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EXPEDITED REVIEW

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

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Objectives We sought to determine both the procedural performance and safety of percutaneous implantation of the second (21-French [F])- and third (18-F)-generation CoreValve aortic valve prosthesis (CoreValve Inc., Irvine, California).

Background Percutaneous aortic valve replacement represents an emerging alternative therapy for high-risk and inoperable patients with severe symptomatic aortic valve stenosis.

Methods Patients with: 1) symptomatic, severe aortic valve stenosis (area <1 cm^2); 2) age $\geq$80 years with a logistic EuroSCORE $\geq$20% (21-F group) or age $\geq$75 years with a logistic EuroSCORE $\geq$15% (18-F group); or 3) age $\geq$65 years plus additional prespecified risk factors were included. Introduction of the 18-F device enabled the transition from a multidisciplinary approach involving general anesthesia, surgical cut-down, and cardiopulmonary bypass to a truly percutaneous approach under local anesthesia without hemodynamic support.

Results A total of 86 patients (21-F, n = 50; 18-F, n = 36) with a mean valve area of 0.66 $\pm$ 0.19 cm^2 (21-F) and 0.54 $\pm$ 0.15 cm^2 (18-F), a mean age of 81.3 $\pm$ 5.2 years (21-F) and 83.4 $\pm$ 6.7 years (18-F), and a mean logistic EuroSCORE of 23.4 $\pm$ 13.5% (21-F) and 19.1 $\pm$ 11.1% (18-F) were recruited. Acute device success was 88%. Successful device implantation resulted in a marked reduction of aortic transvalvular gradients (mean pre 43.7 mm Hg vs. post 9.0 mm Hg, $p < 0.001$) with aortic regurgitation grade remaining unchanged. Acute procedural success rate was 74% (21-F: 78%; 18-F: 69%). Procedural mortality was 6%. Overall 30-day mortality rate was 12%; the combined rate of death, stroke, and myocardial infarction was 22%.

Conclusions Treatment of severe aortic valve stenosis in high-risk patients with percutaneous implantation of the CoreValve prosthesis is feasible and associated with a lower mortality rate than predicted by risk algorithms. (J Am Coll Cardiol 2007;50:69–76) © 2007 by the American College of Cardiology Foundation

Cardiac valve diseases are considered as a major public health problem. A recent large population-based study revealed a steep increase of the prevalence of valvular heart diseases with age (1). In adults $\geq$75 years of age, aortic stenosis was present in as many as 4.6%. Of note, not only does symptomatic valvular heart disease become more prevalent with age but also comorbidities that increase the risk for an operative valve replacement. The latter is the current standard therapy for aortic stenosis, with an operative mortality of $<$5% for first-time isolated aortic valve replacements (2). However, several factors have been identified as independently predictive for an increased risk of periprocedural or postprocedural mortality (3). For example, in patients with reduced systolic left ventricular ejection fraction, the rate of mortality increases to 10% (4). Furthermore, advanced age and renal disease increase the operative

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Abbreviations and Acronyms

AS = aortic stenosis
F = French
MACCE = major adverse cardiovascular and cerebral event
MI = myocardial infarction

mortality risk markedly (odds ratio 4.2) (4,5). The need for alternative treatment options for patients with severe aortic stenosis (AS), particularly in combination with comorbidities, is justified by the fact that as many as one-third of elderly comorbid patients with symptomatic AS were denied surgery in the EuroHeart survey (6). Especially for high-risk patients, the "gold standard" treatment with a conventional surgery may not be the best option. A less-invasive procedure to minimize cardiovascular complications associated with general anesthesia, thoracotomy, and heart-lung machine is required.

After the evaluation of a percutaneous valve replacement strategy in animal models (7–9), Cribier et al. (10) performed the first human implantation of a balloon-expandable aortic valve prosthesis with encouraging results. Nevertheless, the primarily used antegrade approach for valve implantation has shown to be very challenging (11). The innovation of a more flexible delivery catheter for the retrograde approach recently improved the procedural outcome (12). To avoid access site problems and to enhance stabilization during valve implantation, a transapical approach has been developed and is currently being tested (13,14).

An alternative technique with retrograde implantation of a self-expanding valve prosthesis (CoreValve prosthesis, CoreValve Inc., Irvine, California), which uses a porcine bioprosthesis within a nitinol frame, was first described in 2005 by our group (15). Subsequently, we have shown that the implantation procedure of the first- (24-French [F]) and second-generation (21-F) CoreValve device in 10 and 15 patients, respectively, is feasible and when successful results in marked hemodynamic and clinical improvements (16). Further device modifications have been realized since then and have reduced the sheath size from the initial 24-F to the present 18-F device (third-generation) (Figs. 1 and 2). In this report, we describe the procedural success and clinical outcome up to 30 days after implantation of the second- (21-F) and current third-generation (18-F) of the CoreValve revalving system.

Methods

Study design. A prospective multicenter, single-arm safety and performance study was performed that included the HELIOS Heart Center Siegburg, Germany, the Heart Center Leipzig, Germany, and the Institut de Cardiologie de Montreal, Canada. Our objective was to evaluate the feasibility, safety, and clinical outcome of implantation of the 21-F and 18-F self-expanding CoreValve aortic valve prosthesis in high-risk patients with aortic valve disease (stenosis with or without regurgitation) using a retrograde percutaneous transvascular approach. The study was approved by the local medical ethics committees, and all patients signed informed, written consent.

Patient population. A total of 86 consecutive patients were included in the present analysis. The study started in August 2005 with the 21-F device and enrolled a total of 50 patients (n = 25 in Siegburg, n = 14 in Leipzig, and n = 11 in Montreal). At the end of September 2006, the 18-F device became available and was later used exclusively for 36

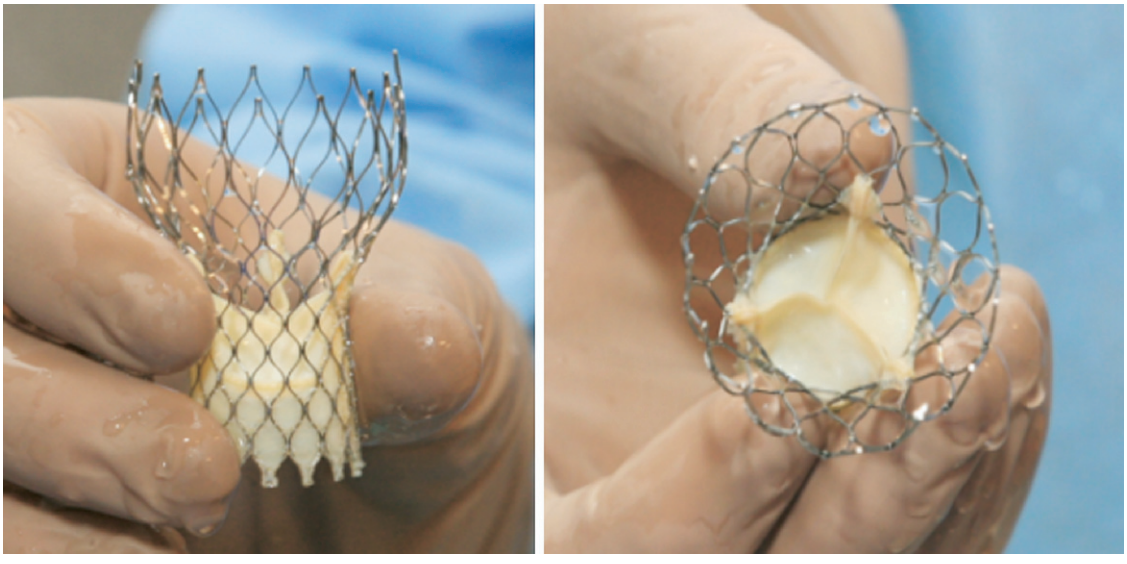

Figure 1 CoreValve Prosthesis

Third generation of the CoreValve prosthesis (18-F) before loading into the delivery catheter.

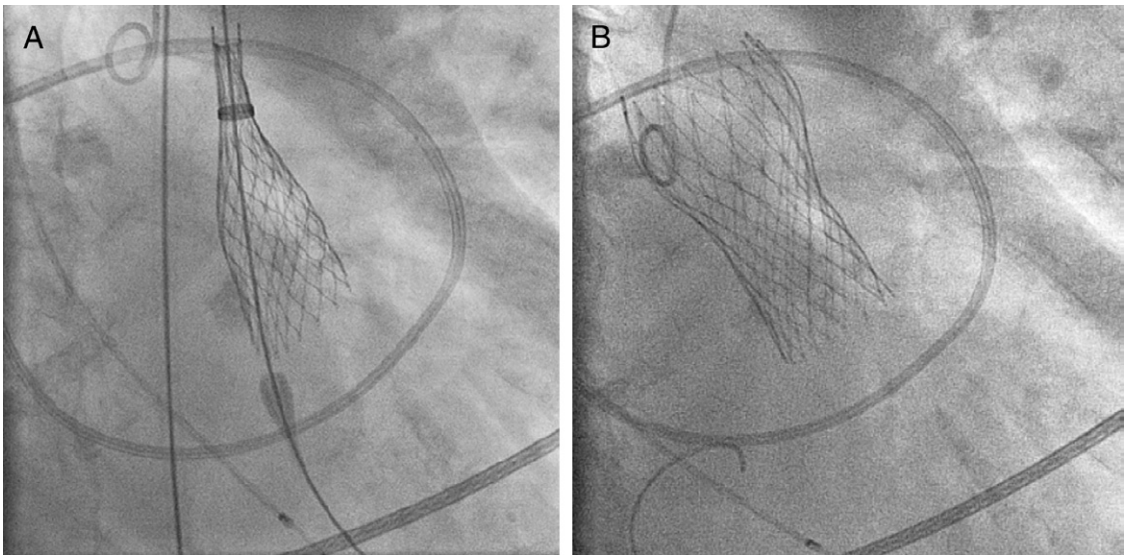

Figure 2 **Implantation of the CoreValve Prosthesis**

(A) Prosthesis partially released (still possible to retrieve the valve); **(B)** prosthesis completely released.

patients until February 2007 (n = 18 in Siegburg, n = 10 in Leipzig, and n = 8 in Montreal).

Inclusion criteria were the following: 1) severe native aortic valve stenosis with an area <1 cm^2 or <0.6 cm^2/m^2, with or without aortic valve regurgitation and age $\geq$80 years or a logistic EuroSCORE of $\geq$20% for the 21-F group and age $\geq$75 years or logistic EuroSCORE $\geq$15% for the 18-F group, respectively, or age $\geq$65 years and at least one of the following complications: cirrhosis of liver, pulmonary insufficiency (forced expiratory volume in one second <1 l), previous cardiac surgery, pulmonary hypertension >60 mm Hg, porcelain aorta, recurrent pulmonary embolus, right ventricular insufficiency, thoracic burning sequelae with contraindication for open chest surgery, history of mediastinum radiotherapy, severe connective tissue disease with contraindication for surgery, or cachexia (body mass index $\leq$18 kg/m^2). 2) Echocardiographic aortic valve annulus diameter $\geq$20 and $\leq$27 mm. 3) Diameter of the ascending aorta $\leq$45 mm at the sinotubular junction.

Exclusion criteria included hypersensitivity or contraindication to any study medication; sepsis or active endocarditis; excessive femoral, iliac or aortic atherosclerosis, calcification, or tortuosity; aortic aneurysm; bleeding diathesis or coagulopathy; recent myocardial infarction or cerebrovascular accident; mitral or tricuspid valvular insufficiency ($>$ grade II); left ventricular or atrial thrombus; uncontrolled atrial fibrillation; previous aortic valve replacement; polyarterial patients with either severe iliac or aortic vascular condition that make an insertion impossible or symptomatic carotid or vertebral arteries narrowing ($>$70%) disease or abdominal/thoracic aortic aneurysm; progressive disease with life expectancy <1 year; pregnancy; or creatinine clearance <20 ml/min.

Preinterventional morphological patient screening included transthoracic as well as transesophageal echocardiography, carotid and arteriovenous duplex ultrasonography, computed tomographic angiography, optional cardiac magnetic resonance imaging, and invasive cardiac evaluation with coronary 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 there was a consensus among an independent cardiologist and cardiac surgeon that conventional surgery would be associated with excessive morbidity and mortality.

Device description and procedure. The CoreValve aortic valve prosthesis consists of a trileaflet bioprosthetic porcine pericardial tissue valve, which is mounted and sutured in a self-expanding nitinol stent (Fig. 1). The prosthetic frame (stent) is manufactured by laser cutting and has an overall length of 50 mm. Further details of the device have been described previously (17). The second-generation (21-F) and third-generation (18-F) (Fig. 1) devices were used in the present study.

Vascular access was obtained either with or without standard surgical cutdown of the common iliac artery, the common femoral artery, or the subclavian artery. The procedure was performed with the patient under general anesthesia or with just local anesthesia in combination with a mild systemic sedative/analgesic treatment. The use of transesophageal echocardiographic guidance and the type of hemodynamic support (extracorporeal percutaneous femorofemoral bypass, tandem heart, extracorporeal membrane oxygenation, or none) was left to the discretion of the

operator. Balloon valvuloplasty with a 20- to 23-mm balloon under rapid pacing was performed before device placement, after which over a stiff guidewire, placed in the left ventricle, the device was deployed retrogradely under fluoroscopic guidance. If used, extracorporal circulatory support was activated just before device placement across the native valve position and terminated immediately after withdrawal of the delivery catheter and confirmation of adequate valve function. Hemodynamic and echocardiographic outcomes were assessed serially during the procedure. Evaluation of postprocedural regurgitations was performed using a supra-aortic angiogram and echo. After the procedure, the patients were transferred to the intensive care unit.

Clinical follow-up and transthoracic echocardiography were performed postprocedure, at hospital discharge, and 30 days after device implantation. Additional clinical and echocardiographic follow-up is planned on a yearly basis for at least 4 years after the implantation.

Antiplatelet and antithrombotic medication. Acetylsalicylic acid (100 mg/day) was administered before the procedure and continued indefinitely. In addition, all patients received clopidogrel (300-mg loading dose), followed by 75 mg daily for at least 6 to 12 months. During the intervention, the patient received weight-adjusted intravenous heparin to achieve an activated clotting time of 300 to 350 s for the duration of the procedure.

Definitions and statistical analysis. Clinical adverse events were adjudicated by an independent clinical events committee. Device success was defined as stable device placement and adequate function as assessed by angiography and echocardiography. Acute procedural success was defined as device success with absence of periprocedural major adverse cardiovascular and cerebral events (MACCEs) in the first 48 h after device implantation. Major adverse cardiovascular and cerebral events consisted of death from any cause, myocardial infarction (creatine kinase-myocardial band $>2 \times$ the upper limit of normal), cardiac tamponade, stroke (as assessed by routine neurological assessment before and after procedure and before hospital discharge), urgent or emergent conversion to surgery or balloon valvuloplasty, emergent percutaneous coronary intervention, cardiogenic shock, endocarditis or aortic dissection. Major bleeding was defined as hemorrhage requiring surgery and/or 3 or more units of blood transfusion.

Categorical variables are presented as frequencies and were compared by chi-square test. Continuous variables are presented as mean ± standard deviation. A 2-tailed unpaired Student *t* test for comparison between groups and a paired Student t test for intragroup comparison was used. A p value of <0.05 was considered statistically significant.

Results

Patient population. Between August 2005 and February 2007, 86 symptomatic patients (30 men and 56 women) with a mean age of 82 years, were included in the study. A total of 50 patients were enrolled for the 21-F and 36 patients for the 18-F device, respectively. Baseline patient characteristics are given in Table 1.

All patients had severe symptomatic AS with a mean transvalvular gradient of 43.7 ± 15.4 mm Hg and peak transvalvular aortic pressure gradient of 70.9 ± 22.8 mm Hg. The preprocedural mean calculated aortic valve area was 0.60 ± 0.16 cm^2 (range 0.3 to 1.0 cm^2) and the systolic left ventricular ejection fraction 54.1 ± 16.3% (range 19% to 80%). In 18 patients, a mild-to-moderate aortic regurgitation was present (n = 16 with grade 2+, n = 2 with grade 3+, respectively) whereas 68 patients presented with a grade 1+ (n = 48) or no aortic (n = 20) regurgitation. The mean calculated logistic EuroSCORE of the study population was 21.7 ± 12.6% and 83% of patients were New York Heart Association functional class III or IV.

Acute procedural and clinical results. Acute device success was achieved in 76 (88%) of 86 enrolled patients (Table 2) with no difference between the 2 groups (88% vs. 89%, p = NS) (Table 2). In 6 patients, misplacement of the valve led to urgent conversion to operative valve replacement (Table 2). In 2 patients, the device did not cross the heavily calcified native valve despite a balloon predilatation and, therefore, only a balloon valvuloplasty was performed. In 2 patients, a suboptimal placement of the prosthesis with remaining aortic

Table 1 Baseline Characteristics (Intention-to-Treat Population)

	Overall (n = 86)	21-F (n = 50)	18-F (n = 36)
Age, years ± SD	82.2 ± 5.9	81.3 ± 5.2	83.4 ± 6.7
Female gender, n (%)	56 (65)	33 (66)	23 (64)
Hypertension, n (%)	62 (72)	36 (72)	26 (72)
Diabetes mellitus, n (%)	27 (31)	18 (36)	9 (25)
Peripheral vascular disease, n (%)	11 (13)	6 (12)	5 (14)
Coronary artery disease, n (%)	48 (56)	24 (48)	24 (67)
Congestive heart failure, n (%)	19 (22)	11 (22)	8 (22)
Prior myocardial infarction, n (%)	11 (13)	7 (14)	4 (11)
Prior stroke, n (%)	10 (11)	3 (6)	7 (20)
Prior bypass graft surgery, n (%)	16 (19)	10 (20)	6 (17)
Prior percutaneous coronary intervention, n (%)	14 (16)	9 (18)	5 (14)
Prior valvuloplasty, n (%)	2 (3)	1 (2)	1 (3)
NYHA functional class			
I and II	15 (17)	7 (14)	8 (22)
III and IV	71 (83)	43 (86)	28 (77)
Left ventricular ejection fraction, % (mean)	54 ± 16	52 ± 18	57 ± 14
Logistic EuroSCORE, % (mean ± SD)	21.7 ± 12.6	23.4 ± 13.5	19.1 ± 11.1
Peak pressure gradient, mm Hg (mean ± SD)	70.9 ± 22.8	66.0 ± 18.8	78.3 ± 26.0*
Mean pressure gradient, mm Hg (mean ± SD)	43.7 ± 15.4	39.5 ± 13.7	49.7 ± 15.9†
Aortic valve area, cm^2 (mean ± SD)	0.60 ± 0.16	0.66 ± 0.19	0.54 ± 0.15‡

*p = 0.003, †p = 0.016, ‡p = 0.003 for 21-F versus 18-F; all other p = NS.
NYHA = New York Heart Association.

Table 2 Procedural Data

	Overall (n = 86)	21-F (n = 50)	18-F (n = 36)
Acute device success, n (%)	76 (88)	44 (88)	32 (89)
Conversion to surgery, n (%)	6 (6)	4 (8)	2 (6)
Only valvuloplasty, n (%)	2 (2)	2 (4)	0
Valve in valve placement, n (%)	2 (2)	0	2 (6)
Valvuloplasty after valve implantation,* n (%)	21 (24)	7 (14)	14 (39)
Procedural time, min (mean ± SD)	173 ± 64	189 ± 55	148 ± 50†

*p = 0.009, based on 76 patients with successful valve implantation. †p = 0.002 for 21-F versus 18-F; all other p = NS.

regurgitation had to be corrected by implantation of a second CoreValve prosthesis (prosthesis-in-prosthesis).

The overall procedural success rate, that includes all MACCE within 48 h (26%) after implantation was 74% (78% for 21-F and 69% for 18-F, p = NS) (Table 3). The overall procedural MACCE rate excluding patients with conversion to valvuloplasty or surgery was 18%. Five deaths occurred periprocedurally: 2 patients died after conversion to balloon valvuloplasty (n = 1) and surgical aortic valve replacement (n = 1), respectively; 3 patients died of pericardial tamponade. The combined procedural rate of death, stroke, and myocardial infarction was 14%.

Overall, cardiac tamponades were observed in a total of 9 patients: 6 of them most likely were caused by wire perforations of the ventricle and treated either with pericardial puncture or surgical pericardiotomy. Two cases of tamponade occurred in the postoperative phase after urgent conversion to operative valve replacement, and one case of tamponade occurred in the postprocedural phase after pacemaker implantation. Neither an aortic dissection nor procedural coronary flow impairment was observed in the entire study population.

Table 3 Procedural MACCE* (Nonhierarchical)

	Overall (n = 86)	21-F (n = 50)	18-F (n = 36)
Death, n (%)	5 (6)	2 (4)	3 (8)
Stroke, n (%)	9 (10)	5 (10)	4 (11)
Major, n (%)	3 (4)	2 (4)	1 (3)
Minor, n (%)	6 (7)	3 (6)	3 (8)
Myocardial infarction, n (%)	0	0	0
Cardiac tamponade			
Procedure related	6 (7)	1 (2)	5 (14)
After conversion to surgery	2 (2)	2 (4)	0
Aortic dissection, n (%)	0	0	0
Coronary flow impairment, n (%)	0	0	0
Conversion to surgery or valvuloplasty, n (%)	8 (9)	6 (12)	2 (6)
Procedural MACCE, n (%)	22 (26)	11 (22)	11 (28)
Procedural MACCE, excluding conversions,† n (%)	14 (18)	5 (11)	9 (26)
Combined death, stroke, MI, n (%)	14 (17)	7 (14)	7 (19)
Procedural success, n (%)	64 (74)	39 (78)	25 (69)

*Includes MACCE within 48 h of valve implantation. †Based on 78 patients with device success, including valve-in-valve (n = 44 for 21-F; n = 34 for 18-F); no significant differences between groups.

MACCE = major adverse cardiac and cerebral events; MI = myocardial infarction; NYHA = New York Heart Association.

Table 4 30-Day Clinical Outcome

	Overall	21-F	18-F
Overall	n = 86	n = 50	n = 36
Death, n (%)	10 (12)	5 (10)	5 (14)
Cardiovascular death, n (%)	9 (10)	5 (10)	4 (11)
MI, n (%)	1 (1)	1 (2)	0
Stroke, n (%)	9 (10)	5 (10)	4 (11)
Combined death, stroke, MI, n (%)	19 (22)	10 (20)	9 (25)
In patients with acute device success	n = 76	n = 44	n = 32
Death, n (%)	7 (9)	3 (7)	4 (13)
Cardiovascular death, n (%)	6 (8)	3 (7)	3 (9)
MI, n (%)	1 (1)	1 (2)	0
Stroke, n (%)	7 (9)	4 (9)	3 (9)
Combined death, stroke, MI, n (%)	14 (18)	7 (16)	7 (22)
In patients with procedural success	n = 63	n = 38	n = 25
Death, n (%)	3 (5)	2 (5)	1 (4)
Cardiovascular death, n (%)	2 (3)	2 (5)	0
MI, n (%)	0	0	0
Stroke, n (%)	0	0	0
Combined death, stroke, MI, n (%)	3 (5)	2 (5)	1 (4)

No significant differences between groups.
MI= myocardial infarction.

Follow-up clinical results. Overall mortality at 30 days was 12% in the intent-to-treat population with a combined rate of death, stroke and myocardial infarction of 22%. In patients with device and procedural success, the mortality was 9% and 5%, respectively (Table 4). With respect to the functional class, a remarkable relief of symptoms was observed with a decline from a mean New York Heart Association functional class of 2.85 ± 0.73 before to 1.85 ± 0.60 after valve implantation ($p < 0.001$).

Acute and follow-up echocardiographic results. The baseline echocardiographic measurements are given in Table 1. In case of a successful procedure, a striking improvement of hemodynamic parameters was observed in all patients, as illustrated in Figure 3 (example of a hemodynamic tracing at baseline and postimplantation) and Figure 4 (mean overall gradient pre vs. postvalve implantation). In 51 (66%) patients, the aortic regurgitation grade remained unchanged or was even reduced after the procedure. On the contrary, a worsening of the preinterventional aortic regurgitation grade after the procedure to grade 2+ was noted in 15 (20%) patients and from 0 to grade 1+ in 11 (14%). All of them were related to paravalvlar leakages as determined by echocardiography. Severe postprocedural aortic regurgitation (3+ or 4+) was not present in any patient. After 30 days, the overall grade of aortic regurgitation remained unchanged with a decrease of aortic regurgitation from grade 2+ to 1+ or 0 in 6 patients and an increase from grade 1+ to 2+ in 5 patients.

Comparison of procedural 21-F versus 18-F data. With the use of the smaller 18-F sheath significant improvements

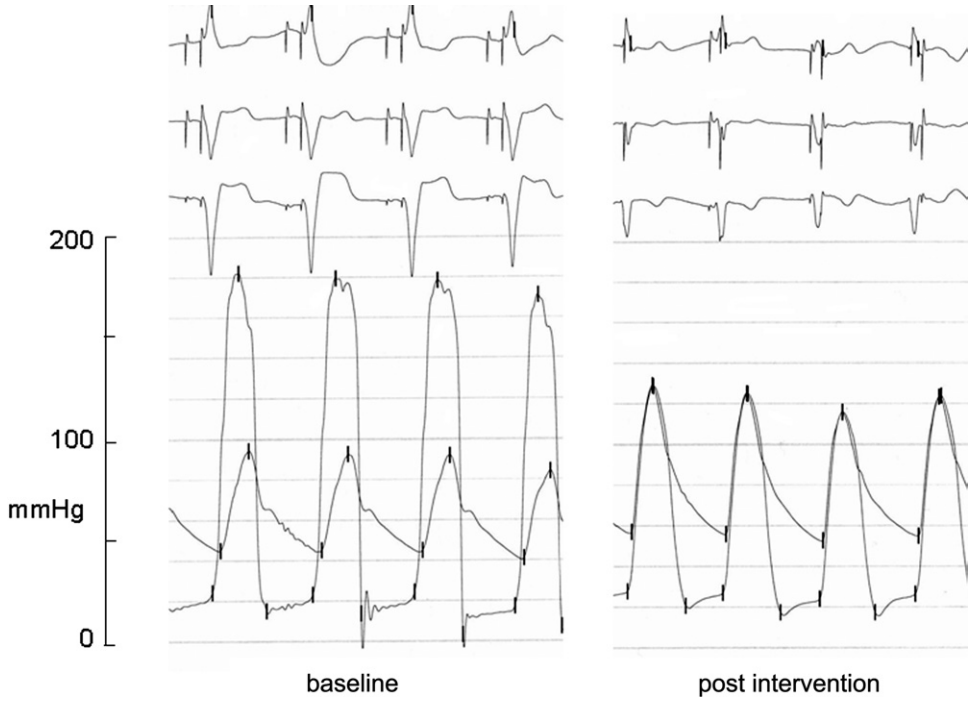

Figure 3 **Hemodynamic Tracing Before and After CoreValve**

Example of simultaneous left ventricular and aortic hemodynamic tracing at baseline and immediately after implantation of prosthesis.

with respect to procedural data were achieved: in the 18-F group, 25% of the procedures were performed only with local anesthesia of the groin (21-F group 0%, $p < 0.001$). Implantations without surgical cut-down for the access site vessel were significantly more frequently performed in the 18-F group (42%) than in the 21-F group (12%, $p = 0.001$). Moreover, 64% treated with the 18-F device had no hemodynamic support (0% with the 21-F device, $p < 0.001$), whereas for the 21-F group, a cardiac assist, extracorporeal membrane oxygenation or a full-bypass support always was applied. As a consequence, the total procedural time decreased markedly from 188 ± 55 min (21-F) to 148 ± 50 min (18-F, $p = 0.002$). A closure device (e.g., with Prostar device, Abbott Vascular, Abbott Park, Illinois) was used in all patients with percutaneous access.

Discussion

This research comprises the largest population treated with a percutaneous valve replacement system for treatment of degenerative, severe, symptomatic aortic stenosis. The analysis of this prospective multicenter study confirms the previously reported feasibility of the procedure (16) with a device success rate of 88% in these selected, high-risk patients. However, the fact that 8 patients of our population needed additional interventions by either second device implantation or conversion to surgery because of suboptimal implantation of the first prosthesis either too low or too high within the native valve area points out that accurate device deployment is crucial and certainly associated with a learning curve.

However, the CoreValve design provides several advantages that facilitate device deployment and reliable implantation: 1) a certain deployment error margin; 2) self-axing properties; 3) beneficial anchoring characteristics in native valve area as well as the ascending aorta; and 4) the ability for device retrieval after partial implantation of the first two-thirds of the prosthesis. This modified deployment technique, as opposed to the rapid complete deployment as favored in the beginning, has been introduced during the study course. Having deployed the distal two-thirds of the prosthesis (Fig. 2), the valve is already sufficiently functioning, whereas the device position can still be adjusted or the device can be pulled back completely.

The encouraging device success rate we have observed in this study goes along with a low procedural and 30-day mortality, which is lower than the predicted operative risk of these patients using the EuroScore risk algorithm (17). The accuracy and value of these risk assessment scores is sometimes controversially discussed. However, these tools are widely used for outcome stratification in high-risk surgical candidates in which large randomized clinical trails are missing. The population enrolled in our series presented with an average logistic EuroScore of 21.7%. The overall

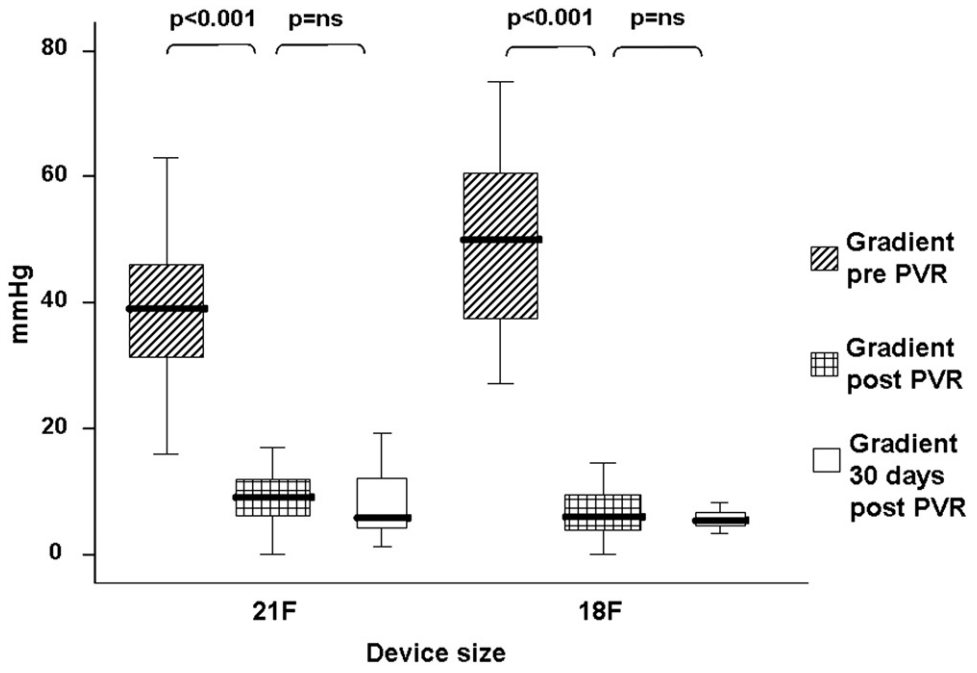

Figure 4 **Mean Aortic Pressure Gradients**

Mean gradient pre- versus postimplantation of prosthesis versus 30-day follow-up (for patients with procedural success). PVR = percutaneous valve replacement.

30-day mortality of 12% as well as the 30-day mortality of 9% in patients with acute device success in our study is therefore encouraging, proving the safety of the procedure with regard to this important clinical end point. In addition, if procedural success is achieved, the 30-day event rate is just 6%.

However, there was a relatively high rate of adverse events at 30 days in the overall intent-to-treat population, largely driven by cerebrovascular events and cardiac tamponades. The latter were induced in 6 cases, most likely by wire perforations during valve insertion and placement. Interestingly, most of these events occurred in the middle of the transition phase from the 21-F to 18-F period, when the less-invasive approach without hemodynamic support was introduced and a new device deployment technique was established. In this phase, it was realized that meticulous distal wire tip control is of particular importance for this procedure, given the characteristics of very stiff wires with a suboptimal tip shape for this procedural setting and their known potential for perforations.

Consequently, to address this issue, mandatory manual wire shaping is now performed before insertion, forming a less traumatic pigtail-like wire tip. In combination with continuous fluoroscopic tip position control, this measure reduced the incidence of wire perforations effectively in the later study phase. A specifically manufactured wire addressing these specific requirements would be certainly helpful to avoid the risk of perforations, a potentially life-threatening event which can occur in surgically treated patients in up to 17% (cardiac effusion) and 4% (tamponade) (18).

The problem of cerebrovascular events when treating patients with severe aortic stenosis is also already known from both the era of balloon valvuloplasty as well as surgical series. The risk of a perioperative cerebrovascular event for patients age ≥80 years of age undergoing coronary bypass surgery or combined bypass surgery and aortic valve replacement has been reported to be as high as 10% and 15%, respectively (3). Therefore, an overall stroke rate of 10%, including minor and major events in our study, is comparable with surgical data in this clinical setting. However, further progress is certainly needed to sufficiently prevent these embolic events during this kind of percutaneous approach. Whether these events are caused by thrombi or liberated plaque particles from the native valve, the ascending aorta or aortic arch, or air emboli is currently unclear. Careful device preparation to avoid air emboli, optimal device positioning without extensive placement maneuvers within the native valve, as well as adequate antiplatelet medication is certainly mandatory to reduce the incidence of embolic events.

The hemodynamic results of this study clearly demonstrate the efficacy of this new technique. As soon as the valve is adequately implanted, there is a striking reduction of the transvalvular gradient, usually without significant regurgitations. However, dilation afterward to fully expand the prosthesis, mainly in heavily calcific degenerated valves, is sometimes needed (24% in this study) to achieve a good hemodynamic outcome. However, this step can be performed safely and reliably, even with slightly oversized balloons, without risk for structural device damage. If

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regurgitation is still detected, it is usually located in the paravalvular area. We found that the acute postprocedural grade of regurgitation can still change in the following days, perhaps as the result of factors such as the self-expanding properties of the device (improvement) or a kind of recoil of the valve segment due to heavy calcifications (worsening). However, we have not observed any significant clinical worsening of regurgitation in the entire population. More long-term data are certainly needed to assess the durability of the acute hemodynamic results. The degeneration pattern of this pericardial valve is expected to be comparable with common aortic valve bioprostheses.

Although the CoreValve technique is still in its infancy, device modifications and procedural advances are proceeding. The device profile reduction to the 18-F catheter resulted in remarkable procedural improvements without different safety outcomes. The procedural duration is significantly reduced as the result of a less-invasive technique without need for ventricular assist devices, general anesthesia, and surgical access-site preparations. This third-generation device allows now a truly percutaneous approach to aortic valve replacement which has the potential to change the standards of care particularly for high-risk surgical candidates with severe AS in the near future.

Study limitations. The current multicenter study describes only the short-term results after CoreValve implantation; assessment of the long-term durability of this prosthesis will require at least a 5-year follow-up. There was no control group in this study, which limited our ability to assess the device efficacy. The results of this study apply only to the patient population enrolled (high-risk patients with aortic stenosis and multiple comorbid conditions). Additional studies are required to determine the suitability of this device for patients who are otherwise good candidates for surgical aortic valve replacement and those with predominant aortic regurgitation.

Conclusions

Percutaneous valve replacement with the CoreValve revalving system for selected patients with severe AS provides an encouraging device success rate, results in marked hemodynamic and clinical improvement, and is associated with a comparably low acute and 30-day mortality rate in this high-risk population. Further progress in terms of implantation technique, device positioning, as well as the device itself is warranted to reduce procedural-related adverse events.

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