end-point that was not affected by the present policy. As a matter of fact, SU-AVR and ST-AVR had similar stays in ICU (median 1 night, $p = 0.258$), whereas the first group had longer hospital stays than the second due to longer permanence in surgical wards ($p = 0.002$). Tentative explications can be made when considering a worse clinical profile (SU-AVR were older and co-morbid), but the incidence of post-operative complications was similar overall. It can therefore be hypothesized that longer permanence was the time required for SU-AVR patients to achieve an adequate number of platelets before safe discharge. Indeed, they had a deeper thrombocytopenia but a similar number of platelets at the end of hospitalization. However, results for both groups compared well with similar investigations in terms of clinical end-points (intubation time, pacemakers, and others), also in terms of end-points with a greater impact on resource consumption [4]. In particular, ICU and ward stay were at least half those reported by Pollari et al. [8], by Minami et al. [15], by Laborde et al. [17], and similar to the TAVR arm of the McCarthy et al. study [18].

From an economic point of view, the overall hospital cost of the index hospitalization for AVR did not significantly differ. At first glance, this seems a neutral result, but considering that higher resource consumption for SU-AVR was expected due to a worse preoperative clinical profile, it can be interpreted as validation of the present internal policy to conserve the sutureless prostheses, for patients who would most benefit. In other words, if we had compared two groups with a hypothetical similar profile, the SU-AVR would have been cost-saving.

Analyzing each individual item of expenditure however, the SU-AVR postoperative ward stay was more expensive than the ST-AVR stay as forecasted by the higher number of days required before starting the rehabilitation program. When operating room costs were also analyzed, the findings agree with Pollari et al. [8], who found were no gross differences between SU-AVR and ST-AVR. On the contrary, the present results did not concur concerning the cost of overall ward stay, which was more expensive for SU-AVR in the present investigation [8]. However, analysis of this aspect is complicated due to the lack of statistical comparisons of economic data between their SU--AVR and ST-AVR groups [8]. Moreover, analysis is also complicated by different administrative cost reporting systems. In Laborde et al. [17], the statistical scrutiny showed that cost savings with the sutureless strategy was not significant for all patients considered. Their findings do agree with those presented here in that a benefit from sutureless valves is apparent for high risk patients [17].

The Minami et al. [15] report is also interesting because it had a similar design to the present investigation. They had a sutureless group with higher EuoSCORE than the stented group, but the cost of the latter was significantly lower, while herein had only a "no difference" result in statistical terms [15]. However, all these investigations were prevalently conducted during the pre-market period of Perceval and the performance of the sutureless device may have been involuntarily emphasized due to attention given to this new type of operation. The cost of prosthesis was not included by anyone and it could have changed the final cost comparison. However, to avoid conclusions relating to an item subject to rapid change over time (and across hospitals and countries), together with the three investigators cited, the present study opted *a priori* not to include it in the analysis.

Finally, in the present study a lower net cost of AVR was found for both groups, SU-AVR and ST-AVR, this compared with other papers that reported economics of conventional AVR, of minimally invasive AVR and of TAVR [6, 8, 15, 17, 19, 20].

Limitations of the study

It is acknowledged that there were several limitations related to the study design and setting. Firstly, it was a non-randomized, single-center retrospective comparison between two cohorts of patients to which prostheses with different implantation techniques were assigned. However, the propensity to receive the sutureless device, i.e., the device with the more restrictive indications, was maximized by enrolling, only patients with anatomical requirements specified in the Perceval IFU, in the concurrent group (ST-AVR). Secondly, the study population was composed of patients evaluated collegially and deemed suitable for surgery (the other patients with aortic stenosis were addressed by TAVR) [21]. For this reason the median operative risk profile, both EuroSCORE II and STS score, was below the threshold suggested by current guidelines (4%) for the definition of "increased surgical risk". However, the definition of "high risk patients" was maintained for SU-AVR group because it was relative to the surgical setting and because this judgment was given after a global

clinical evaluation which also considered factors not captured by the scoring system. Thirdly, all results must be judged bearing in mind the risk of an underpowered sample size and potential of a type II statistical error.

Other limitations pertain to cost analysis. The consumption of material was tracked on an individual basis whenever possible but certain devices were included in the procedural packs and were thus accounted for in this way. Although findings were compared with other studies, mostly from European countries, their health care systems are different in clinical organization and reimbursement models and this may have distorted comparisons. Moreover, a standardized method to analyze resource consumption in aortic valve interventions is not currently available. On the contrary, three similar investigations agreed to exclude the prosthesis cost, considering it a floating and co-founding variable [8, 15, 17]. Finally, the payer was regarded as being the only hospital providing index hospitalization for AVR, without accounting for possible costs of other previous or subsequent hospitalizations/procedures.

Conclusions

Sutureless valves allowed a cohort of patients, considered at relatively high risk, to achieve lower operative times and higher incidence of MIS. These two factors may have favorably impacted many of the post-operative end-points, with a few exceptions (thrombocytopenia and postoperative ward stay). Taking into account the limitations related to the study design, it was found that notwithstanding a worse risk profile of SU-AVR, adverse events and ICU stay did not differ between the two groups. Moreover, overall hospital resource consumption did not differ despite a worse economic impact expected for SU-AVR patients. It can therefore reasonably concluded, that the policy of reserving an expensive device for still operable but more critically ill patients it is probably both valid and worth utilizing. Finally, this investigation is from real-world data which provides additional clinical and economic evidence to support the value-based use of sutureless technology for AVR.

Acknowledgements

The work of colleagues, nurses and technicians of the Cardiovascular and Anesthesia Departments and of the Administration of Poliambulanza Foundation Hospital is much appreciated. We would also like to thank Prof. Robert Coates from Bocconi University, Milan.

Funding: This study was partially supported by an unrestricted grant from LivaNova.

Conflict of interest: Dr. Marco Cirillo and Dr. Giovanni Troise are clinical proctors for LivaNova.

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