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Impact of left ventricular systolic function on clinical and echocardiographic outcomes following transcatheter aortic valve implantation for severe aortic stenosis

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Background This study aimed to evaluate the impact of baseline left ventricular (LV) systolic function on clinical and echocardiographic outcomes following transcatheter aortic valve implantation (TAVI). Survival of patients undergoing TAVI was also compared with that of a population undergoing surgical aortic valve replacement.

Methods One hundred forty-seven consecutive patients (mean age = 80 ± 7 years) undergoing TAVI in 2 centers were included. Mean follow-up period was 9.1 ± 5.1 months.

Results At baseline, 34% of patients had impaired LV ejection fraction (LVEF) (<50%) and 66% had normal LVEF (≥50%). Procedural success was similar in these 2 groups (94% vs 97%, $P = .41$). All patients achieved improvement in transvalvular hemodynamics. At follow-up, patients with a baseline LVEF <50% showed marked LV reverse remodeling, with improvement of LVEF (from 37% ± 8% to 51% ± 11%). Early and late mortality rates were not different between the 2 groups, despite a higher rate of combined major adverse cardiovascular events (MACEs) in patients with a baseline LVEF <50%. The predictors of cumulative MACEs were baseline LVEF (HR = 0.97, 95% CI = 0.94-0.99) and preoperative frailty (HR = 4.20, 95% CI = 2.00-8.84). In addition, long-term survival of patients with impaired or normal LVEF was comparable with that of a matched population who underwent surgical aortic valve replacement.

Conclusions TAVI resulted in significant improvement in LV function and survival benefit in high-risk patients with severe aortic stenosis, regardless of baseline LVEF. Patients with a baseline LVEF <50% were at higher risk of combined MACEs. (Am Heart J 2010;160:1113-20.)

Symptomatic severe aortic stenosis (AS) is associated with high mortality if left untreated,[1] and surgical aortic valve replacement (SAVR) is currently the recommended therapeutic approach.[2] When severe AS is associated with left ventricular (LV) dysfunction, due to either afterload mismatch[3] or primary myocardial dysfunction, SAVR still results in significant improvement of LV function and survival.[4-6] However, patients with depressed LV ejection fraction (EF) undergoing SAVR are associated with higher perioperative and mid-term mortality[4-8] as compared with those with normal LV systolic function. Furthermore, the combination of LV dysfunction with advanced age and significant comorbidities could result in high predicted operative risk[9] that may outweigh the benefits of SAVR and preclude the surgical intervention.[10]

Over the last few years, transcatheter aortic valve implantation (TAVI) has been proposed as a feasible and effective therapeutic alternative in patients with symptomatic severe AS and high operative risk.[11] In fact, studies have shown excellent and sustained transvalvular hemodynamics post-TAVI,[12] together with a significant improvement in symptoms and quality of life.[12,13] In addition, good survival rates have been reported post-TAVI, ranging from 74% to 78% at the 1-year follow-up.[12,14] However, no studies have examined the impact of baseline LV systolic function on the outcomes of patients undergoing TAVI. Therefore, the aims of this study were:

1. to compare early and long-term clinical outcomes post-TAVI in patients with normal versus impaired LV systolic function;

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2. to evaluate early and long-term changes in LV volumes and function post-TAVI in these 2 groups of patients; and
3. to compare the survival of patients undergoing TAVI with that of a group undergoing SAVR matched for age, gender, aortic valve area, and LVEF.

Methods

Patient population

In total, 147 consecutive patients with symptomatic severe AS who underwent TAVI in 2 centers (Leiden University Medical Center, Leiden, The Netherlands, and Centro Cardiologico Monzino, IRCCS, Milan, Italy) were included. Detailed clinical evaluation, transthoracic echocardiography, and invasive angiography of the coronary/aortoiliofemoral arterial systems were performed in all patients before the procedure.[11] In particular, clinical evaluation included the assessment of operative risk based on the logistic EuroSCORE[9] and identification of associated comorbidities and physical frailty according to the criteria of Fried et al.[15] The decision to offer TAVI to patients was evaluated by a multidisciplinary team approach. All patients underwent clinical and echocardiographic evaluation immediately post-TAVI (within 48 hours) and at the 3-, 6-, and 12-month follow-up points.

The current study received no extramural funding. We, the authors, are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of this article, and its final contents.

Transthoracic echocardiography

Patients were imaged using a commercially available ultrasound system (Vivid-7, General Electric, Horten, Norway). Transaortic pressure gradients and AVA were calculated for all patients.[16] Severe AS was defined as a mean transaortic pressure gradient of at least 40-50 mm Hg or an AVA <1 cm^2.[2] Presence of aortic regurgitation and its severity were evaluated as recommended.[17]

LV end-diastolic volume (LVEDV) and LV end-systolic volume (LVESV) were measured and indexed to body surface area.[18] LVEF was derived according to the biplane Simpson method.[18] LV systolic function was defined as normal when LVEF was ≥50% and as impaired when LVEF was <50%.[19] Standard LV ventricular dimensions[18] were also obtained, and LV mass was calculated according to Devereux et al.[18,20]

In addition, LV diastolic function was assessed by the ratio of the transmitral early filling velocity (E wave) to the late diastolic filling velocity (A wave) and the deceleration time of the E wave.[21] Maximal left atrial (LA) area was measured from the standard apical 4-chamber view.[18] Pulmonary artery systolic pressure was calculated as recommended.[21]

TAVI

All patients underwent TAVI with a balloon-expandable Edwards SAPIEN valve (Edwards Lifesciences, Irvine, CA). The procedures were performed at the catheterization laboratory under general anesthesia with transesophageal echocardiography and fluoroscopy guidance. The prosthesis was implanted via the transfemoral or transapical approach, as previously described.[22] The transapical approach was performed in patients with unfavorable iliofemoral anatomy.[22] Procedural success was defined as implantation of a functioning aortic prosthetic valve without intraprocedural mortality.[12] Duration of fluoroscopy, length of the procedure, and the total contrast volume used during the procedure were also recorded.

Follow-up and data collection

Intraprocedural mortality was defined as any death that occurred before extubation in the catheterization laboratory. Intraprocedural adverse events, such as vascular complication, cardiac tamponade, myocardial infarction, and severe aortic regurgitation, were recorded. The diagnosis of acute myocardial infarction was made on the basis of typical electrocardiographic changes and/or ischemic chest pain associated with elevation of cardiac biomarkers.[23]

In-hospital adverse events, defined as those occurring during the index hospital stay, included all cardiovascular events (such as cardiovascular death, heart failure, stroke, and heart conduction block requiring pacemaker) and noncardiovascular events. Combined major adverse cardiovascular events (MACEs), defined as a composite of death, nonfatal stroke, heart failure, or nonfatal myocardial infarction, were recorded. Total early mortality included both intraprocedural, in-hospital deaths and deaths occurring ≤30 days of the procedure.

No patient was lost to follow-up, and the mean follow-up period was 9.1 ± 5.1 months. Long-term follow-up outcomes included all-cause mortality and major cardiovascular and noncardiovascular-related adverse events.

Statistical analysis

Continuous variables are presented as mean ± SD or as median (interquartile range). Categorical variables are presented as frequencies (percentages). Clinical and echocardiographic characteristics of patients were compared based on LV systolic function (LVEF ≥50% vs LVEF <50%) at baseline.[19] Unpaired Student's *t* test or the Mann-Whitney *U*-test was used to compare the continuous variables, as appropriate. To compare categorical variables, we used χ^2 test or Fisher's exact test, as appropriate. Repeated-measures analysis of variance (ANOVA) was used to analyze the repeated paired continuous variables, and post hoc analysis for significant results was performed using Bonferroni's correction. In addition, survival rates were presented as Kaplan-Meier curves, and the log-rank test was used for comparisons between groups. To identify predictors of cumulative major adverse events after TAVI, we used a Cox proportional hazards model. Variables with $P < .2$ in the Cox univariate analysis were used in the multivariate model. Finally, the survival rate of patients who received TAVI was compared with that of a reference cohort who underwent SAVR in the last 10 years at the Leiden University Medical Center matched for age, gender, AVA, and LVEF. A 2-tailed probability value <.05 was considered statistically significant. All statistical analyses were conducted using SPSS version 16 (SPSS, Chicago, IL).

Results

Baseline characteristics

All patients underwent TAVI due to high operative risk (mean logistic EuroSCORE = 21.8% ± 11.0%) and multiple comorbidities (Table I).

Table I. Baseline clinical and echocardiographic characteristics of patients with a baseline LVEF ≥50% and those with that of <50%

	LVEF ≥50% (n = 97)	LVEF <50% (n = 50)	*P* value*
Age (y)	80.5 ± 6.3	79.8 ± 7.5	.57
Male [n (%)]	35 (36)	28 (56)	.023
Logistic EuroSCORE (%)	20.7 ± 10.6	24.0 ± 11.6	.09
New York Heart Association functional class of III or higher [n (%)]	65 (67)	45 (90)	.002
Previous myocardial infarction [n (%)]	15 (16)	12 (24)	.26
Previous coronary bypass surgery [n (%)]	14 (25)	14 (28)	.69
Previous percutaneous coronary intervention [n (%)]	20 (21)	13 (26)	.53
Peripheral vascular disease [n (%)]	35 (36)	17 (34)	.86
Hypertension [n (%)]	78 (80)	35 (70)	.22
Hypercholesterolemia [n (%)]	45 (46)	27 (54)	.39
Diabetes [n (%)]	17 (18)	20 (40)	.005
Smoking [n (%)]	26 (27)	25 (50)	.006
Frailty [n (%)]†	33 (34)	15 (30)	.71
Heart rhythm			
Sinus rhythm [n (%)]	81 (84)	31 (62)	.007
Atrial fibrillation [n (%)]	16 (17)	14 (28)	.13
Pacemaker [n (%)]	3 (3)	9 (18)	.003
Renal dysfunction [n (%)]‡	18 (19)	12 (24)	.39
Hemoglobin (g/dL)	12.2 ± 1.5	13.7 ± 2.6	.22
Echocardiography			
AVA (cm^2)	0.66 ± 0.16	0.68 ± 0.17	.49
Mean aortic gradient (mm Hg)	52 ± 17	40 ± 15	<.001
LVEDV index (mL/m^2)	56 ± 23	79 ± 27	<.001
LVESV index (mL/m^2)	25 ± 18	47 ± 23	<.001
LVEF (%)	61 ± 7	37 ± 8	<.001
LV mass index (g/m^2)	149 ± 40	174 ± 59	.010
Mitral E/A ratio	0.96 ± 0.73	1.27 ± 0.95	.037
Mitral deceleration time (ms)	244 ± 80	223 ± 93	.017
LA area (cm^2)	23.7 ± 5.7	27.2 ± 6.6	.002
Pulmonary artery systolic pressure (mm Hg)	41 ± 10	46 ± 10	.25
Aortic regurgitation grades I and II [n (%)]	75 (77)	38 (76)	.86
Transfemoral approach [n (%)]	48 (50)	27 (54)	.73

* *P* for comparison between baseline LVEF ≥50% and that of <50%.
† Frailty was assessed according to the criteria of Fried et al.[15]
‡ Renal dysfunction is defined as serum creatinine level >130 μmol/L.

Of the total population, 50 patients (34%) had an LVEF <50% and the remaining patients (n = 97, 66%) had an LVEF ≥50% before TAVI. Patients with an LVEF <50% tended to be in a New York Heart Association functional class of III or higher and to have a higher cardiovascular risk profile (with higher prevalence of diabetes and smoking) as compared with patients with an LVEF ≥50% (Table I).

The AVA was similar in patients with an LVEF <50% and those with that of ≥50%, however, the mean transaortic gradient was lower in patients with impaired LV function (40 ± 15 vs 52 ± 17 mm Hg, $P < .001$). In addition, patients with an LVEF <50% exhibited larger LV volumes, higher LV mass, and larger LA area (Table I).

Intraprocedural outcomes

The procedural success rate was 96% (n = 141) in the population. There were 6 cases of unsuccessful procedure: 4 cases of intraprocedural mortality (3 died from vascular complications, and the fourth patient developed massive aortic regurgitation after prosthesis deployment) and 2 procedures were abandoned (due to risk of ventricular rupture via transapical approach in 1 patient, and because the other patient required emergency surgery after iliac artery perforation).

Finally, there were no significant differences in procedural success, intraprocedural mortality, or MACEs between patients with an LVEF ≥50% and those with that of <50% (Table II). The duration of procedure and amount of contrast used were similar (Table II).

Early clinical outcomes

Total early mortality (≤30 days) was 7% (n = 10) in the entire population, which included 4 (3%) intraprocedural deaths (Table II). The remaining deaths were due to heart failure (n = 3), stroke (n = 1), and noncardiac-related respiratory cause (n = 2).

The difference between patients with an LVEF ≥50% and those with that of <50% in terms of early mortality or each individual adverse event (≤30 days) did not reach statistical significance (Table II). However, the MACE rate was significantly higher in the group with an LVEF <50% when compared with the group with an LVEF ≥50% (20% vs 7%, $P = .029$).

Echocardiographic outcomes

Immediately post-TAVI, significant reduction in the mean transaortic gradient (from 48 ± 17 to 11 ± 5 mm Hg, $P < .05$) and a corresponding increase in the effective AVA were observed in all patients (Table III). These desirable transaortic hemodynamics were maintained at long-term follow-up.

All echocardiographic variables obtained at baseline, immediately post-TAVI, and the latest follow-up in patients with a baseline LVEF ≥50% and those with that of <50% are summarized in Table III. The mean echocardiographic follow-up was 7.2 ± 4.2 months (median = 6.3 months). In both groups, LVEDV index did not change significantly post-TAVI. In contrast, LVESV index decreased significantly from 47 ± 23 mL/m^2 at baseline to 45 ± 20 mL/m^2 and then to 40 ± 20 mL/m^2 (ANOVA $P = .004$) in patients with a baseline LVEF <50%, whereas no significant changes in LVESV index were observed in patients with a baseline LVEF ≥50%. Accordingly, LVEF increased significantly from 37% ± 8% to 46% ± 11% post-TAVI and to 51% ± 11% (ANOVA $P < .001$) at follow-up in patients with a baseline LVEF <50%. In the group with a baseline LVEF ≥50%, however, LVEF remained within normal limits over time. Impor-

Table II. Comparison of intraprocedural and early clinical outcomes for patients with a baseline LVEF ≥50% and those with that of <50%

	All (N = 147)	LVEF ≥50% (n = 97)	LVEF <50% (n = 50)	*P* value*
Intraprocedural				
Procedural success [n (%)]	141 (96)	94 (97)	47 (94)	.41
Mortality [n (%)]	4 (3)	2 (2)	2 (4)	.61
Vascular complication [n (%)]	10 (7)	5 (5)	5 (10)	.31
Fatal [n (%)]	3 (2)	1 (1)	2 (4)	.27
Nonfatal [n (%)]	7 (5)	4 (4)	3 (6)	.69
Cardiac tamponade [n (%)]	4 (3)	4 (4)	0	.30
Acute myocardial infarction [n (%)]	2 (1)	1 (1)	1 (2)	.57
Severe aortic regurgitation [n (%)]	2 (1)	2 (2)	0	.43
Fluoroscopy time (min)†	10 (6-13)	10 (7-13)	10 (5-12)	.54
Procedure duration (min)†	95 (71-115)	95 (78-119)	87 (65-110)	.30
Contrast load (mL)†	150 (120-200)	150 (125-200)	140 (100-200)	.29
In-hospital				
Cardiovascular events [n (%)]	16 (11)	10 (10)	6 (12)	.78
Heart failure [n (%)]	5 (3)	2 (2)	3 (6)	.34
Fatal [n (%)]	3 (2)	2 (2)	1 (2)	1.00
Nonfatal [n (%)]	2 (1)	0	2 (4)	.11
Stroke [n (%)]	4 (3)	1 (1)	3 (6)	.11
Fatal [n (%)]	1 (1)	0	1 (2)	.79
Nonfatal [n (%)]	3 (2)	1 (1)	2 (4)	.27
Heart conduction block requiring pacemaker [n (%)]	7 (5)	6 (6)	1 (2)	.42
Infection [n (%)]	2 (1)	0	2 (4)	.11
Early (≤30 days)				
Total mortality [n (%)]	10 (7)	5 (5)	5 (10)	.31
Combined death, stroke, heart failure, or acute myocardial infarction [n (%)]	17 (12)	7 (7)	10 (20)	.029

* *P* for comparison between baseline LVEF ≥50% and that of <50%.
† Data are presented as median (interquartile range).

Table III. Comparison of echocardiographic parameters at baseline, immediately after the procedure, and latest follow-up

	Baseline	Immediately post-TAVI	Latest follow-up	ANOVA *P* within group
Effective AVA (cm^2)				
LVEF ≥50%	0.66 ± 0.16	2.09 ± 0.42*	2.12 ± 0.58†	<.001
LVEF <50%	0.68 ± 0.17	2.08 ± 0.49*	2.00 ± 0.53†	<.001
Mean gradient (mm Hg)				
LVEF ≥50%	52 ± 17	11 ± 5*	11 ± 9†	<.001
LVEF <50%	40 ± 15	10 ± 4*	10 ± 4†	<.001
LVEDV index (mL/m^2)				
LVEF ≥50%	56 ± 23	55 ± 20	55 ± 21	>.99
LVEF <50%	79 ± 27	79 ± 24	78 ± 23	>.99
LVESV index (mL/m^2)				
LVEF ≥50%	25 ± 18	24 ± 17	23 ± 16	.89
LVEF <50%	47 ± 23	45 ± 20	40 ± 20†	.004
LVEF (%)				
LVEF ≥50%	61 ± 7	59 ± 11	60 ± 11	>.99
LVEF <50%	37 ± 8	46 ± 11*	51 ± 11†‡	<.001
LV mass index (g/m^2)				
LVEF ≥50%	149 ± 40	144 ± 36	130 ± 38†‡	.004
LVEF <50%	174 ± 59	172 ± 52	143 ± 37†‡	<.001
Mitral E/A ratio				
LVEF ≥50%	0.96 ± 0.73	1.10 ± 0.89	0.87 ± 0.50‡	.032
LVEF <50%	1.27 ± 0.95	1.30 ± 0.87	0.93 ± 0.61	.24
Mitral deceleration time (ms)				
LVEF ≥50%	243 ± 80	232 ± 83	251 ± 90	.56
LVEF <50%	223 ± 93	204 ± 68	205 ± 115	.61
LA area (cm^2)				
LVEF ≥50%	23.7 ± 5.7	24.3 ± 6.4	23.0 ± 6.2	.068
LVEF <50%	27.2 ± 6.6	27.4 ± 5.7	25.5 ± 6.2†	.028
Pulmonary artery systolic pressure (mm Hg)				
LVEF ≥50%	41 ± 10	39 ± 11	38 ± 12	.11
LVEF <50%	46 ± 10	43 ± 9	39 ± 11†	.012

* *P* < .05 between baseline and immediately post-TAVI.
† *P* < .05 between baseline and latest follow-up.
‡ *P* < .05 between immediately post-TAVI and latest follow-up.

tantly, all patients showed a significant reduction in LV mass index, regardless of the baseline LVEF (Table III).

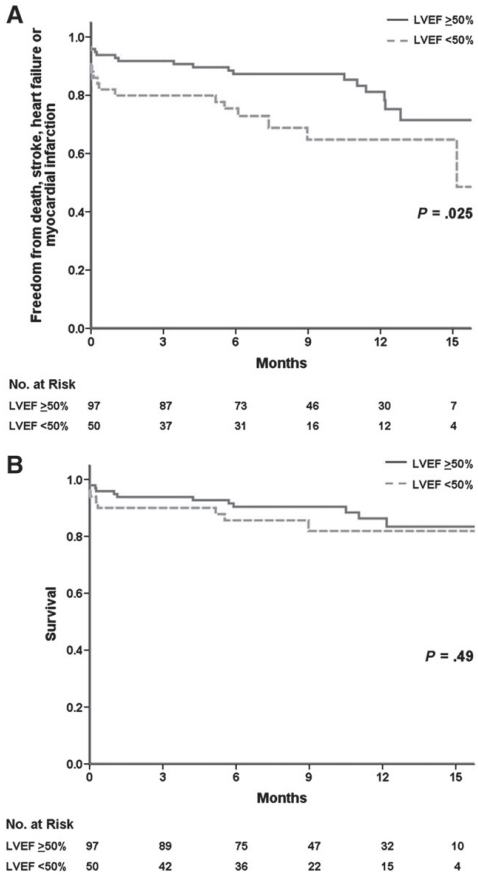
In addition, patients with a baseline LVEF <50% showed significant improvement in LV diastolic function, with a reduction in both LA area and pulmonary artery systolic pressure (Table III). Similarly, patients with a normal baseline LVEF showed a trend toward a decrease in LA area (23.7 ± 5.7 vs 23.0 ± 6.2 cm^2, *P* = .068).

Long-term clinical outcomes

During the follow-up period, there were 12 more cases of death in the total population: 4 cases of cardiovascular death (myocardial infarction, stroke, and infective endocarditis) and 8 cases of noncardiovascular death (gastrointestinal, renal, pulmonary, and orthopedic causes). In addition, further MACEs occurred in 9 patients. Noncardiovascular events (pulmonary diseases) were observed in 2 other patients.

In the Kaplan-Meier analyses of clinical outcomes, the percentage of patients free of MACEs at 6 months and that at 1 year were lower in patients with a baseline LVEF <50% (76% and 65%, respectively) as compared with patients with a baseline LVEF ≥50% (87% and 81%, respectively; log-rank *P* = .025; Figure 1, *A*). In addition, the univariate Cox proportional hazards analysis identified 5 potential baseline predictors of cumulative MACEs: logistic EuroSCORE (hazard ratio [HR] = 1.02, 95% confidence interval [CI] = 1.00-1.05, *P* = .10), presence of frailty (HR = 3.14, 95% CI = 1.59-6.20, *P* = .001), peripheral vascular disease (HR = 1.73, 95% CI = 0.88-3.38, *P* = .11), history of previous coronary artery bypass (HR = 1.75, 95% CI = 0.88-3.47, *P* = .11), and baseline LVEF (HR = 0.98, 95% CI = 0.96-1.00, *P* = .063). In the

Figure 1



A, Kaplan-Meier curves of freedom from death, nonfatal stroke, heart failure, or nonfatal myocardial infarction for patients who underwent TAVI with a baseline LVEF ≥50% and those with that of <50%. **B**, Kaplan-Meier curves of survival for patients who underwent TAVI with a baseline LVEF ≥50% and those with that of <50%.

final multivariate model, presence of frailty (HR = 4.20, 95% CI = 2.00-8.84, $P < .001$) and baseline LVEF (HR = 0.97, 95% CI = 0.94-0.99, $P = .017$) emerged as the only independent predictors of cumulative MACEs.

Nonetheless, the general survival rates at 1, 6, and 12 months in patients with a baseline LVEF ≥50% and those with that of <50% were not significantly different, as illustrated in Figure 1, *B* (95%, 90%, and 86% vs 90%, 86%, and 82%, respectively; log-rank $P = .49$).

TAVI versus surgery

Ninety-nine patients who underwent SAVR at the Leiden University Medical Center were retrospectively recruited from the surgical database and divided into 2 subgroups based on an LVEF <50% (n = 30) or that of ≥50% (n = 69) before surgery to evaluate whether the clinical outcome of TAVI is similar to that of the surgical approach. Table IV summarizes the baseline characteristics of patients who underwent SAVR. These control patients were frequency matched to the studied population in terms of age (79.3 ± 5.6 vs 80.5 ± 6.3 years, $P = .23$), male gender (34.8% vs 36.1%, $P = .86$), and AVA (0.71 ± 0.14 vs 0.66 ± 0.16 cm^2, $P = .06$) for the group with a baseline LVEF ≥50%. In patients with a baseline LVEF <50%, similar matching was performed with regard to their age (77.3 ± 5.0 vs 79.8 ± 7.5 years, $P = .08$), male gender (73.3% vs 56.0%, $P = .12$), and AVA (0.73 ± 0.24 vs 0.68 ± 0.17 cm^2, $P = .37$). Figure 2 demonstrates that survival of patients who underwent TAVI compared favorably with that of patients who underwent SAVR (log-rank $P = .40$), regardless of LV function at baseline.

Discussion

The Euro Heart Survey indicated that apart from advanced age, LV systolic dysfunction is the other major reason to deny surgery in patients with severe AS.[10] In fact, the outcome of SAVR is highly dependent on preoperative LV function.[4,7,24] Recently, TAVI has been introduced as a therapeutic alternative in patients with excessive operative risk. However, little is known on the impact of preoperative LV function on clinical and echocardiographic outcomes post-TAVI.

The present study demonstrates that TAVI is a feasible and effective therapeutic option for high-risk patients with severe AS, irrespective of baseline LVEF. Significant improvements in transvalvular hemodynamics and in LV performance were observed post-TAVI. In particular, patients with an LVEF <50% showed LV reverse remodeling, with marked improvements of LV systolic function and diastolic function.

In addition, early and late all-cause mortality rates were not significantly different between patients with normal and those with impaired LV function, despite a higher rate of combined MACEs in patients with a baseline LVEF <50%. Predictors of cumulative MACEs were the presence of frailty and baseline LVEF. Importantly, the long-term survival curves of patients with normal and those with impaired LV function who underwent TAVI were comparable with those of patients who underwent SAVR (the standard therapy for severe symptomatic AS[2]).

Early clinical outcomes

In the current study, the procedural success rate for TAVI was 96%, in line with results of a recent series that reported improved procedural success rates of 91%-

Table IV. Baseline clinical and echocardiographic characteristics of patients who underwent SAVR with a baseline LVEF ≥50% and those with that of <50%

	LVEF ≥50% (n = 69)	LVEF <50% (n = 30)
Age (y)	79.3 ± 5.6	77.3 ± 5.0
Male [n (%)]	24 (35)	22 (73)
Logistic EuroSCORE (%)	9.6 ± 5.1	17.8 ± 13.0
New York Heart Association functional class of III or higher [n (%)]	30 (44)	14 (47)
Previous myocardial infarction [n (%)]	10 (15)	11 (37)
Previous coronary bypass surgery [n (%)]	8 (11)	7 (23)
Hypertension [n (%)]	35 (51)	11 (37)
Hypercholesterolemia [n (%)]	17 (25)	9 (30)
Diabetes [n (%)]	15 (22)	8 (27)
Smoking [n (%)]	14 (20)	6 (20)
Renal dysfunction [n (%)]*	4 (6)	6 (20)
Hemoglobin (g/dL)	12.6 ± 1.9	13.3 ± 2.0
Echocardiography		
AVA (cm^2)	0.71 ± 0.14	0.73 ± 0.24
Mean aortic gradient (mm Hg)	49 ± 18	33 ± 16
LVEF (%)	60 ± 6	35 ± 8
Concomitant coronary bypass surgery [n (%)]	29 (42)	15 (50)

* Renal dysfunction is defined as serum creatinine level >130 μmol/L.

94%.[12,14] Despite their higher risk profile, patients with a baseline LVEF <50% showed similar success rate (97% vs 94%) and perioperative adverse events relative to patients with a baseline LVEF ≥50% (Table II). Of note, procedure-specific variables, such as procedure duration and total contrast volume, were also similar. Therefore, the present study highlights the feasibility of TAVI in a multicenter setting and regardless of baseline LV function.

The overall early 30-day mortality was 7%, which compares favorably with the recently published multicenter Canadian experience of 10%.[14] Although no significant differences in terms of 30-day mortality were observed between patients with preserved and those with impaired LV function (10% vs 5%, $P = .31$), patients with an LVEF <50% had a more than 2-fold increase in the risk of combined MACEs (20% vs 7%, $P = .03$) as compared with patients with an LVEF ≥50%. Therefore, in patients undergoing TAVI, the presence of LV dysfunction has an additional negative impact on early morbidity with an increased incidence of combined MACEs without affecting the early all-cause mortality significantly.

Echocardiographic outcomes

As a result of chronic LV pressure overload associated with severe AS, the LV wall thickens initially in an attempt to limit wall stress and to maintain adequate systolic function.[16] However, when the wall stress exceeds LV compensatory capacity, LV systolic dysfunction ensues from the effect of afterload mismatch.[3] Consequently, in the absence of significant primary myocardial dysfunction, valve replacement (TAVI or SAVR) results in improvement of LV function.[16] Accordingly, marked LV reverse remodeling and improvement in LV systolic function were observed especially in patients with a baseline LVEF <50%, in whom the mean LVEF increased over time. Thus, the present study confirms that LV dysfunction, when it is due to afterload mismatch associated with severe AS, may be reversible following TAVI.

Significant improvement in other echocardiographic parameters was also observed. LV mass regression occurred in all patients due to the marked improvement in LV hemodynamics post-TAVI. Similarly, as a result of the reduction in LV filling pressure, significant improvement in LV diastolic function was observed (a reduction in LA area and pulmonary artery systolic pressure) (Table III). Of note, this improvement was more marked in patients with a baseline LVEF <50%, who also showed a larger LA area at baseline. LA dilatation has been recognized as a marker of disease progression in patients with AS, reflecting the increase in LV filling pressures associated with severe AS.[25] This study highlights that LA enlargement could also be attenuated post-TAVI.

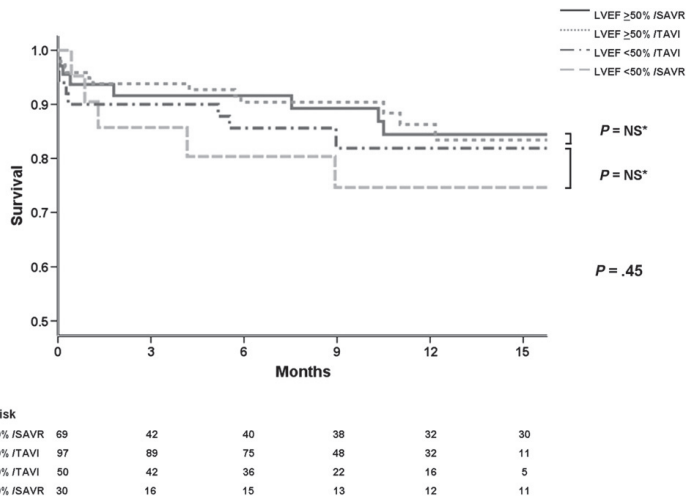
Long-term clinical outcomes

This study shows that during long-term follow-up post-TAVI, patients with a baseline LVEF <50% were associated with higher incidence of combined MACEs as compared with those with a normal LVEF (Figure 1, *A*). Moreover, other than baseline LVEF, the physical performance status of patients (expressed by frailty in the present study) was an independent predictor of MACE-free survival. Similarly, preprocedural functional status, as expressed using a different scoring index (Karnofsky index),[26] has been shown to be able to predict outcome post-TAVI in a recent study of 168 patients who underwent self-expanding prosthesis implantation.[27] These findings suggest that incorporating the functional assessment of high-risk patients with AS in the selection criteria for TAVI may be more appropriate than the currently used scoring systems to identify those patients who will derive maximum benefit from this new intervention.

In terms of all-cause mortality, the cumulative survival rates were similar in both groups (Figure 1, *B*). A possible explanation for this finding is that most deaths occurring after 30 days were not from cardiovascular causes but were related to advanced age and the presence of comorbidities. In the series of Webb et al,[12] who followed up on 168 patients post-TAVI, late mortality was also primarily determined by underlying comorbidities.

Furthermore, in the present study, patients who underwent TAVI had survival curves similar to those of patients who underwent SAVR (Figure 2). In particular, no significant differences were observed in survival rates at 6 months (92% vs 90%) and 1 year (84% vs 86%, log-rank

Figure 2



Kaplan-Meier curves of survival for patients with a baseline LVEF ≥50% and those with that of <50% who underwent SAVR or TAVI. The asterisk indicates comparison between SAVR and TAVI.

P = .82) between patients with a baseline LVEF ≥50% who underwent SAVR and those who underwent TAVI. Similarly, the type of procedure (SAVR or TAVI) did not have an impact on the survival rates at 6 months (80% vs 86%) or 1 year (75% vs 82%, log-rank *P* = .99) in patients with a baseline LVEF <50%. Therefore, the present study suggests that in patients at high operative risk, in whom SAVR would be excluded due to advanced age or depressed LVEF or a combination of factors, TAVI should be strongly considered. In fact, these patients, if left on medical therapy, would have high morbidity and mortality rates. Varadarajan et al[6] studied a cohort of 277 elderly patients (mean LVEF = 52% ± 20%) and showed that patients with symptomatic severe AS and left unoperated have significantly worse prognosis than those undergoing SAVR (52% vs 87% survival rate at 1 year). Moreover, previous studies[5,6,8] have indicated that the presence of LV dysfunction has further negative impact on the survival of patients with severe AS. Tarantini et al[8] reported that in patients with severe AS and depressed LVEF, the mortality rate was very high, with only 16% of patients alive at 2 years. Therefore, the current study suggests that TAVI may improve the survival of high-risk patients with severe AS to a level that is possibly comparable with that of SAVR (the standard therapy for symptomatic severe AS[2]), regardless of baseline LV function.

Limitations

Although the data were prospectively collected, all adverse events were collected from the electronic database of each center. Nonetheless, the investigators endeavored to ensure accuracy of the information provided. In addition, we acknowledge the limitations in comparing TAVI versus SAVR (using a control cohort) and in particular the presence of potential confounding factors despite the matching criteria. For example, due to a selection bias associated with TAVI (after SAVR was denied), patients who underwent TAVI carry significantly higher operative risk compared with those who underwent SAVR. Nonetheless, this inherent difference would have biased the results toward a larger difference in outcomes, favoring those of surgery. On the contrary, the present study shows that patients who underwent TAVI had comparable long-term survival outcome as those who underwent SAVR. The present study may shed some light on the difference in outcomes between these 2 approaches before the results of a randomized controlled trial become available.

Conclusions

The present study shows that the patients with severe AS at high operative risk benefited from TAVI in terms of improvement in LV function and survival, regardless of

baseline LVEF. Although patients with an LVEF <50% were at higher risk of combined MACEs when compared with patients with an LVEF ≥50%, the early and long-term all-cause mortality rates were similar. Importantly, TAVI resulted in a long-term survival that was comparable with that of a matched group of patients who underwent SAVR (the current standard of care for severe AS[2]).

Disclosures

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