Transcatheter aortic valve implantation: first results from a multi-centre real-world registry

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Aims

Treatment of elderly symptomatic patients with severe aortic stenosis and co-morbidities is challenging. Transcatheter aortic valve interventions [balloon valvuloplasty and transcatheter aortic valve implantation (TAVI)] are evolving as alternative treatment options to surgical valve replacement. We report the first results of the prospective multicentre German Transcatheter Aortic Valve Interventions—Registry.

Methods and results

Between January 2009 and December 2009, a total of 697 patients (81.4 ± 6.3 years, 44.2% males, and logistic EuroScore 20.5 ± 13.2%) underwent TAVI. Pre-operative aortic valve area was 0.6 ± 0.2 cm² with a mean transvalvular gradient of 48.7 ± 17.2 mmHg. Transcatheter aortic valve implantation was performed percutaneously in the majority of patients [666 (95.6%)]. Only 31 (4.4%) procedures were done surgically: 26 (3.7%) transapically and 5 (0.7%) transaortically. The Medtronic CoreValve™ prosthesis was used in 84.4%, whereas the Sapien Edwards TM prosthesis was used in the remaining cases. Technical success was achieved in 98.4% with a post-operative mean transaortic pressure gradient of 5.4 ± 6.2 mmHg. Any residual aortic regurgitation was observed in 72.4% of patients, with a significant aortic insufficiency (≥ Grade III) in only 16 patients (2.3%). Complications included pericardial tamponade in 1.8% and stroke in 2.8% of patients. Permanent pacemaker implantation after TAVI became necessary in 39.3% of patients. In-hospital death rate was 8.2%, and the 30-day death rate 12.4%.

Conclusion

In this real-world registry of high-risk patients with aortic stenosis, TAVI had a high success rate and was associated with moderate in-hospital complications. However, careful patient selection and continued hospital selection seem crucial to maintain these results.

Keywords

Aortic stenosis • Aortic valve • Transcatheter aortic valve implantation • Aortic regurgitation

Introduction

Severe symptomatic aortic stenosis has a poor prognosis with conservative treatment.1 Surgical valve replacement is the treatment of choice for these patients and is associated with a better prognosis and improvement in quality of life.2 However, surgical valve replacement may result in severe complications. This is especially true for elderly patients with significant co-morbidities. As a consequence, ~30% of these patients with severe symptomatic aortic stenosis are currently not operated.3

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Percutaneous balloon valvuloplasty was the first catheter-based technique to address this problem. After the first promising results, long-term follow-up data showed high restenosis rates as well as no improvement in the clinical course of patients. Therefore, balloon valvuloplasty remained only an emergency option as a bridge to surgery.

More recently, transcatheter aortic valve implantation (TAVI) has been introduced in 2002 by Cribier et al. to treat older surgical high-risk patients with severe symptomatic aortic stenosis. First single-centre case series have demonstrated the feasibility and efficacy of the balloon-expandable Sapien Edwards™ prosthesis (Edwards Lifesciences LLC, Irvine, CA, USA) as well as the self-expandable CoreValve™, now Medtronic CoreValve™ (Medtronic CoreValve, Irvine, CA, USA), prosthesis. This was confirmed by a larger, multi-centre, post-marketing registry of the Medtronic CoreValve. These promising data have resulted in a rapid adoption of this novel technique in daily clinical practice, with currently more than 6000 implantations of both available types of prostheses. This was accompanied with the recommendation of several cardiac societies for patient selection as well as for performance of the procedures (European Society of Cardiology, American Heart Association and American College of Cardiology, and the German Cardiac Society). Nevertheless, in the absence of randomized controlled clinical trials comparing TAVI with either conservative therapy or conventional surgery and the only available data originating from highly specialized centres or from industry sponsored post-marketing registries, there is a great need to gain independent multi-centre data during the introduction of this new technique to assess its performance in daily clinical practice.

We therefore initiated, immediately after commercial availability of the two valve prostheses in Germany, the independent German Transcatheter Aortic Valve Interventions—Registry to evaluate indications, interventions, and clinical outcome as well as quality of life measurements of the TAVI procedure in routine clinical practice.

Methods

Study design

The German Transcatheter Aortic Valve Interventions—Registry is a multi-centre prospective registry. The aim is to monitor the current use and outcome of transcatheter aortic valve interventions, including TAVI as well as balloon valvuloplasty alone, in daily clinical practice and to evaluate safety, effectiveness and health-economical data. The registry is completely independent from industry, driven by the scientific interest of the participating hospitals and currently financed by the Institut für Herzinfarktforschung (IHF), Ludwigshafen.

Patient population

Since January 2009, all participating hospitals committed to include all consecutive patients with severe symptomatic aortic stenoses treated with either balloon valvuloplasty alone or treated with TAVI. Proposed inclusion criteria for treatment were the following: severe symptomatic aortic valve stenosis with a valve area ≤ 1 cm², with or without aortic valve regurgitation and (i) age ≥ 80 years and a logistic EuroScore ≥ 20% or (ii) logistic EuroScore < 20% and at least one of the following criteria: cirrhosis of liver, pulmonary insufficiency (FEV1 ≤ 1 L), or porcelain aorta. Furthermore, technical feasibility, such as a feasible arterial access and a fitting aortic annulus diameter according to the available prostheses sizes, should have been given.

All patients gave written informed consent before the procedure and also gave written informed consent for processing of their anonymous data.

Pre-interventional patient screening typically included transthoracic as well as transoesophageal echocardiography to confirm diagnosis, multi-slice computer tomography to assess aortic and aortic valve dimensions and morphology, grade and distribution of calcifications, annulus dimension in a multi-planar reconstruction measuring from hinge point to hinge point as well as the access, and invasive cardiac evaluation with coronary angiogram, supra-aortic angiogram, and left ventriculography. The baseline operative risk of the patients was estimated by the logistic EuroScore. The patient was considered high risk if the inclusion criteria were met as confirmed by an independent senior cardiologist and senior cardiac surgeon. The decision to treat a patient as well as the decision to perform a balloon valvuloplasty alone or to do a TAVI was left to the discretion of the treating physician. However, we strongly suggested that such a decision should be made by a multi-disciplinary team, typically consisting of an interventionalist, a cardiac surgeon, and an anaesthesiologist, as suggested by current recommendations.

All decisions regarding the procedure, such as simultaneous revascularization of coronary stenoses > 50% were left to the discretion of the individual centre/physician and not pre-specified by the protocol.

For this first analysis of our registry, we decided to report on all patients included in the registry, but then to restrict our analysis to those treated with TAVI only, to have a homogeneous patient cohort.

Device description

Our registry is open to all available prostheses. However, currently only two prostheses are commercially available in Germany: the Medtronic CoreValve™ and the Sapien Edwards™ prosthesis. The Medtronic CoreValve™ (Medtronic CoreValve) prosthesis consists of a tri-leaflet bioprosthetic porcine pericardial tissue valve, which is mounted and sutured in a self-expanding nitinol stent frame. The size of the delivery system is currently 18 French, which facilitates vascular access and deployment of the device. With the current generation, two different device sizes are available for different annulus dimensions: the 26 mm prosthesis for aortic valve annulus sizes from 20 to 24 mm and the 29 mm prosthesis for aortic valve annulus sizes from 24 to 27 mm. Implantation was done as already reported.

The balloon-expandable Edwards Sapien bovine valve (Edwards Lifesciences LLC) or more recently, the cobalt-chromium bovine valve (Sapien XT) were used. Initial transarterial and transapical procedures were performed with the retroflex delivery catheter; afterwards the Novaflex transarterial catheter incorporating a flexible nose cone and the Ascendra transapical catheter were used. Arterial access was done via a 22 or 24 French delivery system. Two prosthesis sizes were available, with a 23 and 26 mm expanded diameter for aortic valve annulus sizes from 18 to 24 mm. Implantation was done as previously reported.

Adjunctive medication

Pre-treatment included aspirin (100 mg/d, indefinitely) and clopidogrel (600 mg loading dose followed by 75 mg/d for 6–12 months). Heparin was administered according to the patient’s weight to achieve an activated clotting time ≥ 250 s.
The degree of post-procedural aortic regurgitation

The degree of post-procedural aortic regurgitation (AR) was angiographically evaluated at the end of the TAVI procedure after final device deployment and removal of the catheter and guidewire. Qualitative angiographic assessment of the severity of AR was performed by visual estimation of the concentration of contrast medium in the left ventricle, using the method of Sellers et al.20 Aortic regurgitation was classified into four Grades: absent (0), trace or mild (1/4), mild-to-moderate (2/4), moderate-to-severe (3/4), and severe (4/4). The evaluation was performed by the treating physician. Until now, we did not analyse our data on chronic post-interventional AR.

Statistical analysis

Data were collected via the Internet by the IHF at the Heart Centre Ludwigshafen.

For this first analysis of our registry, we focus on the cohort of patients undergoing TAVI, to have a homogeneous patient cohort.

Absolute numbers and percentages as well as means (with standard deviation) are computed to describe the patient population. In case of a non-normal distribution of continuous data, as tested with the Kolmogorov–Smirnov test, medians with quartiles are given. Categorical values were compared by the $\chi^2$ test and continuous variables were compared by the two-tailed Wilcoxon rank-sum test. There was no fixed 30-day evaluation, because many patients then were already in a rehabilitation programme, making it difficult to contact them. Therefore, 30-day events were either reported by the treating hospital or follow-up calls performed by the IHF and then the 30-day death rate was calculated by the Kaplan–Meier survival analysis method. $P$-values $<0.05$ were considered significant. All $P$-values are results of two-tailed tests. The tests were performed using the SAS© statistical package, version 9.1 (Cary, NC, USA).

The authors had full access to, and take full responsibility for, the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Between January and December 2009, a total of 833 transcatheter aortic interventions were performed at 22 hospitals: 136 balloon valvuloplasties only and 697 transcatheter aortic valve implantations (TAVIs). Out of the latter (100%) 666 (95.6%) procedures were done percutaneously and 31 (4.4%) procedures were done surgically. (Figure 1) The mean inclusion per hospital was 39 patients (range: 1–240). The following data refer to only those patients treated with TAVI.

On-site cardiac surgery was is available at 17 of the 22 participating hospitals. In the remaining five hospitals, there is an institutionalized co-operation with a cardiac surgeon team; either the team comes to the hospitals for TAVI procedures or the cardiologists do their TAVI at the surgeon’s hospital.

Patient and pre-interventional characteristics

Mean patient age was 81.4 $\pm$ 6.3 years, 44.2% were male, and the logistic EuroScore was 20.5 $\pm$ 13.2%. Heart failure with a New York Heart Association (NYHA) class $\geq$ III was present in 88.2%. The leading indication for TAVI was high surgical risk. (Table 1)

Left ventricular ejection fraction (LVEF) showed a mean of 52.1 $\pm$ 15.0%, with 14.6% of patients suffering from a severely reduced LVEF of less than 30%. Aortic valve area was 0.6 $\pm$ 0.2 cm² with a median transvalvular gradient of 47 mmHg (quartile: 37–60). The mean aortic annulus diameter was 23.5 $\pm$ 2.6 mm. (Table 2)

Interventional characteristics and types of prostheses used

Most interventions (84.4%) were performed as elective procedures, whereas only 0.6% were performed as emergency procedures. The Medtronic CoreValve™ prosthesis was used in 84.4%, whereas the Edwards Sapien™ prosthesis was used in the remaining cases. Mean intervention time, from arterial puncture until vascular closure, was 86.1 $\pm$ 47.0 min, with a mean fluoroscopy time of 15.0 $\pm$ 6.8 min. Surgical closure of the puncture site was performed in 7.0% of cases. (Table 3)

Technical success, defined as completion of the procedure and lowering of the mean pressure gradient, was achieved in 98.7%. The median residual post-procedural transaortic pressure gradient was 5 mmHg (quartiles: 0–8). Residual AR at the end of the procedure, that includes interventions during the initial procedure to cope with worthwhile regurgitations, was observed in 72.4% of patients. However, a significant residual aortic insufficiency ($\geq$ Grade III) was observed in only 16 patients (2.3%). (Table 4)

Complications and clinical outcome

Median time at the intensive care unit was 2 (quartiles: 1–3) days, and mean time in the hospital was 17.2 $\pm$ 9.2 days. Most patients
(83.7%) were discharged on dual antiplatelet therapy with aspirin and clopidogrel.

A permanent pacemaker had to be implanted in 39.3% of patients, in most cases due to permanent or intermittent third-degree atrioventricular (AV)-block. The pacemaker rate in the Medtronic CoreValve™ group was 42.5% (240/565) vs. 22.0% (22/100) in the Sapien-Edwards™ group. Aortic dissection occurred in 3 (0.4%) patients, pericardial tamponade in 12 (1.8%), and a stroke in 19 (2.8%) patients. The most common complications were severe groin problems sometimes with the need for transfusion in 19.5% of cases. (Table 4) In-hospital mortality was 8.2% (57/697) and the 30-day death rate was 12.4%. In-hospital mortality of patients undergoing percutaneous TAVI was 7.5% (50/666) compared with 22.6% (7/31) in patients undergoing surgical TAVI. In-hospital death rates were 8.8% for the hospitals with, and 3.8% for hospitals, without on-site cardiac surgery ($P = 0.12$).
of 244 patients from the French FRANCE (FRench Aortic National Corevalve and Edwards)—TAVI registry. In this registry, 71% of TAVIs were done percutaneously, 66% transfomerally, and 5% transaxillarily and 29% of patients were treated surgically, with transapical procedures. The Medtronic CoreValve™ prosthesis was used in 32%, whereas the Sapien Edwards™ prosthesis was used in 68% of cases. This shows an inverse use of the two available systems in both countries, which also explains the more frequent surgical TAVI approach in France.

Patient characteristics and selection

The mean patient age of 81.4 ± 6.3 years in our registry is well in line with the 81 ± 6.6 years reported by Piazza et al. in the until now largest published series of TAVIs (646 patients), as well the 82.3 ± 7.3 years as reported by Eltchaninoff et al. The same is true for the estimated surgical risk that was done with the logistic EuroScore in our patients and was 20.5 ± 13.2%, which is somewhat lower than the 23.1 ± 13.8% reported by Piazza et al. and the 25.6 ± 11.4% as reported by Eltchaninoff et al.

The current rapid spread of this new technique carries the danger that patients who are candidates for conventional surgical valve replacement will be treated percutaneously. Piazza et al. already reported an ‘off-label’ use of TAVI in 67% of their 63 patients. The 13% patient decision rate as a reason to perform a TAVI in our registry is alarming and clearly an ‘off-label’ use if the EuroScore is below 20%. In our opinion, ‘off label’ use of TAVI should be vigorously avoided, given the good and predictable results of surgical valve replacement as well as the not-yet-clearly defined risks and missing long-term follow-up data of TAVI.

Intervention

Technical success rate was 98.4% in our series. It should be kept in mind that this included patients in whom during the implantation, rescue interventions, such as a retrieval of not correctly implanted CoreValve™ prostheses, were performed which then resulted in a technical success. Grube et al. reported an increase in the technical success rate from 79 to 97% with increase in operators’ experience and technical improvement of the devices. Piazza et al. reported a technical success rate of 97.2% with a reduction in the mean gradient from 49.4 ± 13.9 to 3 ± 29 mmHg, whereas Eltchaninoff et al. reported a success rate of 97% and a reduction of the mean gradient from 46 ± 16 to 10 ± 5 mmHg.

Clinical outcome and complications

The list of possible severe complications of TAVI is large: cerebral embolism, pericardial tamponade, severe aortic insufficiencies, aortic dissections or aortic, or cardiac ruptures as well as access complications can occur. One of the most common complications, is the need to implant a permanent pacemaker, due to intermittent or persistent third-degree AV-block. This occurred in 39.3% of our patients. Piazza et al. reported a rate of 9.3% and Eltchaninoff et al. of 11.8%. There seems to be a difference in the pacemaker rates between the two available TAVI systems. In the series of Eltchaninoff et al., the pacemaker implantation rate of the Medtronic CoreValve™ was 27.2% compared with 5.3% of the Sapien Edwards™ group. In our series,
the corresponding rates were 42.5% in the Medtronic CoreValve™ group compared with 22% in the Sapien Edwards™ group. This may relate to the higher and longer-lasting radial forces as well as the deeper implantation site of the self-expanding Medtronic CoreValve™, which may more often interrupt the conduction in the bundle of His. The reason why the pacemaker implantation rate in our registry is the highest reported yet is not evident from the data. Most probably it reflects a very low threshold of the treating cardiologists to perform such an implantation after a TAVI procedure at this time.

We observed pericardial tamponade in 1.8% and the stroke rate was 2.8%. These values are comparable with those reported by Piazza et al.12 (1.4 and 0.6%) as well as those reported by Etchaninoff et al.22 (2.0 and 3.6%).

A further frequent complication of TAVI is the occurrence of an AR, which we observed in 72.4% of our patients. The exact diagnosis of the severity of such regurgitation as well as its treatment are two of the most challenging problems of TAVI. The available data for both types of prostheses report a comparable rate of about 70% ARs, which were most often mild to moderate.8,11,19 Severe aortic insufficiency was diagnosed in our series in only 2.3%. However, this rate may underestimate the true problem for two reasons: firstly, severe insufficiencies that were already treated during the implantation procedure11,12 were not counted, and secondly, some insufficiencies initially graded as moderate sometimes turn out to be severe during follow-up. Furthermore, it is of paramount importance to clearly define the underlying pathophysiology, because only with this knowledge an appropriate therapy can be initiated. Severe aortic insufficiency due to too deep implantation of the Medtronic CoreValve™ may be treated with either implantation of a second valve (‘Russian doll’ concept)11,28 or by catheter-based repositioning of the valve10,11,29; para-valvular leakage can be treated by implantation of a plug device30,31 and misplacement of the valve can be treated by retracting the device if it is only partially released, followed by a re-implantation.29 However, such rescue interventions are challenging procedures which are time consuming and may themselves cause complications.

Hospital mortality was 8.2% and the 30-day death rate was 12.4% in our registry. Piazza et al.12 reported a 30-day mortality of 8.0% and Etchaninoff et al. a mortality of 12.7%.22 Overall, this event rate seems to be more related to the advanced age and severe co-morbidities of the patients and to a lesser extent to the complication rate of the intervention itself. This again emphasizes the need for proper patient selection as well as an intensive post-interventional care of the patients. The high in-hospital mortality of 22.6% in our patients undergoing surgical TAVI should be interpreted with caution, mainly because of the low numbers of surgical TAVIs, which might reflect a selection bias of those patients.

Limitations

Although representing the biggest-ever reported series of TAVI procedures until now, our results still reflect the experience in a limited number of cases. Furthermore, until now no formal audit of the participating hospitals has been performed. In this version of our registry only the logistic EuroScore,18 but not the Society of Thoracic Surgeons predicted risk score of mortality22 was evaluated, which makes comparisons with other data more difficult. We also do not have systematic data from the participating centres on patients with severe symptomatic aortic stenoses treated with conventional surgical valve replacement or treated conservatively. In this version of our registry, local access complications were not specifically evaluated: ‘groin problems’ is a too undefined medical term, which needs to be addressed more specifically in future research.

Conclusions

Transcatheter aortic valve implantation is providing a new therapeutic option for older patients with severe co-morbidities suffering severe symptomatic aortic stenosis. Complications rates seem to be acceptable considering the advanced age and frequent co-morbidities of the treated patients. However, before a more widespread use of this technique is considered, further data should be awaited.

Conflict of interest: R.Z., R.H., K.E.H., G.R., J.S. do not have any conflict of interest in combination with this paper. U.G., E.G., A.L., H.S., H.E., S.S. worked as proctors for either Medtronic or Edwards or both and received speakers honoraries. H.R.F. is co-founder and co-inventor of JenaValve™ technology, head of its scientific advisory board, as well as medical advisor to JenaValve™ technology, a company which develops a new transcatheter implantable aortic valve. H.S. is member of the scientific advisory board of JenaValve™ technology.

Appendix

List of participating centres (in order of numbers of included patients, given in brackets)
