Beyond the short-term: Clinical outcome and valve performance 2 years after transcatheter aortic valve implantation in 227 patients

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Objective: Although the procedural feasibility of transcatheter aortic valve implantation has been shown by multiple groups, longer-term data are rare. We report on 2-year follow-up clinical and echocardiographic results after transcatheter aortic valve implantation in 227 patients.

Methods: Patients' mean age was 81 ± 7 years, 59% were female, mean European System for Cardiac Operative Risk Evaluation was $21\% \pm 14\%$, mean Society of Thoracic Surgeons score was $7\% \pm 5\%$, and access routes were transfemoral ($n = 164$), transapical ($n = 54$), axillary ($n = 5$), or transaortic ($n = 4$). A CoreValve (Medtronic Inc, Minneapolis, Minn) prosthesis was implanted in 174 patients, and a SAPIEN prosthesis (Edwards Lifesciences, Irvine, Calif) was implanted in 53 patients. Clinical and echocardiographic investigations were performed at 6 months, 1 year, and 2 years.

Results: Survival was 88.5% at 30 days, 75.9% at 6 months, 74.5% at 1 year, and 64.4% at 2 years. Patients improved significantly in New York Heart Association class after 6 months (from 3.2 ± 0.5 to 1.7 ± 0.7 , $P < .001$) and up to 2 years (1.9 ± 0.7). Cumulative incidences of myocardial infarction, stroke, and life-threatening or major bleeding were 2.7%, 6.2%, and 16.2% at 2 years, respectively. The postprocedural mean transprosthetic gradient was 12 ± 4 mm Hg for all valves and did not change up to 2 years, and the effective orifice area was 1.5 ± 0.4 cm² with no change over 2 years of follow-up. Moderate or severe prosthetic regurgitation was present in 8% of patients at 2 years. In 6% of patients, the paravalvular or valvular regurgitation grade increased significantly over time.

Conclusions: With excellent functional recovery of the patients, good systolic valve function, and overall low morbidity at 2 years, transcatheter aortic valve implantation may be considered the treatment of choice for aortic valve stenosis in elderly patients with an increased risk for surgery with a heart-lung machine. (J Thorac Cardiovasc Surg 2012;143:310-7)

A growing elderly population has resulted in an increase of the number of patients with severe aortic valve stenosis. Surgical aortic valve replacement (SAVR) is the gold standard to treat severe aortic stenosis with proven effectiveness and long-term results. However, a significant number of elderly patients are not treated surgically for increased operative risk.¹ Advancements in transcatheter technology have led to the innovation of transcatheter aortic valve implantation (TAVI), with the first patient treated in 2002 by Cribier and colleagues.² With its less-invasive character by avoiding cardiopulmonary bypass and median sternotomy, TAVI is supposed to allow treatment of

candidates at high surgical risk and improve the usually poor prognosis of the natural history of severe aortic stenosis.

Data from the randomized PARTNER trial cohort A³ recently demonstrated noninferiority of TAVI compared with SAVR treatment with a 1-year follow-up. The most recent publications of several registry studies demonstrated reproducible results up to 1 year.⁴⁻⁶ These findings may lead to a broader application of TAVI in elderly patients. The next step must be to collect longer-term data to prove the effectiveness and durability of this new treatment option.

At the German Heart Center Munich, a transcatheter valve program was initiated in 2007. A total of 580 patients who were considered at high operative risk by clinical judgment and clinical scores (European System for Cardiac Operative Risk Evaluation and Society of Thoracic Surgeons score) have been treated with catheter-based aortic valve implantation by transfemoral, transapical, transsubclavian, or direct ascending aortic access since then.

A total of 227 patients have completed 2 years of follow-up and form the study population, which is, to the best of our knowledge, the largest series from a single center with 2 years of data. The goals of this article are therefore to assess mortality, morbidity, and valve function beyond the

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Abbreviations and Acronyms

EOA	= effective orifice area
LVOT	= left ventricular outflow tract
NS	= not significant
SAVR	= surgical aortic valve replacement
TAVI	= transcatheter aortic valve implantation
VARC	= Valve Academic Research Consortium

short-term in a large number of patients in an all-comers situation. To achieve comparability to other reports, the data were prepared according to the end point definitions recently published by the Valve Academic Research Consortium (VARC).⁷

MATERIALS AND METHODS

Patients and Aortic Valve Implantation Technique

Between June 2007 and March 2009, 227 patients underwent TAVI for severe aortic stenosis. Since the introduction of the TAVI program at the German Heart Center Munich in 2007, all patients with severe aortic stenosis at high risk for conventional cardiac surgery with sternotomy and cardiopulmonary bypass are referred to a TAVI multidisciplinary team discussion by cardiac surgeons, interventional cardiologists, and cardioanesthesiologists. The baseline patient characteristics of the study group are summarized in Table 1. Choice of access site (transfemoral, subclavian, transapical, transaortic) was based on a “transfemoral first” approach.^{8,9} If a transfemoral access was not feasible because of diseased peripheral vessels, a subclavian artery or transapical implantation was considered. The transaortic approach was used as a bail-out in selected patients. In this early-experience population, we mainly used the CoreValve prosthesis (Medtronic Inc, Minneapolis, Minn) if a transfemoral access was eligible, because the smaller introduction sheaths (22F) for the SAPIEN (Edwards Lifesciences, Irvine, Calif) prosthesis were not yet available. The logistic European System for Cardiac Operative Risk Evaluation and Society of Thoracic Surgeons score were not different among patients treated with a CoreValve or a SAPIEN prosthesis. Decisions were based on preprocedural imaging diagnostics (computed tomography scan, angiography, and transesophageal and transthoracic echocardiography) performed in all patients.

All implantations were performed in a hybrid theater. Patients were treated under general anesthesia in the study population. Transfemoral TAVI was carried out with the use of percutaneous closure devices or after surgical cut-down of the femoral artery in case of vessel calcifications or severe obesity. The subclavian artery was dissected free for access through a 4- to 5-cm left or right infraclavicular incision. Transapical valve implantation was performed via a left anterolateral minithoracotomy. For transaortic access, an upper median ministernotomy was performed. After balloon valvuloplasty during rapid ventricular pacing, valve deployment was performed under fluoroscopy on the beating heart in case of the self-expanding CoreValve implantation and during an episode of rapid ventricular pacing in case of the balloon-expanding SAPIEN implantation.

After TAVI, all patients were referred to an intensive care unit and monitored for at least 1 day. Heart rate monitoring was continued until discharge. Platelet inhibition was performed by the application of aspirin 100 mg per day lifelong in all patients. After retrograde TAVI, an additional dose of 75 mg clopidogrel was administered for 6 months postprocedurally. Patients with an indication for warfarin therapy received aspirin and warfarin without clopidogrel.

TABLE 1. Patient baseline characteristics (n = 227)

Parameter	Mean ± SD, or n (%)
Mean age, y	81 ± 7
Female	134 (59%)
Logistic euroSCORE	21% ± 14%
STS score	7% ± 5%
BNP value	7100 ± 14,000 U/L
Mean annulus diameter	23 ± 2 mm
Mean aortic valve area	0.6 ± 0.2 cm ²
Mean aortic gradient	48 ± 17 mm Hg
Implanted valve	
CoreValve (Medtronic Inc, Minneapolis, Minn)	174 (77%)
SAPIEN (Edwards Lifesciences, Irvine, Calif)	53 (23%)
Access site	
Transfemoral	164 (72%)
Transapical	54 (24%)
Subclavian artery	5 (2%)
Ascending aorta	4 (2%)
Coronary heart disease	118 (52%)
Peripheral vessel disease	61 (27%)
Cerebrovascular disease	41 (18%)
Previous stroke	26 (11%)
Pulmonary hypertension > 60 mm Hg	53 (23%)
Previous cardiac surgery	42 (19%)
Atrioventricular valve disease	44 (19%)
Lung disease	52 (23%)
Porcelain aorta	15 (7%)
Atrial fibrillation	51 (22%)
NYHA class III or IV	218 (96%)
Ejection fraction < 35%	42 (19%)
Renal insufficiency (creatinine > 1.5 mg/dL)	48 (21%)

SD, Standard deviation; STS, Society of Thoracic Surgeons; BNP, brain natriuretic peptide; euroSCORE, European System for Cardiac Operative Risk Evaluation.

Follow-up

Clinical and echocardiographic follow-up data were collected at discharge, 6 months, 1 year, and 2 years after the procedure.

Echocardiographic investigations were performed by an experienced echocardiographer with an HP Sonos 5500 and HP Sonos 7500 (Hewlett Packard, Palo Alto, Calif). Peak and mean systolic pressure gradients in the left ventricular outflow tract (LVOT) 1 cm below the valve and across the valve were measured in an apical 3- or 5-chamber view using pulsed-wave Doppler for the LVOT measurements and continuous-wave Doppler for the valve measurements, respectively. The LVOT diameter was measured 1 cm below hinge points of the visible prosthetic leaflets from the inner edges of the stent in a parasternal long-axis zoom view. In patients with sinus rhythm, 3 of the best available signals were averaged. If atrial fibrillation was present, a minimum of 5 measurements was averaged. Effective orifice area (EOA) was obtained by using the continuity equation.¹⁰ Prosthetic regurgitation was assessed by a semiquantitative approach using the extent of the regurgitant jet length (color Doppler), pressure half-time measurement (continuous-wave Doppler), in case of transvalvular regurgitation vena contracta measurement, and in case of paravalvular leakage estimation of percentage of circumference. The severity of regurgitation was graded as none, mild, mild-moderate, moderate, moderate-severe, and severe.

Echocardiographic data were available in 203 of 203 living patients (100%) at discharge, 132 of 159 living patients (83%) at 6 months, 119 of 157 living patients (76%) at 1 year, and 90 of 140 living patients (64%) at 2 years.

FIGURE 1. Two-year Kaplan–Meier survival curve of the study population (227 patients). On the x-axis, the time after TAVI is shown in days. Survivals at 30 days, 6 months, 1 year, and 2 years were 88.5%, 75.9%, 74.5%, and 64.4%, respectively. TAVI, Transcatheter aortic valve implantation.

Medical history and clinical state were obtained during the patient visit in our outpatient clinic, from telephone calls, and from medical reports.

End Point Definitions

Primary end point was all-cause mortality. Causes of death were reported according to the VARC definitions⁷ and the guidelines to report morbidity and mortality after valve procedures.¹¹ Myocardial infarction, stroke, bleeding, acute kidney injury, vascular complications, and the combined efficacy end point at 2 years were reported according to the VARC definitions.⁷

Statistics

Continuous variables are presented as means $\pm$ standard deviation. Categorical variables are presented as simple percentages. Kaplan–Meier estimator curves are used to display survival, freedom from stroke, and freedom from bleeding events within 2 years after TAVI. A paired *t* test was performed to evaluate changes in NYHA classification, self-assessed health state, valve areas, and gradients.

All data were analyzed with SPSS software (v. 17 for Windows; SPSS Inc, Chicago, Ill).

RESULTS

Two-Year Survival

Survivals at 30 days, 6 months, 1 year, and 2 years were 88.5%, 75.9%, 74.5%, and 64.4%, respectively. The course of the Kaplan–Meier survival curve (Figure 1) demonstrates that the majority of deaths occurred within 6 months. Beyond that, the curve shows a slow decline. There was no difference in survival between patients treated by antegrade or retrograde implantation route ($P = .254$, log-rank test) or between patients receiving a CoreValve or

TABLE 2. Periprocedural and two-year morbidity

Event	Periprocedural (≤ 72 h) N (%)	Cumulative at 2 y N (%)
Myocardial infarction	4 (1.8%)	6 (2.7%)
Stroke		
Stroke	6 (2.6%)	15 (6.6%)*
TIA	1 (0.4%)	2 (0.9%)
Bleeding		
Life-threatening/disabling	11 (4.8%)	26 (11.4%)
Major	1 (0.4%)	11 (4.8%)
Minor	1 (0.4%)	12 (5.3%)
Acute kidney injury†		
Stage 2	23 (10.1%)	–
Stage 3	18 (7.9%)	–
Vascular complications		–
Major	18 (7.9%)	
Minor	34 (15.0%)	

TIA, Transient ischemic attack. *Stroke rate was 1 of 54 (2%) in transapically treated patients versus 14 of 173 (8%) in retrogradely treated patients, NS. †Stage 1 was not assessed.

SAPIEN prosthesis ($P = .169$, log-rank test). By using the definitions by Akins and colleagues,¹¹ causes of 87 deaths within 2 years were valve-related in 30% of patients, cardiac in 14% of patients, and noncardiac in 44% of patients, whereas 12% of data were missing. By using the new VARC end point definitions for TAVI trials,⁷ causes of death were cardiovascular in 65 patients (75%) and noncardiovascular in 22 patients (25%).

Two-Year Morbidity and Clinical State

Periprocedural and 2-year morbidity are reported according to the VARC criteria and summarized in Table 2.

Kaplan–Meier estimated freedoms from stroke were 94.9%, 94.3%, 94.3%, and 92.5% at 30 days, 6 months, 1 year, and 2 years, respectively. Kaplan–Meier estimated freedom from any bleeding event (minor, major, and life-threatening/disabling) was 90.1%, 83.7%, 80.7%, and 74.1% at 30 days, 6 months, 1 year, and 2 years, respectively.

General health state on a scale of 0% to 100% (100% = best general health state) was $52\% \pm 17\%$ preoperatively and improved to $63\% \pm 21\%$ at 6 months ($P < .001$). This value stayed unchanged up to 2 years ($63\% \pm 17\%$ at 1 year, $63\% \pm 19\%$ at 2 years, not significant [NS], paired *t* test (Figure 2, A).

Mean NYHA classification was 3.2 ± 0.5 preprocedurally, improved to 1.7 ± 0.7 ($P < .001$) at 6 months, stayed unchanged between 6 months and 1 year (1.8 ± 0.6 , $P = .061$), and declined between 1 and 2 years to 1.9 ± 0.7 ($P = .003$, paired *t* test). The distribution of NYHA classes at different time points is shown in Figure 2, B.

Valve Performance

The EOA, as measured by echocardiography, improved significantly from 0.6 ± 0.2 cm² to 1.5 ± 0.4 cm² at

FIGURE 2. Clinical state after TAVI. A, Self-assessed general health state in % (100% is the best health state) at different time points. B, Distribution of NYHA classes at different time points. *CI*, Confidence interval; *NYHA*, New York Heart Association.

discharge ($P < .001$) and stayed stable at 6 months ($1.5 \pm 0.3 \text{ cm}^2$), 1 year ($1.5 \pm 0.3 \text{ cm}^2$), and 2 years ($1.5 \pm 0.3 \text{ cm}^2$, NS, paired t test). Mean aortic gradients decreased significantly from $48 \pm 17 \text{ mm Hg}$ to $12 \pm 4 \text{ mm Hg}$ ($P < .001$) at discharge. No further changes were detected at 6 months ($12 \pm 5 \text{ mm Hg}$), 1 year ($13 \pm 4 \text{ mm Hg}$), or 2 years ($11 \pm 4 \text{ mm Hg}$, NS, paired t test). The systolic valve function data are shown in Figure 3, A and B. Mean gradients of greater

than 20 mm Hg (defined as prosthetic heart valve dysfunction by the VARC⁴) occurred in 1 of 188 patients (0.5%) at discharge and in 3 of 120 patients (2.5%), 5 of 100 patients (5%), and 1 of 71 patients (1.4%) at 6 months, 1 year, and 2 years, respectively. EOAs of less than 1.2 cm^2 (defined as prosthetic heart valve dysfunction by the VARC⁷) occurred in 29 of 175 patients (16.6%), 18 of 108 patients (16.7%), 15 of 90 patients (16.7%), and 9 of 62 patients (14.5%) at

FIGURE 3. Prosthetic valve function up to 2 years. A, EOA as measured by echocardiography at different time points. B, Mean transprosthetic gradient as measured by echocardiography at different time points. C, Distribution and severity of any prosthetic regurgitation at different time points as assessed by echocardiography. D, Evolution of paravalvular regurgitation. On the x-axis, the severity of paravalvular regurgitation at discharge is shown versus the regurgitation grade at 2 years. *CI*, Confidence interval; *EOA*, effective orifice area.

discharge, 6 months, 1 year, and 2 years, respectively. This finding was equally distributed among the different valve types and sizes.

The distribution and severity of prosthetic regurgitation are shown in Figure 3, C. A regurgitation moderate or higher (defined as prosthetic heart valve dysfunction by the VARC⁷) occurred in 22 of 203 patients (11%), 8 of 130 patients (6%), 9 of 116 patients (8%), and 7 of 89 patients (8%) at discharge, 6 months, 1 year, and 2 years, respectively.

In regard to the evolution of paravalvular prosthetic regurgitation from discharge to 2 years, there was an increase of at least 2 of 5 regurgitation grades in less than 5% of the patients, whereas in the majority of the patients the severity of paravalvular regurgitation improved or did not change significantly (Figure 3, D). The incidence of higher grade paravalvular leakages (moderate or higher) was statistically not different between the CoreValve and the SAPIEN prosthesis. A clinically significant central valvular regurgitation occurred in 3 patients (all with a SAPIEN implantation) with a change from none at discharge to moderate ($n = 1$), moderate-severe ($n = 1$), and severe ($n = 1$) at 2 years.

Combined Efficacy End Point

Combined efficacy at 2 years was 52% (104/202 patients who survived 30 days) according to the VARC criteria⁷ with absence of all-cause death after 30 days, hospitalization for symptoms of valve-related or cardiac decompensation, or prosthetic valve dysfunction (aortic valve area $< 1.2 \text{ cm}^2$ and mean aortic valve gradient $\geq 20 \text{ mm Hg}$ or peak velocity $\geq 3 \text{ m/s}$, or moderate or severe prosthetic valve aortic regurgitation).

DISCUSSION

The new catheter-based valve treatment options will change cardiovascular medicine toward less-invasive treatment with avoidance of cardiopulmonary bypass and sternotomy. With the evidence of noninferiority compared with SAVR in cohort A of the randomized PARTNER trial,³ indications and guidelines will be adopted. However, only periprocedural noninferiority is not sufficient, and longer-term data will be needed. Our data may add important information of the longer-term impact of TAVI therapy.

The findings of our study with a 2 year follow-up of 227 patients after TAVI demonstrate 1) a considerable periprocedural mortality, as was reported by other groups in the early days of TAVI, and low mortality after 6 months; 2) efficacy of the treatment with persistent symptom relief; 3) a low morbidity rate at 2 years except for bleeding events; and 4) a good systolic valve function, whereas prosthetic regurgitation might need further attention.

Survival

The early mortality reported in this early-experience cohort is considerable with 11.5% at 30 days, which compares

well with reports from other groups in 2007 and 2009 with 30-day mortality rates of 12% to 23%.¹²⁻¹⁶ More recent studies demonstrate lower 30-day mortality rates of less than 10%, assuming that there was a “worldwide learning curve” leading to improved results in centers that started later with more experienced proctors and improved devices. Among our most recent 200 TAVI cases (from April 2010) we observed a Kaplan–Meier 30-day survival of 96.6% (Lange et al, unpublished data from the Munich Heart Center database, 2011). The majority of deaths in the study population occurred within 6 months. Beyond 6 months and up to 2 years, only 7.5% (17/227) of the reported patients died. Because the longer-term data are the focus of the present study, we assume a low mortality beyond the short-term and a durable result after TAVI. We might anticipate future 2-year survival of 85% to 90% after TAVI. This may lead to widening the indications for TAVI for younger high-risk patients. In contrast with data from the European PARTNER trial,³ we did not observe differences in 30-day or longer-term survival between antegrade or retrograde implantation routes.

Causes of death were cardiovascular in the majority of the cases when reported according to the VARC definitions, which also include unknown causes of death.⁷ By using the surgical guidelines to report mortality,¹¹ approximately half of the deaths were noncardiac and therefore related to the comorbidities of the patients. However, to achieve comparability to future TAVI studies, it is reasonable to refer to the VARC consensus report.

Clinical State

The short-term improvement in NYHA classification has been reported after treatment of aortic stenosis by TAVI.^{8,17,18} Our data demonstrate stable conditions at 1 year and a slight decline after 2 years with less patients being in NYHA class I. Still, more than 80% of the patients are in NYHA class I or II at 2 years, demonstrating the durable effectiveness of the treatment. Self-assessed general health state remains stable up to 2 years and is significantly improved compared with preprocedural assessment. These data demonstrate a durable symptom relief and thus the longer-term effectiveness of TAVI treatment. The findings justify also offering TAVI treatment to lower-risk octogenarian patients.

Morbidity

Periprocedural incidences of myocardial infarction and stroke rates were low and comparable to other reports,⁴ and only few events occurred within 2 years. Of note, in our cohort, major stroke rate was considerably lower in transapically treated patients (1/54 [2%] vs 14/173 [8%], NS). The hypothesis that the risk of calcium embolization might decrease with less manipulation in the aortic arch via an antegrade route has been proposed¹⁹ but was not proven by all reports.^{5,20} Our observation has encouraged

us to consider a transapical access as the first choice in patients with a history of cerebral infarction. Myocardial infarction is an infrequent complication at long-term and is usually associated with preexisting coronary heart disease. A rare TAVI-specific procedural complication is coronary obstruction with native calcium^{21,22} that may be foreseen in patients with a narrow aortic root. In these patients, implantation of the self-expanding CoreValve might be beneficial. Acute kidney injury with the need for dialysis, which occurred in 8% in the current study, is a frequent problem after TAVI in an elderly cohort with a relatively high incidence of preprocedural renal insufficiency. Reports from other groups indicate 2.5% to 9% new dialysis after TAVI.^{20,23,24} Another study from our group showed that there was an increased in-hospital mortality in patients with acute kidney injury and that preoperative creatinine level is a predictor of acute kidney injury.²⁵ Thus, in patients with elevated creatinine levels, special attention should be paid to fluid and electrolyte management.

Vascular complications may occur in 9% to 30% of transfemoral TAVI cases and have been reported to have an impact on outcomes after TAVI.²⁶⁻²⁸ Previous data from our group²⁹ demonstrate that there is a certain learning curve with large sheaths and vessel closure devices that were not constructed for these large diameters. Future techniques (smaller sheaths, more optimal closure devices) might further reduce these complications. In patients with heavily calcified vessels, we rather opt for a surgical cut-down.

There are few reports on bleeding events beyond procedural data, the incidences ranging from 3% to 30% at 1 year.^{5,6} Bleeding events were frequent in the study population with a Kaplan–Meier estimated freedom from life-threatening or major bleeding of 80% at 2 years. Freedom from any bleeding event was 74% at 2 years. Some 78% (49/63) of all bleeding events occurred beyond the periprocedural 72 hours, assuming that bleeding might be a persistent problem after TAVI. After SAVR with bioprostheses, freedom from bleeding is reported to be as high as 95% at 18 years³⁰ in the typical surgical patient population without anticoagulation, but there is evidence that hemorrhagic complications after SAVR increase with patient age.³¹ The typical TAVI population consists of elderly patients with multiple comorbidities, and thus, dual platelet inhibition, which is empirically administered analogous to percutaneous coronary interventions, might significantly increase the bleeding risk. A larger randomized study is needed to clarify whether these elderly patients could undergo TAVI without dual antiplatelet aggregation therapy.

Valve Performance

As expected for biological valves, there were stable gradients and EOAs at 2 years. Criteria of valve dysfunction were proposed by the VARC. Accordingly, few patients

have an increased gradient of more than 20 mm Hg at 2 years, whereas a reduced valve orifice area of less than 1.2 cm² was found in 14.5% of the patients. In association with the low gradients, this finding is clinically insignificant. In addition, for EOA calculation, the LVOT measurement is the most sensitive parameter. In the present study, the LVOT diameter was measured 1 cm below the hinge points of the visible prosthetic leaflets from inner edges of the stent in a parasternal long-axis zoom view. Other authors measured the LVOT “just underneath the prosthesis”³² or “just below hinge points of the visible prosthetic leaflets from inner edges of the stent.”³³ Thus, because exact definitions for LVOT measurements with the new catheter valves are missing, comparison of EOA data from different groups is limited. Nonetheless, the favorable systolic function of the catheter valves might lead to anticipation of a low degeneration rate and long-term durability. Another concern after TAVI is moderate or severe prosthetic regurgitation, which occurred in 8% of patients at 2 years. There is evidence of impaired in-hospital³⁴ or 1-year⁶ survival with clinically relevant prosthesis regurgitation. Our data demonstrate that paravalvular regurgitation does not decrease in all patients after TAVI (Figure 3, D). Therefore, new technologies addressing this problem are needed. We also identified 3 patients after SAPIEN valve implantation with increasing central leakage at 2 years. This finding might be a sequel of balloon expansion of the valve or a degenerative process.

Combined Efficacy End Point

This is the first study to present the combined efficacy end point according to the VARC criteria at 2 years. The combined efficacy in 227 patients after TAVI at 2 years was 52% in the current study and will have to be compared with results from other reports.

CONCLUSIONS

With excellent functional recovery of patients, good systolic valve function, and overall low morbidity at 2 years, TAVI can be considered the treatment of choice for aortic valve stenosis in elderly patients with increased risk for surgery with a heart–lung machine. Because outcomes were not compared with a control group, future studies are needed to prove an advantage over conventional SAVR.

Prosthetic regurgitation and bleeding events should be addressed in future studies for evaluation of the impact on long-term outcomes. The combined efficacy at 2 years was 52% in the current study and will have to be compared with the results from other reports.

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Discussion

Dr Gregory Fontana (Los Angeles, Calif). Dr Bleiziffer, your program in Munich is unique in that this is one of the largest TAVI experiences in the world but includes both the balloon-expandable and self-expanding devices, and, arguably, the most surgeon-driven program that I am aware of. Drs. Bleiziffer and Lange work as surgeons with all access approaches along with their cardiologists as primary operators and should serve as a model for other surgical programs.

We have limited data available on 2-year clinical and echocardiography follow-up. The data are critical to our development of guidelines for TAVI indications. These are truly excellent results, especially considering the series represent the initial experience with first-generation devices and represent multiple access techniques. I have 2 questions for you.

The first one is about durability. Ten of the patients had mean gradients greater than 20 mm Hg in follow-up, and many more had an aortic valve area less than 1.2 cm². Were you able to identify any leaflet pathology by echocardiography or evidence of early degeneration, and if so, did the porcine or bovine tissue perform differently?

Dr Bleiziffer. What I have in mind is that these small valve orifice areas are somehow difficult to interpret, we think, because

there are no real echocardiography guidelines on how to measure a transcatheter bioprosthesis. The most sensitive parameter for EOA calculation in echocardiography is the LVOT diameter, and it is unclear where should this be measured, below the stent, or within the stent. There are no guidelines. What we do is we measure within the stent, and that might contribute as to why we have slightly smaller EOAs than may be reported from other groups. We think this is not clinically significant in terms of the very low gradients we receive with catheter valves. So maybe these end point definitions proposed by the VARC could also undergo some revision in the future.

Dr Fontana. So none of the valves that you looked at that had these gradients (eg, >20 mm) had anything looking morphologically abnormal? It was just a gradient, a physiologic measurement?

Dr Bleiziffer. No, they did not look abnormal.

Dr Fontana. Second question. Despite your transfemoral-first approach, your transapical and transfemoral survivals are similar, when typically transapical carries a greater risk because of the atherosclerotic burden, at least in the 30-day mortality rates in many series. In addition, there were fewer strokes in the transapical group, only 1, versus 14 in the transfemoral group. Have the results of the first 227 patients influenced your algorithm for valve choice or access strategy?

Dr Bleiziffer. Yes, it has. When patients have stroke in their history, we would rather go for a transapical approach.

Dr Fontana. Thank you.

Dr Eric Manasse (Milano, Italy). Was the rate of readmission during the first year of follow-up different between the cohort of patients who had more than I+ paravalvular regurgitation or intra-aortic and those without regurgitation? Did you perform autopsies in the patients who died in your area?

Dr Bleiziffer. To the first question, we did a subanalysis and saw an increased mortality in patients who left the hospital with a moderate or a higher grade of paravalvular regurgitation, but these were only initial analyses, so we will have a closer look at

that in the future. And, no, I am not aware of autopsies that have been performed.

Dr Manasse. Did you observe an ongoing event of strokes in the late follow-up?

Dr Bleiziffer. Yes, but the stroke rate was low. It was 0.9% of the patients after the postprocedural period, very low.

Dr Tufan Paker (Istanbul, Turkey). I would like to learn about your preferred technique if the patient receiving TAVI has concomitant coronary artery disease. Do you deal with it at the same time or is a second procedure done?

Dr Bleiziffer. We do it as a staged procedure. If there is any coronary that needs intervention, we do it before the TAVI procedure, because we think the rapid pacing that has to be done, at least for balloon valvuloplasty, would be a risk with significant coronary stenosis.

Dr Paker. How do you explain cardiac reason for death dealing with myocardial infarction? I mean, if you do the coronary pathology at the same time, do you change the postoperative results?

Dr Bleiziffer. I don't understand your question.

Dr Paker. When you look at your postoperative results, myocardial infarction is one of the reasons for a cardiac nature death.

Dr Bleiziffer. Yes, but that was rare. There were some single patients who had coronary occlusion during the procedure and died of myocardial infarction, for example.

Dr Paker. Thank you.

Dr Leonard Girardi (New York, NY). I have 1 question for you. On the curves that you presented out to 2 years, there were an ever-increasing number of patients who were no longer in NYHA class I and an ever-increasing number of patients in II and III and even III and IV. Have you taken a look at those patients and what are you ascribing that change to, because you have so many patients in III and IV to start, a very good outcome in the first 6 months, and then it seems to be declining. Is there any reason for that?

Dr Bleiziffer. Of course, I don't have any detailed data on that with me, but those are elderly patients and they also have comorbidities, and, of course, their clinical state gets worse and within years.