European Heart Journal (2011) **32**, 198–204
doi:10.1093/eurheartj/ehq339

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

Ralf Zahn[1]*, Ulrich Gerckens[2], Eberhard Grube[2], Axel Linke[3], Horst Sievert[4], Holger Eggebrecht[5], Rainer Hambrecht[6], Stefan Sack[7], Karl Eugen Hauptmann[8], Gert Richardt[9], Hans-Reiner Figulla[10], and Jochen Senges[11], on behalf of the German Transcatheter Aortic Valve Interventions—Registry Investigators

[1]Abteilung für Kardiologie, Herzzentrum, Ludwigshafen, Germany; [2]Klinik für Kardiologie, Helios Klinikum, Siegburg, Germany; [3]Klinik für Kardiologie, Herzzentrum, Leipzig, Germany; [4]CardioVasculäres Centrum Frankfurt, Katharinen-krankenhaus, Frankfurt, Germany; [5]Klinik für Kardiologie, Universitätsklinikum, Essen, Germany; [6]Abteilung für Kardiologie, Herzzentrum, Bremen, Germany; [7]Abteilung für Kardiologie, Klinikum München Schwabing, München, Germany; [8]Abteilung für Kardiologie, Krankenhaus der Barmherzigen Brüder Trier, Germany; [9]Abteilung für Kardiologie, Segeberger Kliniken, Bad Segeberg, Germany; [10]Abteilung für Kardiologie, Universitätsklinikum Jena, Jena, Germany; and [11]Institut für Herzinfarktforschung, Ludwigshafen, Germany

Received 30 May 2010; revised 16 August 2010; accepted 23 August 2010; online publish-ahead-of-print 23 September 2010

This paper was guest edited by Prof. F. Van de Werf, Department of Cardiology, University Hospital Leuven, Leuven, Belgium

See page 133 for the editorial comment on this article (doi:10.1093/eurheartj/ehq315)

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 cm^2 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™ 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]

* Corresponding author. Kardiologie/Pneumologie/Angiologie, Internistische Intensivmedizin Herzzentrum Ludwigshafen, Bremserstraße 79, D-67063 Ludwigshafen, Germany. Tel: +49 621 503 4000, Fax: +49 621 503 4002, Email: erzahn@aol.com

Percutaneous balloon valvuloplasty was the first catheter-based technique to address this problem. After the first promising results,[4,5] long-term follow-up data showed high restenosis rates as well as no improvement in the clinical course of patients.[6] 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.*[7] 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)[8] as well as the self-expandable CoreValve™, now Medtronic CoreValve™ (Medtronic CoreValve, Irvine, CA, USA), prosthesis.[9–11] This was confirmed by a larger, multi-centre, post-marketing registry of the Medtronic CoreValve.[12]

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.[13] 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,[14] American Heart Association and American College of Cardiology,[15] and the German Cardiac Society[16]). 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[8–11,17] or from industry sponsored post-marketing registries,[12] 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 cm^2, with or without aortic valve regurgitation and (i) age $\geq$80 years and a logistic EuroScore[18] $\geq$20% or (ii) logistic EuroScore $<$20% and at least one of the following criteria: cirrhosis of liver, pulmonary insufficiency (FEV1 $\leq$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 transesophageal 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.[18] 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 interventional cardiologist, a cardiac surgeon, and an anaesthesiologist, as suggested by current recommendations.[14–16]

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.[9–11]

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.[7,8,19]

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 $\geq$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 Kolmogoroff–Smirnov test, medians with quartiles are given. Categorical values were compared by the χ^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%) 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.

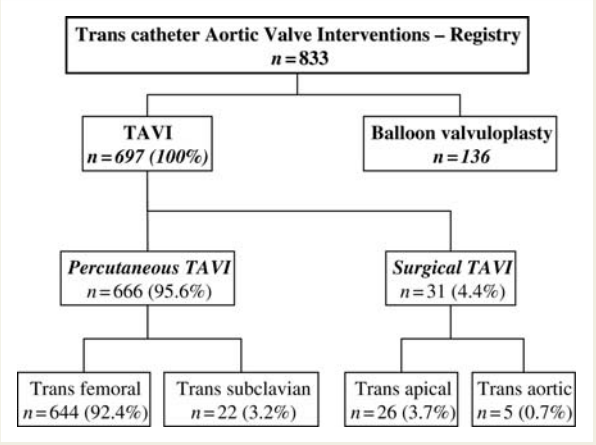

Figure 1 Type of interventions in the Transcatheter Aortic Valve Implantation—Registry.

Patient and pre-interventional characteristics

Mean patient age was 81.4 ± 6.3 years, 44.2% were male, and the logistic EuroScore was 20.5 ± 13.2%. Heart failure with a New York Heart Association (NYHA) class ≥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 ± 15.0%, with 14.6% of patients suffering from a severely reduced LVEF of less than 30%. Aortic valve area was 0.6 ± 0.2 cm^2 with a median transvalvular gradient of 47 mmHg (quartile: 37–60). The mean aortic annulus diameter was 23.5 ± 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 ± 47.0 min, with a mean fluoroscopy time of 15.0 ± 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 (≥ 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 ± 9.2 days. Most patients

Table 1 Patient characteristics

	($n = 697$)
Age (years)	81.4 ± 6.3
Male gender	44.2% (308/697)
Body mass index (kg/m^2)	27.1 ± 10.5
Medical history	
Prior coronary bypass surgery	21.5% (143/693)
Prior PCI	34.2 % (235/688)
Prior valve surgery	3.0% (21/693)
Prior balloon valvuloplasty	13.6% (94/692)
Prior stroke	7.8% (57/692)
Diabetes mellitus	34.6% (239/691)
Chronic obstructive pulmonary disease	24.6% (171/694)
Peripheral arterial obstructive disease	30.3% (210/692)
Renal failure[a]	61.5% (429/697)
Clinical presentation	
NYHA III[b]	70.2% (484/689)
NYHA IV	18.0% (124/689)
ASA I[c]	1.9% (13/685)
ASA II	31.5% (216/685)
ASA III	54.6% (374/685)
ASA IV	10.8% (74/685)
ASA V	1.2% (8/685)
Logistic EuroScore	20.5 ± 13.2%
Indication for intervention	
Surgical high-risk (EuroScore >20%)	39.6% (265/669)
Frailty	17.3% (120/693)
Patients decision	13.0% (90/691)
Limiting concomitant malignancy	3.2% (22/691)
Contraindications for surgery	10.0% (68/682)

[a]Renal failure, glomerular filtration rate <60 mL/min/m^2.
[b]NYHA, New York Heart Association classification of heart failure symptoms.
[c]ASA, American Society of Anaesthesiologists (ASA) physical status classification system.

Table 2 Angiographic and haemodynamic findings

Number of vessels diseased	
No coronary heart disease	39.8% (275/691)
1–vessel disease	19.6% (137/691)
2–vessel disease	13.9% (96/691)
3–vessel disease	26.5% (183/691)
Left main stem diseased	6.0% (41/688)
Left ventricular ejection fraction (EF)	
Ejection fraction (%)	52.1 ± 15.0
Severely reduced (≤30%)	14.6% (101/690)
Aortic valve characteristics	
Aortic valve area (cm^2)	0.6 ± 0.2
Pre-procedural gradient (mmHg)[a]	47 (37–60)
Bicuspid valve	1.7% (12/686)
Severely calcified valve	60.6% (413/682)
Aortic annulus diameter (mm)	23.5 ± 2.6
Low output—low gradient stenosis	12.9% (83/645)
Concomitant aortic insufficiency Grade ≥3	4.3% (30/692)
Other findings	
Concomitant mitral insufficiency Grade ≥3	3.6% (25/692)
Peak systolic pulmonary pressure (mmHg)	44.9 ± 16.6
Pulmonary hypertension	62.8% (430/685)
Atrial fibrillation	23.3% (161/691)
Porcelain aorta	10% (68/682)

[a]Median (quartiles).

Table 3 Type of intervention, type of valve used, and interventional characteristics

Urgency of intervention	
Elective	84.4% (588/697)
Urgent	14.9% (104/697)
Emergency	0.6% (4/697)
Patient under mechanical ventilation	1.0% (7/694)
Intervention during resuscitation	0.0% (0/697)
Type of valve used	
Medtronic CoreValve Revalving system	84.4% (588/697)
26 mm	45.1% (264/585)
29 mm	54.9% (321/585)
Edwards Sapien	15.6% (109/697)
23 mm	43.1% (47/109)
26 mm	56.9% (62/109)
Procedural characteristics	
Intervention time (min)[a]	70 (50–108)
Fluoroscopy time (min)[a]	13 (10–18)
Amount of contrast dye used (mL)	169.2 ± 68.3
Interventional closure of puncture site	86.7% (554/639)
Surgical closure of puncture site	7.0% (45/639)
Concomitant PCI during the same procedure	4.4% (30/689)

[a]Median (quartiles).

(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 in19 (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 ($P = 0.12$).

Table 4 Procedural and clinical events

Procedural results	
Technical successful	98.4% (684/695)
Conversion to open heart surgery	0.7% (5/695)
Unsuccessful termination of the procedure	0.9% (6/695)
Gradient after the procedure (mmHg)[a]	5 (0–8)
Residual aortic insufficiency	72.4% (499/689)
none	27.6% (190/689)
Grade 1	54.9% (378/689)
Grade 2	15.2% (105/689)
Grade 3	2.0% (14/689)
Grade 4	0.3% (2/689)
Implantation of a pacemaker	39.3% (262/667)
Clinical course	
Time at intensive care unit (days)[a]	2 (1–3)
Groin problems	19.5% (130/668)
With need of transfusion	17.1% (115/671)
Severe	4.0% (27/668)
Need for haemodynamic support (IABP or ECLS[b])	1.8% (12/656)
Pericardial tamponade	1.8% (12/670)
Aortic dissection	0.4% (3/670)
Coronary ischaemia	0.1% (1/670)
Myocardial infarction	0.3% (2/673)
Stroke	2.8% (19/670)
Pulmonary embolism	1.3% (9/670)
In-hospital death	8.2% (57/697)
30 day death	12.4%

[a]Median (quartiles).
[b]IABP, intra aortic balloon pump; ECLS, extra corporal life support.

Discussion

The promising results of TAVI, although limited, have caused an unprecedented rapid adoption of this technique in clinical practice.

Registries are an accepted and recommended method to monitor such a process, as they provide important information on the performance of a novel treatment modality in a real-life patient collective at non-specialized centres.[21] Therefore the *German Transcatheter Aortic Valve Interventions—Registry* was initiated, which is purely driven by the scientific interest of the participating hospitals and currently financed independently from industry interests but only by the board values of the IHF, Ludwigshafen. The present analysis is the first report from our registry of the first 833 patients undergoing TAVI at 22 hospitals throughout Germany: 136 balloon valvuloplasties only and 697 TAVIs.

Procedures performed and devices used

Out of our 697 catheter-based TAVIs, 95.6% were done percutaneously and 4.4% procedures were done surgically. The Medtronic CoreValve™ prosthesis was used in 84.4% of patients, whereas the Sapien Edwards™ prosthesis was used in 15.6%. The only comparable data available were recently reported from Eltchaninoff *et al.*[22] of 244 patients from the French ***FRANCE*** (***FR***ench ***A***ortic ***N***ational ***C***orevalve and ***E***dwards)—TAVI registry. In this registry, 71% of TAVIs were done percutaneously, 66% transfemorally, 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.*[12] 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.*[22] The same is true for the estimated surgical risk that was done with the logistic EuroScore[18] in our patients and was 20.5 ± 13.2%, which is somewhat lower than the 23.1 ± 13.8% reported by Piazza *et al.*[12] and the 25.6 ± 11.4% as reported by Eltchaninoff *et al.*[22]

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.*[23] 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, as well as catheter-based correction of prostheses, were performed which then resulted in a technical success. Grube *et al.*[11] 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.*[12] 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.*[22] 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.[8–11,24–27] 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.*[12] reported a rate of 9.3% and Eltchaninoff *et al.*[22] 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.[22] 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 Eltchaninoff *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 procedure[11,12] 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 valve[10,11,29]; para-valvular leakage can be treated by implantation of a plug device[30,31] 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 Eltchaninoff *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 less 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 mortality[32] 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 JenaValveTM technology, head of its scientific advisory board, as well as medical advisor to JenaValveTM technology, a company which develops a new transcatheter implantable aortic valve. H.S. is member of the scientific advisory board of JenaValveTM technology.

Appendix

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

Klinikum Siegburg: U.Gerckens (240), Universität Leipzig Herzzentrum: G.Schuler (123), Herzzentrum Ludwigshafen: R.Zahn (87), Universitätsklinikum Essen: H.Eggebrecht (56), Cardio Vasculäres Centrum (CVC) Frankfurt Sankt Katharinen: H.Sievert (45), Krankenhaus der barmherzigen Brüder Trier: KE Hauptmann (36), Asklepios Klinik St. Georg Hamburg: K.H. Kuck (31), Klinikum Links der Weser Bremen, R. Hambrecht (32), Segeberger Kliniken GmbH: G. Richardt (30), Universitätsklinikum Bonn, Med. Klinik und Poliklinik II: G. Nickenig (27), Elisabeth—Krankenhaus Essen: C.H. Naber (23), Klinikum Schwabing, München: S. Sack (23), Universitätsklinikum Jena: H.R. Figulla (22), Augustinum Klinik München: M. Block (21), Städt. Klinikum München Klinik Bogenhausen: E. Hoffmann (15), Robert-Bosch-Krankenhaus, Stuttgart: U. Sechtem (7), HELIOS Klinikum Wuppertal: H. Gülker (5), Universitäts Klinikum Regensburg: G. Riegger (3), Krankenhaus München—Neuperlach: H. Mudra (3), Herzzentrum Bad Krozingen: FJ Neumann (2), Universitätsklinikum Freiburg: C. Bode (1), Klinikum Coburg: J. Brachmann (1).

References

1. Aronow WS, Ahn C, Kronzon I, Nanna M. Prognosis of congestive heart failure in patients aged > or = 62 y with unoperated severe valvular aortic stenosis. *Am J Cardiol* 1993;**72**:846–848.
2. Vahanian A, Baumgartner H, Bax J, Butchart E, Dion R, Filippatos G, Flachskampf F, Hall R, Iung B, Kasprzak J, Nataf P, Tornos P, Torracca L, Wenink A. Guidelines on the management of valvular heart disease: the task force on the management of valvular heart disease of the European Society of Cardiology. *Eur Heart J* 2007;**28**:230–268.
3. Iung B, Cachier A, Baron G, Messika-Zeitoun D, Delahaye F, Tornos P, Gohlke-Barwolf C, Boersma E, Ravaud P, Vahanian A. Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery? *Eur Heart J* 2005;**26**:2714–2720.
4. Cribier A, Savin T, Saoudi N, Rocha P, Berland J, Letac B. Percutaneous transluminal valvuloplasty of acquired aortic stenosis in elderly patients: an alternative to valve replacement? *Lancet* 1986;**1**:63–67.
5. NHLBI Balloon Valvuloplasty Registry Investigators Participants. Percutaneous balloon aortic valvuloplasty. Acute and 30-day follow-up results in 674 patients from the NHLBI Balloon Valvuloplasty Registry. *Circulation* 1991;**84**:2383–2397.
6. Otto CM, Mickel MC, Kennedy JW, Alderman EL, Bashore TM, Block PC, Brinker JA, Diver D, Ferguson J, Holmes DR Jr. Three-year outcome after balloon aortic valvuloplasty. Insights into prognosis of valvular aortic stenosis. *Circulation* 1994;**89**:642–650.
7. Cribier A, Eltchaninoff H, Bash A, Borenstein N, Tron C, Bauer F, Derumeaux G, Anselme F, Laborde F, Leon MB. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. *Circulation* 2002;**106**:3006–3008.
8. Webb JG, Pasupati S, Humphries K, Thompson C, Altwegg L, Moss R, Sinhal A, Carere RG, Munt B, Ricci D, Ye J, Cheung A, Lichtenstein SV. Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis. *Circulation* 2007;**116**:755–763.
9. Grube E, Laborde JC, Gerckens U, Felderhoff T, Sauren B, Buellesfeld L, Mueller R, Menichelli M, Schmidt T, Zickmann B, Iversen S, Stone GW. Percutaneous implantation of the CoreValve self-expanding valve prosthesis in high-risk patients with aortic valve disease: the Siegburg first-in-man study. *Circulation* 2006;**114**:1616–1624.
10. Grube E, Schuler G, Buellesfeld L, Gerckens U, Linke A, Wenaweser P, Sauren B, Mohr FW, Walther T, Zickmann B, Iversen S, Felderhoff T, Cartier R, Bonan R. Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patients using the second- and current third-generation self-expanding CoreValve prosthesis: device success and 30-day clinical outcome. *J Am Coll Cardiol* 2007;**50**:69–76.
11. Grube E, Buellesfeld L, Mueller R, Sauren B, Zickmann B, Nair D, Beucher H, Felderhoff T, Iversen S, Gerckens U. Progress and current status of percutaneous aortic valve replacement: results of three device generations of the CoreValve Revalving system. *Circ Cardiovasc Interv* 2008;**1**:167–175.
12. Piazza N, Grube E, Gerckens U, den Heyer P, Linke A, Luha O, Ramondo A, Ussia G, Wenaweser P, Windecker S, Laborde F, de Jaegere P, Serruys PW. Procedural and 30-day outcomes following transcatheter aortic valve implantation using the third generation (18F) CoreValve Revalving system: results from the multicentre, expanded evaluation registry 1-year following CE mark approval. *EuroIntervention* 2008;**4**:242–249.
13. Serruys PW, Piazza N, Cribier A, Webb JG, Laborde JC, de Jaegere P. (eds) *et al. Transcatheter Aortic Valve Implantation. Tips and Tricks to Avoid Failure*. New York: Informa Healthcare; 2010.
14. Vahanian A, Alfieri OR, Al-Attar N, Antunes MJ, Bax J, Cormier B, Cribier A, De JP, Fournial G, Kappetein AP, Kovac J, Ludgate S, Maisano F, Moat N, Mohr FW, Nataf P, Pierard L, Pomar JL, Schofer J, Tornos P, Tuzcu M, van HB, von Segesser LK, Walther T. Transcatheter valve implantation for patients with aortic stenosis: a position statement from the European Association of Cardio-Thoracic Surgery (EACTS) and the European Society of Cardiology (ESC), in collaboration with the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur J Cardiothorac Surg* 2008;**34**:1–8.
15. Rosengart TK, Feldman T, Borger MA, Vassiliades TA Jr, Gillinov AM, Hoercher KJ, Vahanian A, Bonow RO, O'Neill W. Percutaneous and minimally invasive valve procedures: a scientific statement from the American Heart Association Council on Cardiovascular Surgery and Anesthesia, Council on Clinical Cardiology, Functional Genomics and Translational Biology Interdisciplinary Working Group, and Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation* 2008;**117**:1750–1767.
16. Figulla HR, Cremer J, Walther T, Gerckens U, Erbel R, Osterspey A, Zahn R. Positionspapier zur kathetergeführten Aortenklappenintervention. *Der Kardiologe* 2009;**3**:199–206.
17. Buellesfeld L, Wenaweser P, Gerckens U, Mueller R, Sauren B, Latsios G, Zickmann B, Hellige G, Windecker S, Grube E. Transcatheter aortic valve implantation: predictors of procedural success—the Siegburg-Bern experience. *Eur Heart J* 2010;**31**:984–991.
18. Roques F, Nashef SA, Michel P. Risk factors for early mortality after valve surgery in Europe in the 1990s: lessons from the EuroSCORE pilot program. *J Heart Valve Dis* 2001;**10**:572–577.
19. Webb JG, Altwegg L, Boone RH, Cheung A, Ye J, Lichtenstein S, Lee M, Masson JB, Thompson C, Moss R, Carere R, Munt B, Nietlispach F, Humphries K. Transcatheter aortic valve implantation: impact on clinical and valve-related outcomes. *Circulation* 2009;**119**:3009–3016.
20. Sellers RD, Levy MJ, Mplatz K, Lillehei CW. Left retrograde cardangiography in acquired cardiac disease: technique, indications and interpretations in 700 cases. *Am J Cardiol* 1964;**14**:437–447.
21. Gitt AK, Bueno H, Danchin N, Fox K, Hochadel M, Kearney P, Maggioni AP, Opolski G, Seabra-Gomes R, Weidinger F. The role of cardiac registries in evidence-based medicine. *Eur Heart J* 2010;**31**:525–529.
22. Eltchaninoff H. on behalf of the FRANCE Registry Investigators. FRANCE Registry: trans-catheter aortic valve implantation in France. Early results. [Abstract]. *Circulation* 2009.
23. Piazza N, Otten A, Schultz C, Onuma Y, Garcia GH, Boersma E, De JP, Serruys PW. Adherence to patient selection criteria in patients undergoing transcatheter aortic valve implantation with the 18F CoreValve RevalvingTM System—Results from a single-center study. *Heart* 2010;**96**:19–26.
24. Masson JB, Kovac J, Schuler G, Ye J, Cheung A, Kapadia S, Tuzcu ME, Kodali S, Leon MB, Webb JG. Transcatheter aortic valve implantation: review of the nature, management, and avoidance of procedural complications. *JACC Cardiovasc Interv* 2009;**2**:811–820.
25. Zahn R, Schiele R, Kilkowski C, Zeymer U. Aortic insufficiency after transcatheter aortic valve implantation: on the importance to clarify the underlying pathophysiology. *Clin Res Cardiol* 2010;**99**:193–197.
26. Zahn R, Schiele R, Kilkowski C, Klein B, Zeymer U, Werling C, Lehmann A, Gerckens U, Saggau W. Correction of aortic regurgitation after transcatheter aortic valve implantation of the Medtronic CoreValveTM prosthesis due to too low implantation by transcatheter repositioning. *J Heart Valve Dis* 2010; in press.
27. Kahlert P, Knipp SC, Schlamann M, Thielmann M, Al-Rashid F, Weber M, Johansson U, Wendt D, Jakob HG, Forsting M, Sack S, Erbel R, Eggebrecht H. Silent and apparent cerebral ischemia after percutaneous transfemoral aortic valve implantation: a diffusion-weighted magnetic resonance imaging study. *Circulation* 2010;**121**:870–878.
28. Piazza N, Schultz C, de Jaegere PP, Serruys PW. Implantation of two self-expanding aortic bioprosthetic valves during the same procedure-Insights into valve-in-valve implantation ("Russian doll concept"). *Catheter Cardiovasc Interv* 2009;**73**:530–539.
29. Vavouranakis M, Vrachatis DA, Toutouzas KP, Chrysohoou C, Stefanadis C. "Bail out" procedures for malpositioning of aortic valve prosthesis (CoreValve). *Int J Cardiol* 2009; (Epub ahead of print).
30. Shapira Y, Hirsch R, Kornowski R, Hasdai D, Assali A, Vaturi M, Sievert H, Hein R, Battler A, Sagie A. Percutaneous closure of perivalvular leaks with Amplatzer occluders: feasibility, safety, and short-term results. *J Heart Valve Dis* 2007;**16**:305–313.
31. Hammerstingl C, Werner N, Nickenig G. Symptomatic paravalvular leakage after mechanical aortic valve replacement in a critically ill patient: why not just "plug" the hole? *Eur J Echocardiogr* 2009;**10**:576–578.
32. Edwards FH, Peterson ED, Coombs LP, DeLong ER, Jamieson WR, Shroyer ALW, Grover FL. Prediction of operative mortality after valve replacement surgery. *J Am Coll Cardiol* 2001;**37**:885–892.