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Results of Transfemoral or Transapical Aortic Valve Implantation Following a Uniform Assessment in High-Risk Patients With Aortic Stenosis

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Objectives We sought to describe the results of a strategy offering either transfemoral or transapical aortic valve implantation in high-risk patients with severe aortic stenosis.

Background Results of transfemoral and transapical approaches have been reported separately, but rarely following a uniform assessment to select the procedure.

Methods Of 160 consecutive patients at high risk or with contraindications to surgery, referred between October 2006 and November 2008, 75 were treated with transcatheter aortic valve implantation. The transfemoral approach was used as the first option and the transapical approach was chosen when contraindications to the former were present. The valve used was the Edwards Lifesciences SAPIEN prosthesis.

Results Patients were age 82 ± 8 years (mean ± SD), in New York Heart Association functional classes III/IV, with predicted mean surgical mortalities of 26 ± 13% using the European System for Cardiac Operative Risk Evaluation and 16 ± 7% using the Society of Thoracic Surgeons Predicted Risk of Mortality. Fifty-one patients were treated via the transfemoral approach, and 24 via the transapical approach. The valve was implanted in 93% of the patients. Hospital mortality was 10%. Mean (± SD) 1-year survivals were 78 ± 6% in the whole cohort, 81 ± 7% in the transfemoral group, 74 ± 9% in the transapical group ($p = 0.22$), and 60 ± 10% in the first 25 patients versus 93 ± 4% in the last 50 patients treated ($p = 0.001$). In multivariate analysis, early experience was the only significant predictor of late mortality.

Conclusions Being able to offer either transfemoral or transapical aortic valve implantation, within a uniform assessment, expands the scope of the treatment of aortic stenosis in high-risk patients and provides satisfactory results at 1 year in this population. The results are strongly influenced by experience. (J Am Coll Cardiol 2009;54: 303–11) © 2009 by the American College of Cardiology Foundation

Aortic stenosis (AS) is the most frequent valvular heart disease in Western countries (1). Surgical aortic valve replacement (AVR) is the reference treatment. The possibilities of treatment have expanded with the development of transcatheter aortic valve implantation (TAVI) techniques (2–16). Feasibility and favorable short-term outcomes of TAVI have been demonstrated, but mid- and long-term results need to be further evaluated (17). In addition, the transfemoral and transapical approaches have been studied separately, but very rarely as part of a strategy taking advantage of the availability of both techniques (18).

The aim of this study was to describe immediate and 1-year results of TAVI following a uniform assessment leading to the use of the transfemoral approach as the first option, or of the transapical approach in case of contraindications to the transfemoral approach.

Methods

Patients. From October 2006 to November 2008, among all patients with severe symptomatic AS consecutively referred for TAVI by primary or tertiary hospitals or by

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Abbreviations and Acronyms

AS = aortic stenosis

AVR = aortic valve replacement

EuroSCORE = European System for Cardiac Operative Risk Evaluation

NYHA = New York Heart Association

STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality

TAVI = transcatheter aortic valve implantation

TEE = transesophageal echocardiography

TTE = transthoracic echocardiography

independent cardiologists, those who actually had a high surgical risk or contraindications to AVR were evaluated for TAVI.

Screening included clinical evaluation, transthoracic echocardiography (TTE) and, if necessary, transesophageal echocardiography (TEE), coronary angiography, aortic and femoroiliac angiography, and multislice computed tomography. After multidisciplinary evaluation including cardiologists, cardiovascular surgeons, anesthesiologists, and geriatricians, using imaging and medicosurgical conferences, the decision to perform TAVI was made in patients with severe symptomatic AS; contraindications to, or high risk for AVR (European System for Cardiac Operative Risk Evaluation [EuroSCORE] ≥20% or Society of Thoracic Surgeons Predicted Risk of Mortality [STS-PROM] ≥10%); life expectancy >1 year (17,19–20); anatomy suitable for intervention (17,21); and no need for coronary bypass surgery.

These patients represent the study population. The transfemoral approach was considered as the first option, and the transapical approach was used when there were contraindications to the transfemoral route, which were mainly unsuitable femoroiliac accesses and severely calcified aortic arch and descending aorta (17). In patients with contraindications to both approaches, AVR was reconsidered if the operative risk was not considered prohibitive. In patients who were too frail to undergo any invasive intervention or with comorbidities that clearly limited short-term life expectancy or precluded future quality of life (mainly malignancies and cognitive disorders), a medical treatment was decided upon. The formal decision algorithm is shown in Figure 1. The device used was the Edwards-SAPIEN valve (Edwards Lifesciences Inc., Irvine, California).

Transfemoral TAVI. Procedures were performed under general anesthesia, with fluoroscopic and TEE guidance. After retrograde crossing and pre-dilation of the native valve, the prosthesis was pushed by a flexible catheter (RetroFlex, Edwards Lifesciences) positioned within the aortic valve, and then delivered by balloon inflation under rapid ventricular pacing. Technical aspects of the procedure have been detailed previously (3–7,15,17).

Transapical TAVI. After anterolateral mini-thoracotomy and pericardiotomy, the left ventricular apex was punctured through purse-string sutures. Then, a sheath was introduced in the left ventricle and the prosthesis was implanted using the antegrade route via the Ascendra (Edwards Lifesciences) system (11–14).

Follow-up. Hospital clinical and echocardiographic data were obtained before discharge. All adverse events were prospectively recorded. After the hospital phase, clinical and TTE follow-up was obtained in all survivors at 1 to 3 months, 6 months, 1 year, and then annually.

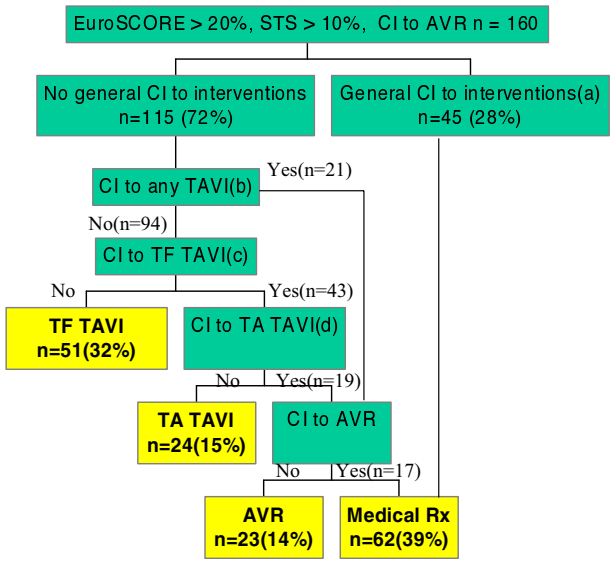

Figure 1 **Management of High-Risk Patients With Aortic Stenosis**

Algorithm for treatment in 160 high-risk patients referred for transcatheter aortic valve implantation (AVR). **(a)** Frailty (n = 5); life expectancy too short (n = 20); quality of life too poor (n = 20). **(b)** Annulus diameter too large (n = 12); bicuspid aortic valve (n = 5); intracardiac thrombus (n = 4). **(c)** Inadequate iliac arteries (n = 41); porcelain aorta (n = 6); abdominal aortic aneurysm with thrombus (n = 4). **(d)** Severe respiratory failure (n = 10); subaortic left ventricular hypertrophy (n = 3); miscellaneous (n = 6). Several contraindications may have been encountered in 1 patient. AVR = aortic valve replacement; CI = contraindication; EuroSCORE = European System for Cardiac Operative Risk Evaluation; STS = Society of Thoracic Surgeons; TA = transapical; TAVI = transcatheter aortic valve implantation; TF = transfemoral.

Outcomes. Outcomes were described according to the guidelines for reporting mortality and morbidity after cardiac valve interventions (22). Implantation success was defined by valve implantation in the correct position. Major vascular complications were defined as lesions requiring immediate or delayed vascular operations other than a simple arterial suture, or leading to hospital death.

Statistical analysis. Data were expressed as mean ± SD, except for the length of stay, which was expressed as median with 25th to 75th percentiles. To assess experience, a binary variable was used to separate the first 25 patients from the last 50 patients. The Mann-Whitney *U* test was used to compare continuous variables in the transfemoral and transapical groups, and categorical variables were compared by the chi-square or Fisher exact test. Survival rates between groups were compared using the log-rank test. Analysis of the predictive factors of late survival was performed using a multivariate Cox model including early versus late experience, transfemoral or transapical approach, and patient risk score (EuroSCORE or STS-PROM score). All tests were 2-sided. A p value <0.05 was considered to indicate a

statistically significant difference. Statistical analysis was performed using statistical software Statistica version 5.0 (Statsoft Inc., Tulsa, Oklahoma).

Results

Patients. Among patients consecutively referred for TAVI, 160 were at high risk or had contraindications to surgery. The algorithm for treatment is shown in Figure 1. Of these patients, 51 (32%) were treated with transfemoral TAVI and 24 (15%) were treated with transapical TAVI because of contraindications to the transfemoral approach. Twenty-three (14%) were reoriented toward conventional AVR, mainly due to the presence of an aortic annulus, which is too large for TAVI (>25 mm), associated with a surgical risk profile that was not considered prohibitive (EuroSCORE 20 ± 11%, range 6% to 50%). Sixty-two patients (39%) were considered too frail, with a life expectancy too short to undergo any invasive intervention, or had technical contraindications to both TAVI and AVR and were treated medically (EuroSCORE 32 ± 19%, range 3% to 86%).

The population studied here consisted of the 75 patients who were treated with either transfemoral or transapical TAVI. Its characteristics are detailed in Table 1. Overall, the population was at high surgical risk, and the risk profile tended to be even more severe in the transapical than in the transfemoral subset. Seven patients (9%) had both EuroSCORE <20% and an STS-PROM <10%. For them, indications for TAVI were represented by absolute contraindications to conventional AVR due to severe respiratory failure (n = 3), chest radiation sequelae (n = 2), a voluminous intracerebral aneurysm (n = 1), or morbid obesity (n = 1).

In-hospital outcomes. In-hospital outcomes are detailed in Table 2. Implantation success was achieved in 70 patients (93%). In all cases, aortic valve area and mean transprosthetic gradient were satisfactory. Technical failures occurred only in the transfemoral approach. Reasons for failure included the inability to pass the iliac artery in 3 patients, to cross the aortic valve with the prosthesis in 1 patient, and hemopericardium in 1 patient due to perforation of the left

Table 1 Baseline Characteristics of the Study Population

Characteristics	Overall (n = 75)	Transfemoral TAVI (n = 51)	Transapical TAVI (n = 24)	p Value
Age, yrs, mean ± SD	82 ± 8	82 ± 7	82 ± 10	0.75
Female sex	34 (45)	26 (51)	8 (33)	0.15
NYHA functional class				0.70
II	4 (5)	2 (4)	2 (8)	
III	40 (53)	27 (53)	13 (54)	
IV	31 (41)	22 (43)	9 (38)	
Coronary artery disease	45 (61)	25 (49)	20 (87)	0.001
Previous MI	15 (20)	4 (8)	11 (48)	0.001
Previous PCI	11 (22)	7 (20)	4 (27)	0.60
Previous CABG	23 (31)	11 (22)	12 (52)	0.01
Peripheral artery disease	11 (15)	4 (8)	7 (30)	0.02
Renal failure	28 (38)	16 (31)	12 (52)	0.09
Severe COPD	20 (27)	14 (27)	6 (26)	0.9
Cancer	20 (27)	14 (27)	6 (26)	0.9
Porcelain aorta	9 (12)	3 (6)	6 (26)	0.01
≥2 comorbidities	43 (58)	26 (51)	17 (74)	0.06
Aortic valve area, mean ± SD				
cm^2	0.64 ± 0.16	0.63 ± 0.16	0.65 ± 0.17	0.72
cm^2/m^2	0.37 ± 0.09	0.36 ± 0.10	0.37 ± 0.09	0.94
Mean gradient, mm Hg ± SD	52 ± 15	54 ± 15	48 ± 14	0.07
LVEF, %	51 ± 15	52 ± 16	48 ± 13	0.24
Logistic EuroSCORE, %				
Mean ± SD	26 ± 13	25 ± 13	28 ± 13	0.43
Range	6–65	6–65	11–57	
STS-PROM, %				
Mean ± SD	16 ± 7	15 ± 7	18 ± 9	0.09
Range	3–41	3–26	7–41	
CI to surgery*	34 (45)	19 (37)	15 (63)	0.04

Values are expressed as n (%) unless otherwise stated. *Mainly porcelain aorta, sequelae of chest radiation, or severe respiratory failure. Previous CABG was not considered an absolute CI to surgery.

CABG = coronary artery bypass grafting; CI = contraindication; COPD = chronic obstructive pulmonary disease; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TAVI = transcatheter aortic valve implantation.

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Table 2 In-Hospital Outcomes in the Study Population

Outcomes	Overall (n = 75)	Transfemoral TAVI (n = 51)	Transapical TAVI (n = 24)	p Value
Implantation success	70 (93)	46 (90)	24 (100)	0.05
Aortic valve area				
cm^2	1.73 ± 0.41	1.70 ± 0.37	1.80 ± 0.48	0.46
cm^2/m^2	1.01 ± 0.21	0.97 ± 0.20	1.08 ± 0.27	0.13
Mean gradient, mm Hg				
Mean ± SD	10 ± 4	11 ± 4	9 ± 4	0.11
Range	3–21	6–21	3–20	
Paravalvular aortic regurgitation				0.36
Grade 0	5 (7)	3 (6)	2 (8)	
Grade I	52 (75)	33 (72)	19 (80)	
Grade II	9 (13)	8 (18)	1 (4)	
Grade III	4 (5)	2 (4)	2 (8)	
"Valve after valve"	3 (4)	1 (2)	2 (8)	0.20
Major vascular complications	8 (11)	6 (12)	2 (8)	0.65
Stroke	3 (4)	3 (6)	0	0.23
Tamponade	4 (5)	2 (4)	2 (8)	0.15
Heart block*	4 (5)	3 (6)	1 (4)	0.75
In-hospital death	8 (10)	4 (8)	4 (16)	0.22
Per procedure	2 (3)	2 (4)	0	
Cardiac	7 (9)	4 (8)	3 (12)	
Noncardiac	1 (1)	0	1 (4)	
Length of stay in ICU (days), median [25th–75th percentiles]	3 [2–5]	2.5 [2–4]	5 [3–8]	<0.001
Length of hospital stay (days), median [25th–75th percentiles]†	12.5 [9–16]	13 [9–16]	12 [9–18]	0.89

Values are expressed as n (%) or mean ± SD unless otherwise stated. *Requiring pacemaker implantation. †From procedure to discharge.
ICU = intensive care unit; TAVI = transcatheter aortic valve implantation.

ventricle, leading to intraprocedural death. There was neither prosthesis embolization nor conversion to on-pump surgical AVR. Immediately after implantation, paravalvular leaks were observed in more than one-half of the patients. They were grade II or greater in 13 patients (17%), but were grade III or greater in only 4 patients (5%). The incidence of aortic regurgitation grade II or greater was related to a larger annulus diameter ($p < 0.001$) and greater patient height ($p < 0.01$). Five patients underwent redilation for paravalvular leaks. In 1 patient, redilation did not improve the degree of regurgitation. In another, redilation induced a massive intravalvular regurgitation, and emergent implantation of a second prosthesis into the first one ("valve after valve") was necessary, with good results. At the end of the procedure, 2 patients had grade III paravalvular aortic regurgitation, with no hemodynamic consequences (no change in the clinical condition or pattern of the aortic pressure and no increase in left ventricular filling pressures). Two other patients had a second valve implanted into the first one in a higher position because the placement of the first one was deemed too low.

Three strokes (6%) occurred after transfemoral TAVI. They were diagnosed immediately after the procedure in 2 patients and 5 days later in a third, with full recovery within 2 months in all cases. No causative factor was found. There were no strokes in the transapical group. Four atrioventricular blocks requiring pacemaker implantation occurred (5%): 2 per procedure, 1 at day 4, and 1 2 weeks after the procedure. No coronary event leading to clinical, angiographic, or electrocardiographic consequences was observed. However, troponin levels were not systematically recorded.

The most frequent major complications were vascular in 8 patients (11%). There were 4 iliac dissections in the transfemoral group: 3 were treated by surgical grafting, with uneventful outcomes in 2 patients, and post-operative death at day 4 in 1 patient; 1 was treated by iliac stenting, complicated by acute leg ischemia due to stent occlusion on day 1, requiring emergency surgery, with a favorable outcome. There was 1 femoral injury at the entry site requiring surgical grafting, and 1 hematoma in the contralateral groin requiring a surgical evacuation. Two vascular complications occurred in the transapical group: 1 was secondary to the delayed rupture of the femoral arterial access site (1 week after TAVI), and 1 to thrombosis of the common iliac artery in the context of septic shock in a patient with severe peripheral artery disease, leading to death.

Four tamponades occurred: 2 during transfemoral procedures (1 perforation of the left ventricular apex, previously mentioned, and 1 rupture of the aortic annulus), leading to intraprocedural deaths; 1 4 h after a transapical procedure, with satisfactory recovery after surgical drainage, and 1 2 days after a transapical procedure, due to rupture of the left ventricular apex, requiring emergent reintervention and leading to multiorgan failure and death at day 39. Causes of

Table 3 Causes of Death in 75 Patients Treated With TAVI

Time	Approach	Days to Death	Cause of Death
In-hospital	TF	0	Hemopericardium (LV perforation); intraprocedural death
In-hospital	TF	0	Hemopericardium (annular rupture); intraprocedural death
In-hospital	TF	1	Sudden, unexplained death
In-hospital	TA	2	Intractable arrhythmias, heart failure
In-hospital	TF	4	Iliac dissection; multi-organ failure after vascular surgery
In-hospital	TA	18	Septic shock, leg ischemia
In-hospital	TA	39	LV rupture at day 2, multiorgan failure after reintervention
In-hospital	TA	61	DRESS syndrome
Post-discharge	TA	31	Pulmonary infection
Post-discharge	TA	77	Progressive physiological deterioration
Post-discharge	TF	79	Chronic renal failure, sudden unexplained death
Post-discharge	TF	165	Pulmonary infection
Post-discharge	TF	347	Heart failure (grade II paraprosthetic AR*)
Post-discharge	TF	445	Heart failure (grade III paraprosthetic AR*)

*As initially determined by transesophageal echocardiography, and then evaluated by transthoracic echocardiography during follow-up.
AR = aortic regurgitation; DRESS = drug rash with eosinophilia and systemic syndrome; LV = left ventricular; TA = transapical; TF = transfemoral; other abbreviations as in Table 1.

deaths are detailed in Table 3. All-cause in-hospital mortality was 10%.

A comparison of hospital outcomes between the first 25 and last 50 patients is shown in Table 4. According to predictive mortality risk scores, the risk profile tended to be worse in the first than in the last patients. It showed a higher implantation success rate and a significant decrease in the frequency of severe paravalvular regurgitation and hospital mortality in the last compared with the first patients. In the patients redirected to AVR, in-hospital mortality was 14%.

Midterm outcomes. Mean follow-up duration was 10 ± 6 months (range 1 to 27 months). Six deaths occurred after discharge. Their causes are detailed in Table 3. One-year survival rates were 78 ± 6% for the whole TAVI cohort, 81 ± 7% and 74 ± 9% for the transfemoral and transapical subsets, respectively (Fig. 2). Survival rates of the first 25 patients are compared with those of the last 50 patients in Figure 3. At 1 year, the survival rate was 60 ± 10% among the first patients compared with 93 ± 4% among the last patients (p = 0.001). With models using the EuroSCORE and the STS-PROM, multivariate analysis showed that early experience was the only significant predictor of late mortality (hazard ratio: 8.9, 95% confidence interval: 2.3 to 34.6; p = 0.002, and hazard ratio: 7.2, 95% confidence interval: 1.9 to 27.1; p = 0.004, respectively) (Table 5).

A pericardial effusion occurred 1 month after a transapical TAVI and was treated with surgical drainage. A false aneurysm of the apex of the left ventricle occurred 2 months after a transapical TAVI and was treated by surgical closure, with an uneventful recovery. There was no other reintervention, hemolysis, or permanent valve-related impairment.

Table 4 Comparison of Risk Profiles and Hospital Outcomes in First 25 and Last 50 Patients Treated With Transcatheter Aortic Valve Implantation

Variable	First 25 Patients	Last 50 Patients	p Value
EuroSCORE, %	31 ± 14	23 ± 11	0.02
STS-PROM, %	17 ± 7	15 ± 7	0.17
CI to surgery	13 (52)	21 (42)	0.41
Implantation success	21 (84)	49 (98)	0.02
Paravalvular regurgitation			0.04
Grade 0	1 (5)	4 (8)	
Grade I	13 (62)	39 (80)	
Grade II	4 (19)	5 (10)	
Grade III	3 (14)	1 (2)	
Major vascular complications	4 (16)	4 (8)	0.29
Stroke	0	3(6)	0.21
Tamponade	2 (8)	2 (4)	0.76
Heart block*	0	4 (8)	0.1
In-hospital death	6 (24)	2 (4)	0.01

Values are expressed as n (%) or mean ± SD unless otherwise stated. *Requiring pacemaker implantation.
Abbreviations as in Table 1.

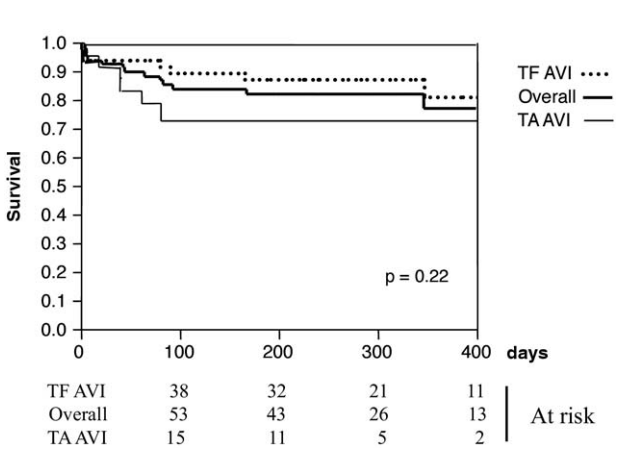

Figure 2 Survival After TAVI

Kaplan-Meier survival in the 75 patients treated with transcatheter aortic valve implantation, and in those treated with transfemoral or transapical approaches. AVI = aortic valve implantation; other abbreviations as in Figure 1.

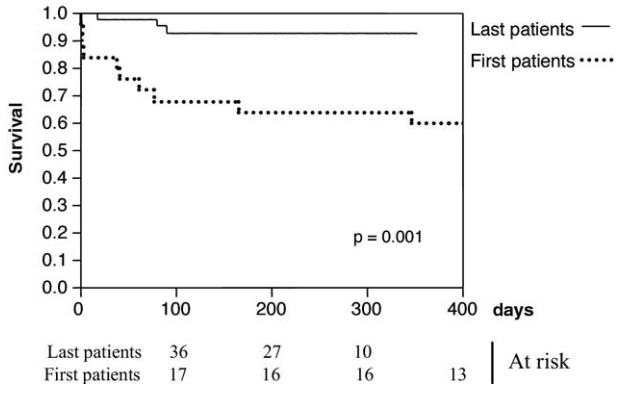

Figure 3 **Impact of Learning Curve on Survival After Transcatheter Aortic Valve Implantation**

Kaplan-Meier survival in the first 25 versus last 50 patients treated with transcatheter aortic valve implantation.

At the last follow-up of the 61 survivors, 20 (33%) were in New York Heart Association (NYHA) functional class I, 35 (57%) were in class II, and 6 (10%) were in class III.

Follow-up of the echocardiographic parameters is shown in Figures 4A and 4B. No structural valve deterioration or dysfunction was observed. In the patients redirected to AVR, 1-year survival was 83 ± 8%.

Discussion

This prospective study reports the management of patients with severe symptomatic AS and high risk for, or contraindications to AVR, using all contemporary techniques of TAVI (i.e., either transfemoral or transapical approach following a uniform assessment). In this strategy, as compared with the use of the transfemoral approach alone, a higher number of patients were allowed to undergo intervention. One-year survival and functional results were good. Outcome was closely related to experience.

Number of patients being treated. The European Heart Survey showed that many high-risk patients with AS are not offered operations (1,2). The development of TAVI led to an increase in the number or patients who can undergo interventions. Furthermore, the availability of both transfemoral and transapical approaches increased the number of those patients, in comparison with the use of the transfemoral approach alone. Although only one-third of the patients studied were candidates for transfemoral TAVI, use of the transapical approach extended the feasibility of TAVI to 47%. Moreover, reconsideration of conventional surgery in some others further increased the number of patients treated effectively, up to 61%. Most remaining patients who were treated medically had severe comorbidities, severely limiting their life expectancy or precluding any functional benefit from TAVI.

Another study, conducted with the Edwards SAPIEN valve, using either transfemoral or transapical approaches, concluded that 75% of the patients evaluated for TAVI actually underwent the procedure (18). However, this study included only 29 patients.

Our results are closer to those previously reported using the CoreValve Revalving System (CRS, CoreValve Inc., Irvine, California), which showed that among high-risk patients referred for TAVI, 28% were not eligible and 14% were redirected toward surgical AVR (23). But because of the absence of alternative transapical approaches with this latter device, the use of TAVI was restricted to 39% of the patients; 3% underwent percutaneous aortic balloon valvuloplasty only, and another 16% refused treatment.

In the future, the number of candidates for TAVI will be closely conditioned by the ability to decrease the sheath size for the transfemoral approach and increase the valve size for all approaches, which are currently the main technical limitations of the technique.

In-hospital mortality. Recent studies have shown that AVR can be performed in properly selected elderly patients, with operative mortality rates around 10% (24–27). However, this figure cannot be extrapolated to the population of the present study, characterized by a high surgical risk or presenting contraindications to AVR. High risk was shown by the predicted mortality rate, which was, on average, 26% for the EuroSCORE and 16% for the STS PROM. The 10% hospital mortality observed in this series compares favorably with these predicted mortality rates. But it is acknowledged that predictive scores have limitations, particularly the Logistic EuroSCORE, which tends to overestimate risk in the most severe patients (28,29).

The present mortality rate compares favorably with the 23% 30-day mortality observed in the first French feasibility studies, which addressed patients recruited on a compassionate basis (5). It is consistent with the 12% mortality rate reported by Webb et al. (7) in 50 patients whose risk profile was similar to that observed in the present series (EuroSCORE 28%) and who were treated by transfemoral TAVI using the Edwards SAPIEN prosthesis. Piazza et al. (10) reported an 8% 30-day mortality rate in 600 patients who were treated with transfemoral TAVI using the CoreValve Revalving System and included in a multicenter registry. However, their

Table 5 **Multivariate Analysis of the Predictors of Late Mortality in Patients Treated With TAVI**

Model	Hazard Ratio	95% Confidence Interval	p Value
Model using the EuroSCORE			
Early* versus late† experience	8.9	2.3–34.6	0.002
Transapical versus transfemoral	2.7	0.9–8.1	0.08
Logistic EuroSCORE (1-point increase)	0.98	0.93–1.02	0.28
Model using the STS-PROM			
Early* versus late† experience	7.2	1.9–27.1	0.004
Transapical versus transfemoral	2.5	0.8–7.7	0.12
STS-PROM score (1-point increase)	0.99	0.93–1.06	0.86

*First 25 patients. †Last 50 patients.
Abbreviations as in Table 1.

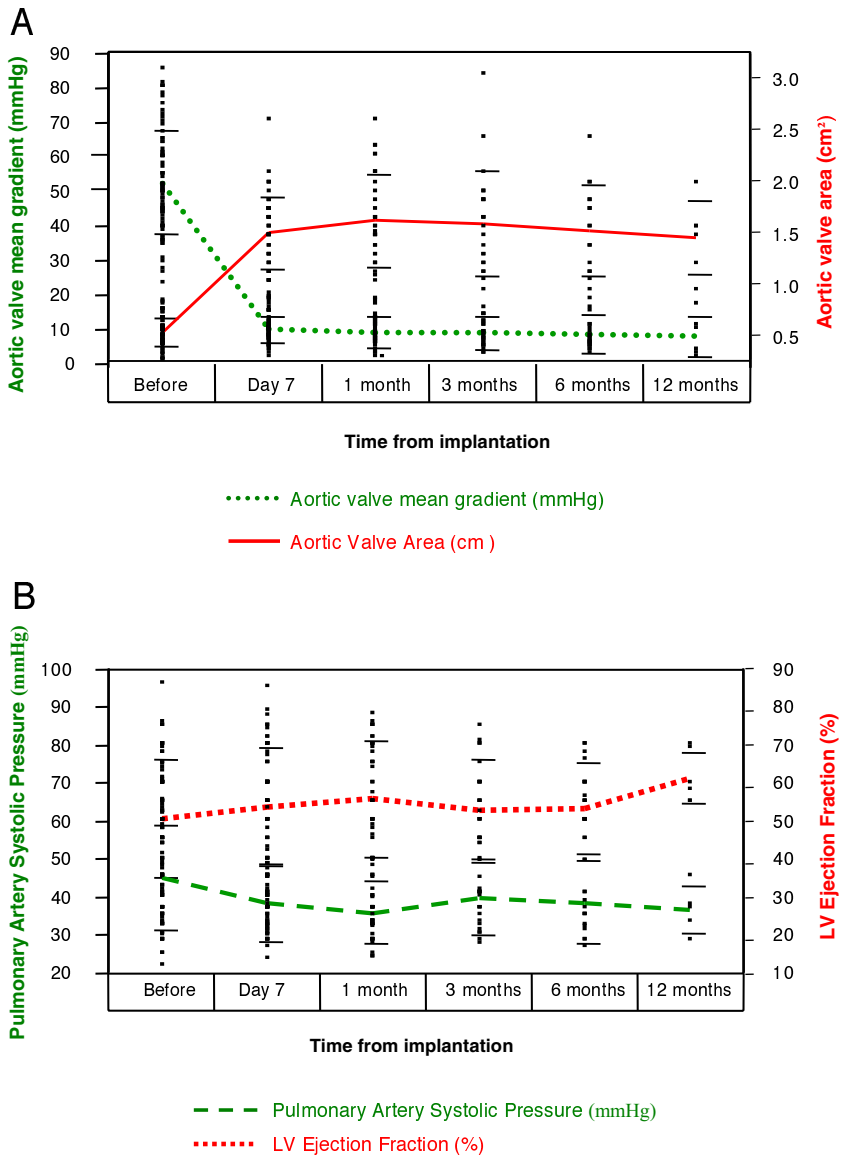

Figure 4 **Echocardiographic Follow-Up After Transcatheter Aortic Valve Implantation**

(A) Aortic valve area and mean transvalvular gradient follow-up after transcatheter aortic valve implantation. **(B)** Left ventricular (LV) ejection fraction and systolic pulmonary artery pressure follow-up after transcatheter aortic valve implantation.

overall risk profile tended to be lower than in the previous studies (EuroSCORE 23%). In comparison, hospital mortality rates reported in transapical TAVI series tended to be higher: 14% in the multicenter experience reported by Walther et al. (12), and 22.5% in the feasibility study reported by Svensson et al. (14).

In the present series, hospital mortality was predominantly due to cardiovascular causes. This was also the case in the series reported by Cribier et al. (5) and Webb et al. (7). As observed in those previous reports, there was no valve-related death.

Morbidity. Nonfatal morbidity could be considered acceptable due to the high-risk nature of the population. Strokes were rare (4%). All stroke patients recovered without sequelae. Consistent with previous reports, no stroke occurred after transapical TAVI (12). The incidence of complete atrioventricular blocks requiring pacemaker implantation was low (5%), consistent with previous publications on the Edwards SAPIEN prosthesis (4–7,15) and lower than rates reported with the CoreValve Revalving System (9,10). There was no myocardial infarction, coronary obstruction, or induced mitral valve dysfunction. Contrary to most previous TAVI series, there was no embolization. Adequate pre-procedure annulus sizing and continuous TEE monitoring during TAVI may have contributed to this result.

Thus, the main cause of severe morbidity with the transfemoral approach remained vascular complications due to the large diameters of the sheaths. This rate has already been decreased by the reduction of the diameters with the CoreValve Revalving System (9).

1-year results. Post-discharge mortality was due to noncardiac causes in one-half of the patients. These findings are consistent with those previously reported by Cribier et al. (5). Overall, late survival was consistent with that from previous reports on transfemoral or transapical TAVI, when used separately.

The 81% 1-year survival rate obtained in the present series with the transfemoral approach compares favorably to those previously reported, ranging from 45% to 80% (5,7,9). In patients who could not be treated by the transfemoral route and who underwent the transapical procedure, 1-year survival tended to be lower, but the difference did not reach statistical significance. The 74% 1-year survival rate observed here after transapical TAVI also compares favorably with the 72% survival at 3 months and the 60% survival at 6 months observed in a recent feasibility study (14). This rate is more consistent with the 76% survival rate reported at 110-day follow-up in a multicenter study (12).

Functional results were good, with 90% of patients in NYHA functional class I or II at last follow-up; 94% were in NYHA functional class III or IV before intervention. This is of particular importance in the elderly, in whom the aim of intervention is essentially to improve the quality rather than the duration of life.

Predictive factors of outcome. As previously reported (7), this study shows the presence of a learning period with a direct impact on patients' outcomes. In fact, the incremental improvements acquired during the TAVI program may have affected patient selection, as well as the implantation technique itself, and post-procedural management. The short- and mid-term outcomes were better in the last than in the first patients and this difference remained highly significant in multivariate analysis adjusting for risk profile and the type of procedure. The 2 fatal vascular complications were observed at the beginning of the experience. This was also the case for the 2 grade ≥II post-implantation paravalvular leaks associated with midterm mortality. The decrease in the incidence of paravalvular leaks in the later experience may have been related to better echocardiographic evaluation of annulus diameters and positioning of the prosthesis.

Multivariate analysis also suggested that the transapical approach, compared with the transfemoral approach, is associated with a negative trend, albeit not significant, on outcomes. The strategy used here is likely to restrict the transapical approach to the highest risk patients, in particular, those with peripheral artery disease. In the present series, patients who underwent the transapical approach had more frequent coronary artery disease, previous coronary artery surgery and myocardial infarction, renal failure, and extracardiac comorbidities. Thus, the higher risk profile of the current transapical group may, at least in part, explain the difference in results. Although several complications of TAVI are common to both approaches, transapical TAVI requires a thoracotomy, potentially leading to specific postoperative complications.

The fact that the STS-PROM and the EuroSCORE were not predictive of in-hospital outcome may be due to clinical or morphologic variables unrecognized by these scores, or to the influence of the learning curve.

Study limitations. This study reflects a single-center experience on a relatively limited number of patients. Sample size is an issue with respect to multivariate analysis since the number of end points is too small to avoid over-fitting. However, the present study allowed a uniform assessment and selection strategy in the entire population, as well as data collection and analysis. It is also an initial experience. As the learning curve had a crucial and direct influence on clinical outcomes, the true benefit/risk ratio of the technique may have been underestimated in the present report. This study was not randomized, and no fair conclusion on the comparative clinical benefits of transfemoral and transapical approaches can be drawn from its results.

Conclusions and Future Directions

Today, TAVI allows patients who are at very high surgical risk or with contraindications to surgical AVR to benefit from an effective treatment of AS, and the availability of both transfemoral and transapical approaches increases the number of patients who can be treated. One-year results are satisfactory in terms of survival as well as functional improvement, in particular, given the patients' risk profile. The close impact of the learning curve on patients' outcomes underlines the necessity of proper training, and the restriction of these procedures to high-volume centers (17). In the future, randomized controlled trials and comprehensive registries with longer follow-up will help to better define the safety and durability, and subsequently, indications of the technique, and the respective places of transfemoral and transapical approaches.

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REFERENCES

1. Iung B, Baron G, Butchart EG, et al. A prospective survey of patients with valvular heart disease in Europe: the Euro Heart Survey on valvular disease. Eur Heart J 2003;24:1231–43.
2. Iung B, Cachier A, Baron G, et al. Decision making in elderly patients with severe aortic stenosis: why are so many denied surgery? Eur Heart J 2005;26:2714–20.
3. Cribier A, Eltchaninoff H, Bash A, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. Circulation 2002;106:3006–8.
4. Cribier A, Eltchaninoff H, Tron C, et al. Early experience with percutaneous transcatheter implantation of heart valve prosthesis for

the treatment of end-stage inoperable patients with calcific aortic stenosis. J Am Coll Cardiol 2004;43:698–703.
5. Cribier A, Eltchaninoff H, Tron C, et al. Treatment of calcific aortic stenosis with the percutaneous heart valve: mid-term follow-up from the initial feasibility studies: the French experience. J Am Coll Cardiol 2006;47:1214–23.
6. Webb J, Chandavimol M, Thompson CR, et al. Percutaneous aortic valve implantation retrograde from the femoral artery. Circulation 2006;113:842–50.
7. Webb JG, Pasupati S, Humphries K, et al. Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis. Circulation 2007;116:755–63.
8. Grube E, Laborde JC, Gerckens U, et al. Percutaneous implantation of the CoreValve self-expanding valve prosthesis in high-risk patients with aortic valve disease. The Sieburg first-in-man study. Circulation 2006;114:1616–24.
9. Grube E, Schuler G, Buellesfeld L, et al. 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.
10. Piazza N, Grube E, Gerckens U, et al., on behalf of the clinical centres who actively participated in the registry. Procedural and 30-day outcomes following transcatheter aortic valve implantation using the third generation (18Fr) CoreValve ReValving System: results from the multicentre, expanded evaluation registry 1-year following CE mark approval. EuroInterv 2008;4:242–9.
11. Walther T, Falk V, Borger MA, et al. Minimally invasive transventricular beating heart aortic valve implantation–proof of concept. Eur J Cardio Thor Surg 2007;31:9–15.
12. Walther T, Simon P, Dewey T, et al. Transapical minimally invasive aortic valve implantation: multicenter experience. Circulation 2007; 116:I240–5.
13. Ye J, Cheung A, Lichtenstein SV, et al. Six-month outcome of transventricular transcatheter aortic valve implantation in the initial seven patients. Eur J Cardio Thor Surg 2007;31:16–21.
14. Svensson LG, Dewey T, Kapadia S, et al. United States feasibility of transcatheter insertion of a stented aortic valve by the left ventricular apex. Ann Thorac Surg 2008;86:46–55.
15. Eltchaninoff H, Zajarias A, Tron C, et al. Transcatheter aortic valve implantation: technical aspects, results and indications. Arch Cardiovasc Dis 2008;101:126–32.
16. Descoutures F, Himbert D, Lepage L, et al. Contemporary surgical or percutaneous management of severe aortic stenosis in the elderly. Eur Heart J 2008;29:1410–7.
17. Vahanian A, Alfieri O, Al-Attar N, et al. 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 Heart J 2008;29:1463–70.
18. Rodés-Cabau J, Dumont E, De LaRochellière R, et al. Feasibility and initial results of percutaneous aortic valve implantation including selection of the transfemoral or transapical approach in patients with severe aortic stenosis. Am J Cardiol 2008;102:1240–6.
19. Rockwood K, Stadnyck K, MacKnight C, McDowell I, Herbert R, Hogan DB. A brief clinical instrument to clarify frailty in elderly people. Lancet 1999;353:205–6.
20. Lee SJ, Lindquist K, Segal MR, Covinsky KE. Development and validation of a prognostic index for 4-year mortality in older adults. JAMA 2006;295:801–8.
21. Zedgi R, Ciobotaru V, Noghin M, et al. Is it reasonable to treat all calcified stenotic aortic valves with a valved stent? J Am Coll Cardiol 2008;51:579–84.
22. Akins CW, Miller C, Turina MI, et al. Guidelines for reporting mortality and morbidity after cardiac valve interventions. J Thorac Cardiovasc Surg 2008;135:732–8.
23. Otten AM, van Domburg RT, van Gameren M, et al. Population characteristics, treatment assignment and survival of patients with aortic stenosis referred for percutaneous valve replacement. EuroInterv 2008;4:250–5.
24. Bonow RO, Carabello BA, Chatterjee K, et al. ACC/AHA guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Valvular Heart Disease). J Am Coll Cardiol 2006;48:e1–148.
25. Vahanian A, Baumgartner H, Bax J, et al. 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;28:230–68.
26. Kolh P, Kerzmann A, Honore C, Comte L, Limet R. Aortic valve surgery in octogenarians: predictive factors for operative and long-term results. Eur J Cardiothorac Surg 2006;31:600–6.
27. Edwards MB, Taylor KM. Outcomes in nonagenarians after heart valve replacement operation. Ann Thorac Surg 2003;75:830–4.
28. Dewey TM, Brown D, Ryan WH, Herbert MA, Prince SL, Mack MJ. Reliability of risk algorithms in predicting early and late operative outcomes in high risk patients undergoing aortic valve replacement. J Thorac Cardiovasc Surg 2008;135:180–7.
29. Grossi EA, Schwartz CF, Yu PJ, et al. High-risk aortic valve replacement: are outcomes as bad as predicted? Ann Thorac Surg 2008;85:102–6.

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