One-year multicentre outcomes of transapical aortic valve implantation using the SAPIEN XT™ valve: the PREVAIL transapical study‡

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Abstract

OBJECTIVES: The study aimed to evaluate 1-year outcomes of the multicentre PREVAIL transapical (TA) study of TA-aortic valve implantation (AVI) in high-risk patients.

METHODS: From September 2009 to August 2010, a total of 150 patients, aged 81.6 ± 5.8 years, 40.7% female, were included at 12 European TA-AVI experienced sites. Patients received 23 (n = 36), 26 (n = 57) and 29 mm (n = 57) second-generation SAPIEN XT™ (Edwards Lifesciences, Irvine, CA, USA) valves. The mean logistic EuroSCORE was 24.3 ± 7.0, and mean Society Thoracic Surgeons score was 7.5 ± 4.4%.

RESULTS: Survival was 91.3% at 30 days and 77.9% at 1 year. Subgroup analysis revealed survivals of 91.7/88.9, 86.0/70.2, 96.55/91.2% for patients receiving 23-, 26- and 29-mm valves at 30 days and at 1 year, respectively. Transthoracic echocardiography revealed preserved left ventricular ejection fraction and low gradients. Aortic incompetence was none in 41/48, trace 30/36, mild 22/12 and moderate in 7/4% at discharge and 1 year. Walking distance increased from 221 (postimplant) to 284 m (at 1 year, P = 0.0004). Three patients required reoperation due to increasing aortic incompetence during follow-up. Causes of mortality at 1 year were cardiac (n = 7), stroke (n = 1) and others (n = 5).

CONCLUSIONS: The European PREVAIL multicentre trial demonstrates good functionality and good outcomes for TA-AVI using the second-generation SAPIEN XT prosthesis and the ASCENDRA-II delivery system. The 29-mm SAPIEN XT valve was successfully introduced and showed excellent results.

Keywords: Aortic stenosis • Aortic valve implantation • Transcatheter • Transapical

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) has been established as a routine procedure in many European Heart centres, especially in order to treat elderly high-risk patients with aortic stenosis (AS) [1–5]. TAVI is routinely performed using a retrograde transfemoral (TF) or an antegrade transapical (TA) approach. In addition, retrograde access routes, such as a trans-subclavian (TS) or transaortic (TAo), are being used more frequently in some centres. Since 2008, two TAVI systems have been Commune European (CE) approved for routine use: the CoreValve™ (Medtronic, Inc., Minneapolis, MN, USA), which is used for retrograde accesses (TF, TS and TAo) and the SAPIEN™, which is used for retrograde access (TF, TS and TAo) and for an antegrade TA approach.

The SAPIEN XT™ valve has been modified while retaining many of the established features of the previous SAPIEN™ valve: it is a balloon-expandable device, and for TA implantation, has the same procedural steps as described previously [6]. The frame has a new design and is manufactured from cobalt–chromium, leading to a lower crimp profile geometry. The leaflets have a...
scallop-shaped design and are in a semi-closed position with an overall increased coaptation area. In parallel, the newly designed 29-mm SAPIEN XT™ valve was introduced into clinical practice.

The PREVAIL TA trial was conducted to evaluate the performance of the SAPIEN XT™ valve. A total of 150 patients were included in the study between September 2009 and August 2010. Due to the good initial results of the PREVAIL study, CE approval was granted for the SAPIEN XT™ valve in Spring 2010. The initial results of the PREVAIL TA study including 30-day outcomes have been presented and will be shortly published [7]. We report here the 1-year outcomes of this multicentre European trial on TA-AVI.

METHODS

A total of 150 high-risk elderly patients were included in this study between September 2009 and August 2010. The 29-mm valve was introduced soon after the trial had started. Patients were treated at 12 centres, all of whom had previous experience with TA-AVI including (number of patients treated): Essen, Germany (33); Leipzig, Germany (30); Karlsruhe, Germany (16); Bad Bevensen, Germany (15); Hamburg, Germany (15); London Kings, UK (11); Cologne, Germany (8); Bad Nauheim, Germany (8); Paris, France (5); London St. Thomas, UK (4); Vienna, Austria (4); Munich DHZ, Germany (1). The study was performed after approval by the ethical committees. All patients gave written informed consent. Patients with a high-operative risk as indicated by a logistic EuroSCORE between 15 and 40% were included in this study, and those on chronic dialysis were excluded.

In parallel to using the SAPIEN XT™ prostheses, the ASCENDRA-II™ delivery system (Edwards Lifesciences, Inc., Irvine, CA, USA), as discussed elsewhere [7], was used in this study. In brief, the pusher is integrated into the handle of the ASCENDRA-II™ system to allow for easier pusher retrieval during valve implantation. In addition, de-airing is easier, facilitated by a new de-airing valve and it also has a smaller 24-F sheath for patients who are receiving 23 and 26 mm valves. The 29-mm SAPIEN XT™ valve is implanted by means of the previous-generation ASCENDRA-II™ delivery system with a 26-F sheath. Figure 1 illustrated the 23-mm SAPIEN XT™ valve (frame height 14.3 mm), a 26-mm valve (frame height 17.2 mm) and a 29-mm SAPIEN XT™ valve (frame height 19.1 mm), respectively.

The TA-AVI procedure was performed as described previously [6]. In short, under general anaesthesia, a femoral arterial sheath (6F) and a femoral venous guidewire were placed, and a pigtail catheter positioned into the ascending aorta. TA access was gained through a left anterolateral minithoracotomy, pericardiotomy with retention stitches and Teflon pledget reinforced apical purse-string sutures. Following apical puncture, a stiff guidewire was placed antegrade into the descending aorta by means of a right Judkins catheter. After balloon valvuloplasty (20 mm balloon, brief episode of right ventricular pacing [RVP]), the 24-F ASCENDRA-II™ sheath (26-F sheath for the 29-mm prosthesis) was inserted bluntly, with the crimped SAPIEN XT™ valve attached, the system de-aired, the valve positioned intra-annularly and the pusher retrieved. Valve implantation was performed after control angiography and under RVP, followed by system retrieval and apical closure. Valve-size selection was performed by the local Heart Teams. In general, it was based on transoesophageal echocardiographic measurements of the aortic annulus diameter while taking computer tomographic measurements into account at some of the centres as well. A 23-mm SAPIEN XT™ valve was used for an aortic annulus diameter of 18–22 mm, a 26-mm SAPIEN XT™ valve for an aortic annulus diameter of 21–25 mm and a 29-mm SAPIEN XT™ valve for an aortic annulus diameter of 24–27 mm, respectively.

Edwards Lifesciences LLC was the sponsor of this study. Data were monitored and statistically analysed by experienced...
RESULTS

Patient demographics of this study were as follows: patients were aged 82 ± 6 (range 61–95 years); 41% were female, logistic EuroSCORE was 24 ± 7% and Society Thoracic Surgeons score was 7.5 ± 4.4%. A total of 36 (24%) patients received a 23-mm SAPIEN XT™ valve, and 57 (38%) patients each received a 26- and a 29-mm SAPIEN XT™ valve, respectively. The overall survival at 30 days was 91%, correct valve implantation was performed in 98%, there was no patient with coronary ischaemia due to potential coronary obstruction, annular dissection occurred in 1 (0.7%) patient and temporary haemodynamic support using cardiopulmonary bypass was required in 6 (4%). Intraoperative access complications due to the TA puncture occurred in 1 (0.7%) patient.

A summary of adverse events at 30 days and at 1 year together with the overall Kaplan-Meier freedom rate from the respective events is given in Table 1. In detail, data on endocarditis, myocardial infarction, significant paravalvular leak (3+ or 4+), pericardial effusion, need for permanent pacemaker, renal failure, respiratory failure, stroke and transitory psychotic syndrome (disorientation) are depicted.

A total of 5 (3.3%) patients required reoperation or conversion to conventional aortic valve surgery due to increasing paravalvular leakage at up to 1 year. In detail, these were: a patient (23-mm SAPIEN XT™ valve) with annular dissection who died on the operative day; 1 patient (23-mm SAPIEN XT™ valve) due to paravalvular leak 3+ on postoperative day (POD) 14 who is alive; 1 patient (26-mm SAPIEN XT™ valve) due to paravalvular leak 3+ on POD 31 who suffered sudden cardiac death on POD 71; 1 patient (29-mm SAPIEN XT™ valve) due to paravalvular leak 3+ on POD 52 who is alive and 1 patient (26-mm SAPIEN XT™ valve) due to paravalvular leak 3+ on POD 100 who is alive. Thus, 3 of 5 (60%) patients who were converted to conventional surgery at any time are alive at 1 year.

The causes of death at up to 30 days and 1 year are given in Table 2. This gives an overview of the usual causes of death in an elderly and high-risk population. Total mortality was 13 of 150 (8.7%) at 30 days and 22 of 137 (16.1%) at 1 year. The mean duration until late death was 198 days.

Some relationship between comorbidities and outcome was revealed during statistical analysis: as such, patients who died within 1-year had a significantly higher incidence of previous vascular stent or percutaneous angioplasty (P < 0.0001), pulmonary disease with a functional expiratory volume 1 < 1.0 (P = 0.007), absence of sinus rhythm (P = 0.02) and tricuspid regurgitation ≥ 2° (P = 0.02).

Overall survival of the PREVAIL TA cohort of 150 patients was 78% (117 patients at risk) at 1 year. The Kaplan-Meier survival curve for the overall cohort is presented in Fig. 2. Overall survival of the PREVAIL TA trial at up to 1 year, together with valve-size-related subgroup analysis is given in Fig. 3. One-year survival of patients receiving a 23-mm SAPIEN XT™ valve was 80.6% (29 patients at risk), 1-year survival for patients receiving a 26-mm SAPIEN XT™ valve was 66.7% (38 patients at risk) and
1-year survival for patients receiving a 29-mm SAPIEN XT™ valve was 87.7% (50 patients at risk), respectively.

Echocardiographic results are given in Table 3, indicating preoperative baseline as well as 30-day, 6-month and 1-year follow-up. Postaortic valve implantation patients had sufficient valve opening areas and low gradients. Left ventricular ejection fraction is well preserved.

Data on potential overall aortic valve incompetence are given in Table 4, indicating the same preoperative baseline as well as 30-day, 6-month and 1-year follow-up time intervals. Few patients only had higher degrees of aortic valve incompetence, and there was no increase in incompetence noted over time.

Functional improvement after TA-AVI was assessed by measuring the overall walking distance, which increased significantly.
Table 3: Echocardiographic results at preoperative baseline, 30-day postaortic valve implantation as well as 6 months and 1 year postoperatively

<table>
<thead>
<tr>
<th>Echo parameter</th>
<th>Preoperative baseline (n = 150)</th>
<th>30 days (n = 112)</th>
<th>6 months (n = 106)</th>
<th>1 year (n = 87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AV area (cm²)</td>
<td>0.7 ± 0.2</td>
<td>1.7 ± 0.4</td>
<td>1.7 ± 0.5</td>
<td>1.8 ± 0.6</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>56.9 ± 12</td>
<td>59.0 ± 11</td>
<td>57.1 ± 12</td>
<td>56.3 ± 10</td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>41.8 ± 16</td>
<td>9.8 ± 5</td>
<td>10.1 ± 4</td>
<td>10.8 ± 5</td>
</tr>
<tr>
<td>Peak gradient (mmHg)</td>
<td>69.4 ± 24</td>
<td>18.8 ± 9</td>
<td>19.2 ± 8</td>
<td>20.4 ± 8</td>
</tr>
</tbody>
</table>

Table 4: Echocardiographic results regarding total aortic valve incompetence for the study population

<table>
<thead>
<tr>
<th>Total aortic insufficiency</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (None)</td>
<td>29 (19.3%)</td>
</tr>
<tr>
<td>+1 Trace</td>
<td>41 (27.3%)</td>
</tr>
<tr>
<td>+2 Mild</td>
<td>56 (37.3%)</td>
</tr>
<tr>
<td>+3 Moderate</td>
<td>21 (14.0%)</td>
</tr>
<tr>
<td>+4 Severe</td>
<td>3 (2.0%)</td>
</tr>
<tr>
<td>NAV/missing</td>
<td>2 (1.3%)</td>
</tr>
</tbody>
</table>

NAV: not available.
Results are given for preoperative baseline, 30-day, 6-month and 1-year follow-up.

from 221 ± 101 up to 284 ± 117 mm on average for the whole population (P = 0.0004). In addition, New York Heart Association (NYHA) functional class improved in all patients: whereas at preoperative baseline, 82% of the patients were in NYHA Class III or IV at 1-year follow-up and 82% were in NYHA Class I or II. Details on the distribution of NYHA functional classes are given in Fig. 4.

DISCUSSION

TAVI has gained increasing interest and importance after the broader clinical introduction of these techniques approximately 5 years ago. A landmark year was 2008 when two devices, the Medtronic CoreValve™ (Medtronic, Inc.) and the Edwards SAPIEN™ valve received initial CE approval, with thousands of patients treated at many centres since then. The Edwards SAPIEN™ valve was the only valve to date to allow retrograde TF and antegrade TA implantation, thus allowing direct access to the native aortic valve as well as the treatment of patients in whom retrograde access is not feasible. Further developments of the SAPIEN™ valve resulted in the SAPIEN XT™ prosthesis, which offers improved leaflet design and a lower profile stent. Together with the improved ASCENDRA-II™ delivery system, this should lead to even more reliable and standardized procedures in high-risk elderly patients with AS. The PREVAIL TA study was performed to introduce the new SAPIEN XT™ prosthesis in 2009 to obtain CE approval for this device, which was granted in Spring 2010. A multicentre European study was thus conducted and following the initial and 30-day results [7], we report here on the intermediate-term outcomes at up to 1-year follow-up. This study was conducted using standardized protocols together with a data adjudicating clinical events committee as well as corelab evaluation of the results. Therefore, firm conclusions can be drawn from the outcomes of the 150 high-risk elderly patients who were treated at 12 European centres.

Overall results of the PREVAIL TA trial are excellent, especially in view of the high-risk profiles of the patients treated. They compare favourably to the recent literature results on TA-AVI [8-14]. Outcomes at 1 year compare well with those of the PARTNER trial [14]. PREVAIL TA is the first multicentre study ever included high-risk elderly patients and obtained better than 90% survival in the short-term follow-up at up to 30 days postoperatively. Results at 1 year revealed good survival of 78% on average for all three different valve sizes. Subgroup assessment indicated better survival in those patients who received a 29-mm SAPIEN XT™ in comparison with a 26-mm SAPIEN XT™ prosthesis. This may in part be related to some patient selection and waiting list issues: the larger (29 mm) prosthesis only became available 4 months after the initiation of this study. Patients were obviously waiting for this device, which can be seen by the relatively large number of 29-mm valves that were implanted. Patients on a waiting list per se lead to better-than-average outcomes due to the fact that the sicker ones may have died or were treated with conventional aortic valve replacement before inclusion in the study. However, it may also have something to do with the larger size of the valve itself, as we know from SOURCE [9] that patients with 26-mm valves inserted have improved outcomes.

The causes of death during the early and intermediate period up to 1 year are, unfortunately, those seen and expected in an elderly and high-risk population. Different causes contributed to the overall numbers as shown in Table 2.

When evaluating the results presented, it has to be considered that, at many centres, the routine practice is to use a TF approach whenever feasible. Selection of such a ‘TF-first’ approach, however, is not substantiated by any scientific literature at present. Due to this selection bias, results may be worse with TA access whenever compared with TF results. However, this direct comparison should be avoided as it lacks scientific evidence. Therefore, in most series where vascular access is chosen in favour of TF-AVI, outcomes are not directly comparable with the TA approach. Usually sicker patients, who present with relevant additional comorbidity such as peripheral vascular disease, are directed towards the TA approach. In fact, data from the Canadian multicentre trial clearly indicate that TF and TA-AVI are comparable regarding longer-term outcomes at 1 and 2 years, despite a significantly higher risk profile in the TA series [15]. Based on the excellent outcomes of this study and the reported outcomes from the literature, we recommend taking a broader view of patient allocation towards TF or TA: we recommend a balanced allocation of patients to both procedures as long as no direct comparable data are available that favours one access approach. The overall assumption of ‘TF being less invasive’ may be relatively subjective. It is especially important to consider hard endpoint criteria such as mortality and stroke when judging invasiveness. Data from the presented PREVAIL TA study have clearly indicated that TA-AVI leads to excellent and comparable outcomes with respect to these endpoints.
Of course, even in this study, the rate of patients suffering from peripheral vascular disease was high, being 33%. The relevance of the risk factor ‘peripheral vascular disease’ is underlined by the fact that patients with any previous vascular interventions, and thus the presence of this comorbidity, had a significantly higher risk of mortality in this study. Thus, the good outcomes of the PREVAIL study were obtained in relatively sick patients.

We saw a very low incidence of complications with the TA approach. Only 1 of 150 patients (0.7%), at multicentre patient inclusion, suffered from such a complication. Therefore, the TA access is safe. In addition, we did not observe any late apical complications, such as potential apical pseudoaneurysms during the first year after the implantation. Most importantly, echocardiography proved the well-preserved left ventricular ejection fraction after the TA approach. The very low (0.7%) access-related complication rate has to be considered a positive factor regarding overall outcomes, especially in comparison with patients who receive a TF approach. In conclusion, the TA approach can be considered safe and standardized.

Fortunately, only a few patients required conversion to conventional surgery; 1 patient on the day of AVI and the other 4 patients at later dates, all due to moderate or severe paravalvular leakage. The outcomes of these conversions were good, with satisfactory survival at 1 year. Thus, conventional surgery should always be considered as a bailout option, even in high-risk patients, as recommended by the current position paper [16] and as indicated by the individual heart teams.

In summary, excellent outcomes were obtained at 30 days and at 1 year in a multicentre trial on TA-AVI using the Edwards SAPIEN XT™ valve, which led to CE approval. The TA approach is a valuable, antegrade, direct and truly minimally invasive option for aortic valve implantation. The heart teams should consider both the TF and the TA approaches as comparable options to treat high-risk elderly patients with AS.

**ACKNOWLEDGEMENTS**

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**Conflict of interest**: Olaf Wendler worked as a proctor and consultant for the Edwards Lifesciences transcatheter heart valve program and also received speakers honoraria. Holger Schroefel has, within the past 12 months, had the following financial interests, arrangements and affiliations with these organizations: honoraria for lectures (Edwards Lifesciences, Philips Healthcare, Symetis S.A.); participation in clinical trials (Edwards Lifesciences, Symetis S.A.); proctoring fees (Edwards Lifesciences, Symetis S.A.). All other authors: none declared.

**REFERENCES**

APPENDIX. CONFERENCE DISCUSSION

Dr D. Berdajs (Lausanne, Switzerland): This is a multicentre case-control study with 150 patients. You are presenting a new model of the Edwards valve. I have three questions for you.

The first question, on your second slide you tell us that the coaptation of the leaflets is somewhat better as compared to the previous version of the valve. Do you think that this coaptation form may augment the durability of the valve? The second question concerns the three patients having a stroke in the follow-up period. Do you believe that this is perhaps related to the anticoagulation or antiplatelet therapy regimen? Thirdly, I believe that one of your slides tells us that in the patients who died there is a higher incidence of pulmonary events. Do you believe that this may be avoided by transaortic implantation of the valve?

Dr Walther: First, I didn’t mention that I think the coaptation length is larger. These leaflets are in a semi-closed fashion. That means that centre back flow is sufficient to close the leaflets, and we can avoid the problem that may arise in a small aortic root if there is not sufficient centre back flow. The Sapien valve required some lateral back flow through the upper wire frame of the valve, and this is not required anymore to safely close the leaflets. So that kind of leaflet malfunction shouldn’t occur that frequently anymore.

Your second question concerned stroke and anticoagulation/antiplatelet regimens. We have different regimens; most centres will go only for aspirin. We have a 95% freedom from stroke at one year and this is in an elderly high-risk population. It is just the normal course of life that stroke will occur in some patients: only three patients had additional strokes during 30 days of follow-up. So I think this is pretty acceptable.

Dr Berdajs: Would you recommend to us an anticoagulation therapy, I don’t know, for the first three months or for six months and after that antiplatelet therapy?

Dr Walther: Well, it is difficult. Of course, after SYNTAX we thought we didn’t give enough anticoagulation to our patients. On the other hand, we are treating elderly high-risk patients who may be at risk for some bleeding if you give too much. So it is a bit of a balance. I personally, in a regular patient, would go only for aspirin. If I have any concern, short distance to coronaries and so on, or a previous coronary stent, for example, then give additional medication. And the third question?

Dr Berdajs: The third question was about patients who died. Incidence of pulmonary events was higher in this group. Now the question is, you are doing a lateral thoracotomy. If we could avoid these kind of complications by doing a hemi-sternotomy and then implanting the valve in the retrograde way by opening the aorta, what would you think about that?

Dr Walther: What should I say to that? Of course you can do a small mini-incision on the sternum. That is the access I use for all my aortic valves, routine aortic valves, and I don’t open the pleural space. This may translate into lower risk of pulmonary problems. Firstly, we had only one patient who died due to pulmonary problems during follow-up, so this is pretty low. Secondly, from my experience with 800 transcatheter valves, half transfemoral, half transapical, during four years in Leipzig, and right now with some 250 valves to do per year, patients can die from pulmonary problems anyhow. They can die when they have awake transfemoral percutaneous procedures. They can get a pneumonia three days later because they are sick, they are frail, they are not mobilized, and they catch some bug or whatever.

So I don’t think that this affected it.

For the transaortic approach, do you want to hear my statement? Well, I think we should push on the antegrade straightforward intuitive approach, because that is the better one I think.

Dr S. Salizzoni (Tolono, Italy): I have a question. In your series you showed that you had five reinterventions, and I imagine that they were standard aortic valve replacement, is that correct?

Dr Walther: Yes, sure.

Dr Salizzoni: Have you ever thought that these patients may benefit from a valve-in-valve instead of a surgical aortic valve replacement, because you previously considered them at very high risk?

Dr Walther: Well, valve-in-valve in a patient with a third degree aortic incompetence can be a tricky procedure, because you probably need to over-dilate the Sapien, which may be feasible, maybe not, and you put the patient at some risk, so, of course, you have to balance it. In the truly inoperable, severe porcelain aorta, 90 year old patient, two previous operations, etc., you may consider that. But otherwise if you see an option (and we are treating these elderly patients who are high risk) that you could also operate conventionally, then we opted for conventional surgery. Obviously the results are good: three of them are alive at one year.