Better Short-Term Outcome by Using Sutureless Valves: A Propensity-Matched Score Analysis

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Background. Sutureless aortic valve prostheses have the potential of shortening ischemic time. However, whether shorter operative times may also result in improved patient outcomes and have an effect on hospital costs remains to be established.

Methods. From March 2010 to April 2013, 566 patients underwent aortic valve replacement with bioprostheses; of these, 166 received a sutureless valve, and 400 received a stented valve. Redo and associated procedures were included. A propensity-score analysis was used to create two groups (sutureless and stented) with 82 matched pairs with comparable preoperative characteristics. Hospital outcome, follow-up, and health care resource consumption were compared.

Results. There were 3 hospital deaths in the stented group and 2 in the sutureless group (p = 0.69). Aortic cross-clamp, cardiopulmonary bypass, and operation times were significantly shorter in the sutureless group (p < 0.001). Patients in the sutureless group required blood transfusion less frequently (1.2 ± 1.3 vs 2.5 ± 3.7 units, p = 0.005), with a similar need for reexploration for bleeding (2 vs 5, p = 0.221). The sutureless group had a shorter intensive care unit stay (2.0 ± 1.2 vs 2.8 ± 1.3 days, p < 0.001), hospital stay (10.9 ± 2.7 vs 12.4 ± 4.4 days, p = 0.001) and intubation time (9.5 ± 4.6 vs 16.6 ± 6.4 hours, p < 0.001), and a lower incidence of postoperative atrial fibrillation (p = 0.015), pleura effusions (p = 0.024), and respiratory insufficiency (p = 0.016). Pacemaker implantation and occurrence of neurologic events were similar between groups (p > 0.05). A lower rate of postoperative complications resulted in reduced resource consumption in the sutureless group for diagnostics (<2,153 vs €1,387), operating room (<3,879 vs €3,527), and hospital stay (<9,873 vs €6,584), with a total cost saving of approximately 25% (€17,905 vs €13,498).

Conclusions. A shorter procedural time in the sutureless group is associated with better clinical outcomes and reduced hospital costs.


Aortic valve replacement (AVR) with biological or mechanical prostheses using the median sternotomy as conventional access is still the gold standard for treatment of severe aortic stenosis [1]. Given the increasing comorbidities and age of patients, there is a tendency toward biological valve implants avoiding long-term anticoagulation. In an effort to improve the outcomes of patients with stented biological valves, stentless valves were introduced into clinical practice in the early 1990s. These valves were designed to be less obstructive, resulting in lower transvalvular gradients. However, the implantation technique of stentless valves is more complex and demanding, with prolonged cross-clamp and bypass times [2]. Despite modern techniques of cardioprotection, aortic cross-clamp time still remains an independent predictor of morbidity and death in patients undergoing cardiac operations [3].

AVR in high-risk patients carries a significant risk of morbidity and death; therefore, alternative options have been considered in this population to minimize this risk. Transcatheter aortic valve implantation (TAVI) is one such emerging alternative option [4]. Although the concept of TAVI appears attractive, the calcified aortic valve is not removed but is pressed against the aortic wall, without decalcification of the annulus. Hence, paravalvular leakage remains an important issue with this technology [5]. Access site-related problems and device malpositioning and migration are also additional important concerns.

These concerns and issues prompted the emergence of a further alternate option, the sutureless aortic valve

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prosthesis. This is a stent-mounted aortic valve prosthesis that can be placed in a sutureless fashion with a conventional surgical technique [6]. This technology includes a classic extracorporeal circulation, cross-clamping of the aorta, and an aortotomy, allowing complete removal of the diseased native valve. Sutureless implantation of heart valves has a significant advantage over the classic technique of suturing the valve in place because it shortens implantation time and therefore myocardial ischemia time.

Currently, the largest published sutureless experience available is with the Perceval device (Sorin Group, Saluggia, Italy) [6–8]. The Perceval sutureless prosthesis (Fig 1) is a bovine pericardial valve mounted on a self-expanding nitinol frame with Carbofilm (Sorin) coating. It is collapsed within a specific holder before being released in the correct intraannular position, without the need for sutures. Otherwise, potentially different device acquisition costs would have to be factored in the analysis to have a more comprehensive picture. At the moment, we have only an article describing a probabilistic patient-level simulation model on this topic [9].

This report provides a comparison between the Perceval valve and the traditional biological prostheses in an attempt to better define the role of sutureless AVR in the treatment of critical aortic valve stenosis. An evaluation of health care costs is included.

Patients and Methods

We collected data of all patients who were diagnosed with severe aortic valve stenosis eligible for surgical intervention at our center, from March 2010 to April 2013. A specific program was initiated at our institution during that time involving the sutureless Perceval prosthesis. Every week, during an interdepartmental conference, we evaluated all patients affected by severe aortic valve stenosis referred to our center from peripheral hospitals, private practices, or our emergency department, considering comorbidities and surgical risk to determine the best treatment.

The Perceval sutureless valve was implanted as part of the premarket study Perceval S Valve Clinical Trial for Extended CE Mark (Cavalier Study) and later (after European Community approval in 2011) as routine use in all patients aged older than 65 years with an indication for AVR, considered eligible for surgical repair, and with compatible echocardiographic findings (symmetric aortic annulus with a diameter between 19 and 27 mm and a sinotubular junction-to-annulus ratio of <1.3).

During the premarket study, patients signed an additional informed consent for the study use of the new type of prosthesis, which had not yet received Conformité Européene approval. All patients also signed an informed consent for the use of personal data and follow-up contact. The local Ethics Committee approved the study.

Alternatively, a stented bioprosthesis was implanted in all patients aged older than 65 years with an indication for AVR, who were considered eligible for surgical repair, if echocardiographic findings were not compatible with Perceval indications (eg, bicuspid valve) or no surgeon trained in Perceval implantation was available at the time of the procedure.

During the study period, 566 patients were operated on with or without associated coronary artery bypass grafting (CABG), distributed between the stented and sutureless groups (400 and 166 each). Propensity score matching (1:1) was performed to control selection bias as a result of nonrandom assignment to the groups, resulting in 82 matched pairs having the same propensity score. Postoperative outcomes of the sutureless and stented groups were compared, including in-hospital and valve-related complications and follow-up survival.

During follow-up, all patients were clinically assessed at our outpatient clinic and were evaluated with questionnaires for events between visits. In particular, the need for rehospitalization for cardiovascular and other causes was recorded. Moreover, for the matched-pair samples, we recorded the total hospital costs obtained blinded from our economic department.

The Perceval implantation technique was described previously [10]. All patients in both groups underwent transesophageal echocardiography during the operation, and no paravalvular leak—even if minimal—was tolerated. A minimally invasive approach (with a J-sternotomy) was used for all operations, except in patients with a previous cardiac operation (redo) or an indication with associated CABG, in whom a full sternotomy was performed. In case of associated CABG, distal coronary anastomoses preceded prosthesis implantation, and proximal surgical sutures were performed during primary cross-clamping, after tangential clamping.
of the ascending aorta, or avoided completely by using mammary arteries. General anesthesia with orotracheal intubation was used in both groups.

Statistical Analysis
The propensity score was defined as the probability of receiving the Perceval valve and was estimated using a multivariate regression analysis. The following patient characteristics and major preoperative risk factors were entered into the model: age, gender, body surface area, logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE), previous cardiac operations, previous percutaneous transluminal coronary angioplasty, hypertension, pulmonary hypertension exceeding 50 mm Hg, hyperlipidemia, left ventricular ejection fraction, renal disease (creatinine clearance <85 mL/min), previous myocardial infarction, chronic obstructive pulmonary disease, peripheral vascular disease, and New York Heart Association functional class.

Once the propensity score had been estimated for each patient, a receiver operating characteristic curve area proved the performance of the model (C statistic = 0.823). Categoric variables are summarized as frequencies (%) and continuous variables as mean ± standard deviation. Normal distribution of data was assessed with the Shapiro-Wilk test. Continuous variables were compared by two-tailed paired t test and categoric variables by the χ² test. Not normally distributed data were tested using the Mann-Whitney test. Cumulative survival curves were computed according to the Kaplan-Meier method. The log-rank test was used to compare survival and freedom from valve-related complications.

Resource Use and Costs
In-hospital preprocedural and postprocedural resource use data were retrospectively collected from electronic patient records. Associated costs were retrieved from the hospital financial department. Costs were identified according to the German diagnostic related group matrix. To avoid bias related to different valces prices across different hospitals, countries, and over time, the costs of the prostheses used in both groups were not included in the analysis. Indeed, costs of innovative technologies are subject to rapid changes over time and vary across countries. The costs analysis was performed according to 10 cost centers, comprising normal ward, intensive care unit (ICU), dialysis unit, operating room, anesthesia, cardiac diagnostic therapy, endoscopic diagnostics, radiology, laboratory, and other diagnostics, and the three main cost element groups of labor, material, and infrastructure. Costs were aggregated and reported according to three main categories:

- operating room, including anesthesia;
- hospital stay, including ICU and cardiac surgical ward; and
- diagnostic, radiology, and laboratory, including cardiac diagnostic therapy, endoscopic diagnostics, radiology, laboratory, and other diagnostics.

Results
Preoperative clinical and echocardiographic characteristics of the overall study population are reported in Table 1. The two populations showed many statistically different variables, including age, body surface area, diabetes, logistic EuroSCORE, redo, pulmonary hypertension, and associated operations, pointing to a higher risk in the Perceval population. Propensity matching resulted in 82 matched pairs available for analysis. Preoperative clinical and echocardiographic characteristics of all matched pairs are reported in Table 2. No single value was statistically significant.

In the sutureless group we observed a faster operation in operative time, cardiopulmonary bypass time, and cross-clamp time (Table 3). The in-hospital mortality rate was similar in the matched groups (Table 3), but a different outcome was recorded for hospital and ICU stay, atrial fibrillation, pleura effusion, respiratory insufficiency, and need for blood transfusion (Table 3). Follow-up (13 ± 6 months) was complete (80 patients for sutureless and 79 for stented). Overall survival was 96.8%, and freedom from valve-related death was 99.4%. No differences were observed in sutureless compared with the stented population in survival (Fig 2), whereas freedom from valve-related death was 100% vs 98.7% (p = 0.31), freedom from stroke was 98.8% vs 97.5% (p = 0.55), freedom from endocarditis was 100% vs 98.7% (p = 0.31), and freedom from reoperation was 100% vs 98.7% (p = 0.31).

Cost data were available for all patients. Total health care costs were higher for the stented group than for the sutureless group (€17,905 vs €13,498), including hospital

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sutureless</th>
<th>Stented</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>79.5 ± 5.4</td>
<td>64.4 ± 9.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender</td>
<td>75 (45.2) 160 (40)</td>
<td>0.259</td>
<td></td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.78 ± 0.3 1.9 ± 0.3</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>50 (30.1) 88 (22)</td>
<td>0.013</td>
<td></td>
</tr>
<tr>
<td>NYHA class</td>
<td>2.9 ± 0.4 3.0 ± 0.5</td>
<td>0.052</td>
<td></td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>21 (12.6) 72 (18)</td>
<td>0.537</td>
<td></td>
</tr>
<tr>
<td>Logistic EuroSCORE, %</td>
<td>14 ± 7.4 9.9 ± 7.5</td>
<td>0.021</td>
<td></td>
</tr>
<tr>
<td>Previous cardiac operation</td>
<td>21 (12.6) 24 (6)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>LVEF</td>
<td>0.572 ± 0.081 0.553 ± 0.172</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>31 (18.7) 36 (9)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Associated CABG</td>
<td>58 (34.9) 88 (22)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Surgical approach</td>
<td>79 (47.6) 112 (28)</td>
<td>0.021</td>
<td></td>
</tr>
<tr>
<td>Full sternotomy</td>
<td>84 (50.6) 288 (40)</td>
<td>0.021</td>
<td></td>
</tr>
<tr>
<td>J sternotomy</td>
<td>3 (1.8) 0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*Categorical data as number (%).

CABG = coronary artery bypass grafting; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association.
hospitalization costs and the percentage of cost-saving for the main three cost categories.

**Comment**

Sutureless aortic bioprosthetic valves have been recently introduced into clinical practice and bear the potential advantage of a short and simple implantation, thus reducing surgical time. The sutureless technique was introduced in the 1970s and showed promising midterm and long-term results [11]. However, the mechanical valve prostheses of the older ball-and-cage variety are no longer used because of their high thrombogenic risk and differed remarkably from the sutureless bioprosthetic valves used today. The possibility of decreasing ischemic time may be crucial in minimally invasive operations.

In a recent retrospective observational study of Gilmanov and colleagues [12] conducted in 137 patients undergoing Perceval aortic valve implantation through a right anterior minithoracotomy, mean aortic cross-clamp time was 59 minutes, although surgeons were highly experienced with minimally invasive procedures using the Perceval bioprosthesis. Flameng and colleagues [6] reported a mean aortic cross-clamp time of 17 minutes in patients undergoing sutureless implantation with the same prosthesis under full sternotomy. Whether this difference in aortic cross-clamp time (1 hour vs less than 20 minutes) may have a significant effect on patient outcome remains to be clearly elucidated. In a propensity-matched cohort, Gilmanov and colleagues [13] demonstrated that the minimally invasive approach allows for better results than conventional operations, despite a longer aortic cross-clamp time of 83.8 vs 71.3 minutes ($p < 0.0001$). In addition, minimally invasive AVR through a right anterior minithoracotomy was associated with better outcomes than ministernotomy, with comparable aortic cross-clamp times of 89.7 and 84.3 minutes, respectively ($p = 0.07$) [14].
Shorter aortic cross-clamp times have been shown to be relevant for patient outcome [3, 15]. In particular, in a recent retrospective analysis of approximately 1,000 patients undergoing surgical AVR, Ranucci and colleagues [16] reported that aortic cross-clamp time was an independent predictor of severe cardiovascular morbidity, with an increased risk of 1.4% per 1-minute increase. In addition, high-risk patient populations, such as those with diabetes or depressed left ventricular ejection fraction, were found to benefit the most from a reduction in aortic cross-clamp time [16].

As supported by our findings, the Perceval aortic valve offers the opportunity to combine both advantages, in that it makes minimally invasive implantation easier and faster than if using another type of bioprosthetic valve [17]. Our results also suggest that shorter procedural times are associated with a better postoperative outcome, with a lower incidence of atrial fibrillation, pleural effusion, respiratory insufficiency, and need for blood transfusions, likely related to reduced systemic inflammatory effects of cardiopulmonary bypass. In our opinion, the clinical benefit may also be related to a shorter aortic cross-clamp time, as previously suggested [16]. Nonetheless, the mechanisms underlying the better outcome are yet not well understood and go beyond the scope of our study.

The use of the Perceval bioprosthesis combines the advantages of stentless valves in terms of hemodynamic performance with those of a simple implantation technique using a minimally invasive approach [10]. Notwithstanding this, the category of patients for whom Perceval implantation is indicated still remains a matter of debate. Current guidelines [1] and data from Placement of Aortic Transcatheter Valve (PARTNER) Cohort B [18] confirm the benefits of TAVI in inoperable or extreme high-risk surgical patients and the indication for conventional AVR in patients at intermediate-risk or low-risk patients.

Between these two options is a “gray zone” of patients for whom the better indication for TAVI or surgical AVR is still unclear. D’Onofrio and colleagues [19] recently compared early clinical and echocardiographic outcomes of patients undergoing sutureless Perceval AVR vs TAVI using propensity-score matching analysis. Their data showed lower mortality and paravalvular leak rates in the Perceval group. Although the primary aim of our study was not to evaluate the incidence of paravalvular leak, this was very low in both groups: it occurred in 1 patient with 2+ aortic regurgitation from the sutureless group (1.2%) and in 1 patient from the stented group due to infective endocarditis. Given that the occurrence of paravalvular leak is associated with increased death after TAVI [20], the low incidence of this phenomenon should be taken into consideration in high-risk patients who fall in the “gray zone.” In this respect, our results may be affected by the potential development of late paravalvular leak and the lack of long-term follow-up of this condition. However, in another study from our group comparing TAVI vs sutureless AVR, the reduced occurrence of paravalvular leak at follow-up was in favor of the sutureless technique [21].

In this specific subset of high-risk patients, another interesting but less investigated issue is the cost-benefit ratio. In the PARTNER Cohort B trial, TAVI was more cost-effective than medical therapy [22] and also proved to be more cost-effective compared with surgical AVR, but only in the short-term. The occurrence of paravalvular leak at long-term follow-up was not recorded, a limitation that was also acknowledged by the authors and that may even lead to a reversal of the study results [23].

Few studies have evaluated costs of AVR so far, and to the best of our knowledge, this study is the first that has assessed how better postoperative outcomes translate into economic benefits. A recent report by Osnabrugge and colleagues [24] compared hospital and follow-up costs of surgical AVR of intermediate-risk patients in
Netherlands. Absolute values of total costs reported by Osnabrugge and colleagues for the surgical AVR were higher (€33,354) than ours, but relative weights of main cost categories were comparable in the two studies. The absolute cost difference can be explained by differences in unit cost, cost structure, and different cost reporting systems existing in Germany and Netherlands. Moreover, observed results are consistent with the preliminary results of a cost analysis based on a probabilistic model simulation [9] and confirm the model prediction capability. Indeed, the technical and clinical benefits of Perceval are reflected in reduced resource consumption at the ICU, complication-related costs, and operating room costs.

In conclusion, by combining the advantage of shorter procedural times with a subsequent better outcome and reduced health care costs, sutureless AVR might become the first-line surgical treatment for patients with severe aortic valve stenosis. Nevertheless, despite the promising preliminary results, a longer follow-up is warranted before a definite conclusion can be drawn.

References

stay, do you have the analysis of how many patients were performed via a minimally invasive approach, and what impact they have on cost?

DR POLLARI: As a standard in our group, we perform always the J sternotomy in all patients, if possible; obviously, except the associated procedures and the redo patients. In our series from 82 patients, excluded circa 30 patients, all the others were performed with a J sternotomy.

DR BADHWAR: For clarification though, in this study you had coronary artery bypass grafting (CABG) patients; therefore, they have to be sternotomy.

DR POLLARI: In patients with associated CABG, we performed the full sternotomy.

DR BADHWAR: Second question, in your calculation for total operating room (OR) costs, you refer to anesthesia, etc as only €5,000. The device cost itself is substantial, and the device cost differential is probably significant. For clarification for our important interpretation of your cost analysis and therefore your conclusions, was the device cost included in your analysis?

DR POLLARI: As I showed in my presentation, we excluded the prosthesis cost for two reasons. In the first evaluation, we recognized a too strong advantage for the sutureless group, because many of these patients were part of a premarket study for which the prosthesis was not paid from the hospital. The second reason is that the price of this prosthesis changed in the last 2 years. So we eliminated this bias from our study, thus eliminating the prosthesis cost from both group. And I have no clear-cut answer for the cost of this prosthesis at this moment.

DR BADHWAR: Last comment. In situations when both prostheses are equivalent price, that makes excellent sense. Given the fact that both prostheses have very different price points, that may be a significant limitation that you may want to disclose in your manuscript.

DR ADEL TASH (Riyadh, Saudi Arabia): Thank you very much for the excellent presentation. The gentleman also mentioned one of the points that I wanted to mention is that the cost of the prosthesis is very different: there is a big difference between the sutured and sutureless valves. This is the first comment.

The second is a question that is about the use of the permanent pacemaker percentage in the Perceval group. We know that in the sutureless valve, the need for a permanent pacemaker is higher, a little bit higher than the sutured valve, less than the transcatheter aortic valve implantation but a little bit higher than the sutured valve. In the morning, there was a presentation from Montreal and they mentioned a 17% need for a permanent pacemaker. What was the percentage in your hospital and was that cost added to the total cost of the procedure?

DR POLLARI: The incidence in our study was about 5%, and there was no significant difference in the two groups.

DR FRANK FAZZALARI (Rochester, MI): I have one more question, about cost. How did you calculate cost? Did you use hospital charges? Did you use hospital payments or cost-to-charge ratios, or did you do a true time-driven activity-based cost analysis?

DR POLLARI: The cost analysis was performed from our hospital finance department according to the German diagnosis related group (DRG) matrix. The study period was in the last 3 years, so from 2010 and 2013, each patient’s cost was calculated with the corresponding DRG for that year.

DR FAZZALARI: Thank you.

DR ERNESTO JIMENEZ (Tampa, FL): One quick question. Did you extubate the sutureless valves in the OR?

DR POLLARI: No. We don’t extubate the patients in OR.

DR THOMAS MACGILLIVRAY (Boston, MA): So I guess as a corollary to that, were there standard protocols for how patients were weaned from the ventilator and extubated?

DR POLLARI: Our standard protocol is the fast-track.

DR MACGILLIVRAY: For both?

DR POLLARI: For all the patients.