Journal of the American College of Cardiology Vol. 53, No. 20, 2009

ISSN 0735-1097/09/$36.00
doi:10.1016/j.jacc.2009.01.060

FOCUS ISSUE: VALVULAR HEART DISEASE

Comparison of the Hemodynamic Performance of Percutaneous and Surgical Bioprostheses for the Treatment of Severe Aortic Stenosis

Marie-Annick Clavel, DVM, MSc,* John G. Webb, MD,† Philippe Pibarot, DVM, PhD,* Lukas Altwegg, MD,† Eric Dumont, MD,* Chris Thompson, MD,† Robert De Larochellière, MD,* Daniel Doyle, MD,* Jean-Bernard Masson, MD,† Sebastien Bergeron, MD,* Olivier F. Bertrand, MD, PhD,* Josep Rodés-Cabau, MD*

Québec City, Québec, and Vancouver, British Columbia, Canada

Objectives This study was undertaken to compare the hemodynamic performance of a percutaneous bioprosthesis to that of surgically implanted (stented and stentless) bioprostheses for the treatment of severe aortic stenosis.

Methods Fifty patients who underwent percutaneous aortic valve implantation (PAVI) with the Cribier-Edwards or Edwards SAPIEN bioprosthetic valve (Edwards Lifesciences, Inc., Irvine, California) were matched 1:1 for sex, aortic annulus diameter, left ventricular ejection fraction, body surface area, and body mass index, with 2 groups of 50 patients who underwent surgical aortic valve replacement (SAVR) with a stented valve (Edwards Perimount Magna [SAVR-ST group]), or a stentless valve (Medtronic Freestyle, Medtronic, Minneapolis, Minnesota [SAVR-SL group]). Doppler echocardiographic data were prospectively obtained before the intervention, at discharge, and at 6- to 12-month follow-up.

Results Mean transprosthetic gradient at discharge was lower ($p < 0.001$) in the PAVI group (10 ± 4 mm Hg) compared with the SAVR-ST (13 ± 5 mm Hg) and SAVR-SL (14 ± 6 mm Hg) groups. Aortic regurgitation (AR) occurred more frequently in the PAVI group (mild: 42%, moderate: 8%) compared with the SAVR-ST (mild: 10%, moderate: 0%) and SAVR-SL (mild: 12%, moderate: 0%) groups ($p < 0.0001$). At follow-up, the mean gradient in the PAVI group remained lower ($p < 0.001$) than that of the SAVR-ST group, but was similar to that of the SAVR-SL group. The incidence of severe prosthesis-patient mismatch was significantly lower ($p = 0.007$) in the PAVI group (6%) compared with the SAVR-ST (28%) and SAVR-SL (20%) groups. However, the incidence of AR remained higher ($p < 0.0001$) in the PAVI group compared with the 2 other groups.

Conclusions PAVI provided superior hemodynamic performance compared with the surgical bioprostheses in terms of transprosthetic gradient and prevention of severe prosthesis-patient mismatch, but was associated with a higher incidence of AR. (J Am Coll Cardiol 2009;53:1883–91) © 2009 by the American College of Cardiology Foundation

Surgical aortic valve replacement (SAVR) is the treatment of choice for patients with symptomatic severe aortic stenosis. Two main types of bioprostheses, stented and stentless valves, are currently used for SAVR with excellent hemodynamic results in the vast majority of patients. However, the hemodynamic performance of the prosthetic valves is not equivalent to that of the normal native valve, and consequently, a substantial proportion of the patients are left with some degree of prosthesis-patient mismatch (PPM) after SAVR (1). Importantly, the occurrence of severe PPM, defined as an indexed valve effective orifice area (EOAi) ≤0.65 cm^2/m^2, has been associated with reduced functional improvement and increased morbidity and mortality rates at short-term and midterm follow-up after SAVR (1–3).

See page 1892

From the *Quebec Heart & Lung Institute/Laval Hospital, Laval University, Québec City, Québec, Canada; and †St. Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada. This study was funded, in part, by a grant (MOP 57745) of the Canadian Institutes of Health Research, Ottawa, Ontario, Canada. Dr. Pibarot holds the Canada Research Chair in Valvular Heart Disease, Canadian Institutes of Health Research, and has received honoraria from Edwards Lifesciences, Inc., Sorin Medical, St. Jude Medical, and Medtronic. Dr. Rodés-Cabau is a consultant for Edwards Lifesciences, Inc. Dr. Webb is a consultant to Edwards Lifesciences, Inc., St. Jude Medical, Guided Delivery Systems, and Kardium. Dr. Dumont served in a proctorship for transapical aortic valve replacement for Edwards Lifesciences, Inc.

Manuscript received October 15, 2008; revised manuscript received January 6, 2009, accepted January 25, 2009.

JACC Vol. 53, No. 20, 2009
May 19, 2009:1883–91

Abbreviations and Acronyms

AR = aortic regurgitation
EOA = effective orifice area
EOAi = indexed effective orifice area
LVEF = left ventricular ejection fraction
PAVI = percutaneous aortic valve implantation
PPM = prosthesis-patient mismatch
SAVR = surgical aortic valve replacement

In recent years, percutaneous aortic valve implantation (PAVI) has emerged as an alternative to the treatment of severe aortic stenosis in patients considered at high or prohibitive surgical risk (4–9). This patient selection has led to carrying out PAVI interventions in very old patients with multiple comorbidities and severely calcified aortic valves. The Cribier-Edwards or the Edwards SAPIEN bioprosthesis (Edwards Lifesciences, Inc., Irvine, California) is a balloon-expandable percutaneous valve that consists of a metallic structure of stainless steel containing a biological valve. Unlike SAVR, which involves the removal of the native aortic valve before valve implantation, the mechanism of PAVI consists of the expansion of the stent containing the new valve against the native calcified aortic valve. The implantation of a percutaneous bioprosthesis within a "left-in-place" severely calcified valve might lead to incomplete and/or irregular expansion of the prosthetic valve (10), but preliminary acute and midterm hemodynamic results obtained with PAVI have been promising, with low transprosthetic gradients and large prosthetic valve effective orifice area (EOA) in most patients, although some degree of residual aortic regurgitation (AR), usually paravalvular, is common after this procedure (4–9). However, how the hemodynamic results obtained with PAVI compare to those obtained with SAVR remains unknown. The objective of this study was to compare the hemodynamic performance of a percutaneous bioprosthesis, the Edwards (Cribier or SAPIEN) valve, to that of surgically implanted (stented and stentless) bioprostheses for the treatment of symptomatic severe aortic stenosis.

Methods

The study included a total of 50 patients with symptomatic severe aortic stenosis who underwent successful PAVI with the Cribier-Edwards or Edwards SAPIEN valve in St. Paul's Hospital, Vancouver, British Columbia, Canada, and in the Quebec Heart & Lung Institute/Laval Hospital, Quebec City, Canada. All patients had complete clinical and echocardiographic follow-up at 6 to 12 months, and were included in a prospective registry database. These patients were obtained from a series of 89 consecutive patients who underwent PAVI, after excluding those who had unsuccessful PAVI (failure to implant the valve or procedural death, n = 8), those who died before the 6-month to 1-year follow-up (n = 13), and those with a follow-up either carried out in other centers or incomplete (n = 18). The procedures were performed under compassionate clinical use approved by the Department of Health and Welfare (Ottawa, Ontario, Canada), and all patients signed informed consent for the procedures.

The 50 PAVI patients were case-matched with 50 patients who had undergone successful SAVR with a stented Carpentier-Edwards Perimount Magna bioprosthesis (Edwards Lifesciences [SAVR-ST group]), and with 50 patients who had undergone successful SAVR with a stentless Freestyle bioprosthesis (Medtronic, Minneapolis, Minnesota [SAVR-SL group]), from a prospective registry database including all patients who had undergone SAVR in the Quebec Heart & Lung Institute/Laval Hospital since 1993. Each PAVI patient was matched 1:1 with both a SAVR-ST and a SAVR-SL patient for sex (exact match), aortic annulus diameter (within 0.05 mm), and left ventricular ejection fraction (LVEF) (within 5%) as determined by echocardiography, body surface area (within 0.3 m^2), and body mass index (within 5 kg/m^2). The presence of a bicuspid aortic valve was a contraindication for PAVI, and we therefore excluded patients with a bicuspid valve from the study. All clinical and echocardiographic data were collected prospectively at baseline, at hospital discharge, and at 6- to 12-month follow-up. Some of the patients included in the PAVI group had already been included in 2 previous studies (5,7).

PAVI procedures. PAVI was performed with the use of the Cribier-Edwards valve or the Edwards SAPIEN valve, which are balloon-expandable prostheses that consist of a tubular slotted stainless steel stent with an attached pericardial trileaflet valve and fabric sealing cuff. Two valve sizes of 23- and 26-mm expanded diameter were available. The procedures were performed by transfemoral approach in 38 (76%) patients and by transapical approach in 12 (24%) using techniques described in detail in previous reports (4–9). Briefly, the procedures were performed by a team of interventional cardiologists and cardiac surgeons, under general anesthesia, without cardiopulmonary bypass, and with fluoroscopy and transesophageal echocardiography guidance. The 23-mm valve was selected if the aortic annulus was between 16 and 21 mm by transesophageal echocardiography, and the 26-mm valve was selected if the aortic annulus was between 22 and 25 mm. Patients received aspirin (80 mg/day) indefinitely and clopidogrel (75 mg/day) for 3 to 6 months.

SAVR procedures. The 2 surgical bioprostheses used in this study were the Magna valve, which is a stented bioprosthesis fabricated from bovine pericardium sheets mounted on a stent (SAVR-ST group), and the Freestyle valve, which is a stentless bioprosthesis manufactured from the whole porcine aortic valve (SAVR-SL group). The SAVR interventions were performed through standard midline sternotomy with cardiopulmonary bypass. Excision of the native aortic valve and annular debridement was performed in all cases before valve implantation. The size of both stented and stentless valves was determined by the diameter of the aortic annulus as measured by pre-calibrated cylindrical sizers and proprietary valve sizers. The Magna (stented) valve was implanted in the supra-annular position with interrupted, radial, noneverting, pledget-supported

sutures; whereas the Freestyle (stentless) valve was inserted in subcoronary position using a 2-layer suture technique. Patients received aspirin (80 to 325 mg/day) for the first 12 post-operative weeks.

Doppler echocardiography. All patients in the 3 groups underwent a Doppler echocardiographic examination at baseline before intervention, at hospital discharge, and at 6- to 12-month follow-up. The following measurements were obtained in all patients: aortic annulus diameter, LVEF calculated with the Simpson method, mean transvalvular gradient calculated with the Bernoulli formula, and the valve EOA measured by the continuity equation. The EOA was indexed for body surface area (EOAi), and the occurrence of severe PPM was defined as an EOAi ≤ 0.65 cm^2/m^2 (1). The presence, degree, and type (paravalvular versus transvalvular) of AR was recorded in all patients. The degree of AR was classified as follows: trivial, mild, moderate, and severe (11,12).

Statistical analysis. Categorical variables were expressed as percentages and continuous variables as mean (SD) unless otherwise specified. For each outcome variable, the mixed model analysis was performed to analyze 3 experimental factors: 1 associated to the subjects matched and analyzed as random block effects, 1 associated to the comparison among procedures (PAVI, SAVR-ST, SAVR-SL), and 1 linked to the time period. The procedure and period time factors were analyzed as repeated measures factors with an interaction term between them. For dichotomous variables, a binomial probability distribution function was obtained using the logit link transformation. Differences were considered statistically significant when $p < 0.05$. The data were analyzed using SAS statistical software, version 9.1.3 (SAS Institute Inc., Cary, North Carolina).

Results

Baseline and procedural data. Baseline clinical and echocardiographic data are shown in Table 1. The PAVI patients were older ($p < 0.0001$) compared with the SAVR-ST and SAVR-SL patients. The mean values of the matching variables in the whole study population were as follows: aortic annulus diameter: 20.1 mm; LVEF: 54%; body surface area: 1.7 m^2; and body mass index: 26 kg/m^2. There were no significant differences in the values of mean transvalvular gradients between groups, but patients in the PAVI group had lower baseline EOAi values compared with both SAVR-ST and SAVR-SL groups ($p = 0.011$).

Valve sizes grouped according to type of implanted valve are shown in Table 2. About two-thirds of the PAVI patients received a 26-mm valve, and one-third a 23-mm valve. The 21- and 23-mm valves were the most commonly implanted in both the SAVR-ST (72%) and SAVR-SL (70%) groups. Aortic root enlargement and Bentall procedures were not used in the SAVR patients because of the potentially increased operative risk associated with these procedures, especially in the elderly population with calcified aortic root.

Doppler echocardiography data. Doppler echocardiography data at hospital discharge are shown in Table 3. Mean transprosthetic gradient at discharge was lower ($p < 0.001$) in the PAVI group (10 ± 4 mm Hg) than in the SAVR-ST (13 ± 5 mm Hg) or SAVR-SL (14 ± 6 mm Hg) groups; and EOA and EOAi were larger ($p < 0.01$) in the PAVI group (1.61 ± 0.40 cm^2 and 0.90 ± 0.26 cm^2/m^2, respectively) than in the SAVR-ST (1.29 ± 0.25 cm^2 and 0.76 ± 0.16 cm^2/m^2, respectively) or SAVR-SL (1.38 ± 0.38 cm^2 and 0.80 ± 0.21 cm^2/m^2, respectively) groups. The incidence of severe PPM was higher ($p = 0.042$) in the SAVR-ST (26%) and SAVR-SL (28%) groups than in the PAVI group (11%). As shown in Table 4, the overall incidence of prosthetic regurgitation was higher ($p < 0.0001$) in the PAVI group (78%) than in the SAVR-ST (48%) or SAVR-SL (34%) groups. Mild AR was present in 42% of the PAVI patients compared with 10% and 12% of the SAVR-ST and SAVR-SL patients, respectively ($p < 0.001$). Four (8%) of the PAVI patients had moderate AR at hospital discharge compared with none of the SAVR patients ($p = 0.24$). The AR was considered of paravalvular origin in 94%, 56%, and 58% of the cases in the PAVI, SAVR-ST, and SAVR-SL groups, respectively. Figure 1 shows the absence of any significant association between the degree of valve oversizing and the

Table 1 Data of the Clinical and Echocardiographic Variables at Baseline

	PAVI (n = 50)	SAVR-ST (n = 50)	SAVR-SL (n = 50)	p Value
Age, yrs	83 ± 7	75 ± 6*	70 ± 9*†	<0.0001
Male, n (%)‡	27 (54)	27 (54)	27 (54)	1.000
Body surface area, m^2‡	1.76 ± 0.25	1.72 ± 0.20	1.74 ± 0.17	0.311
Body mass index, kg/m^2‡	25.2 ± 5.2	25.7 ± 3.6	27.0 ± 5.1	0.068
Aortic annulus diameter, mm‡	20.2 ± 2.0	20.0 ± 1.6	20.1 ± 1.7	0.779
Indexed annulus diameter, mm/m^2‡	11.6 ± 1.3	11.8 ± 1.1	11.7 ± 1.2	0.730
LVEF, %‡	54 ± 16	55 ± 15	56 ± 14	0.105
Mean gradient, mm Hg	47 ± 17	42 ± 16	43 ± 8	0.211
Effective orifice area, cm^2	0.60 ± 0.14	0.68 ± 0.20	0.69 ± 0.24	0.053
Indexed effective orifice area, cm^2/m^2	0.34 ± 0.10	0.40 ± 0.12*	0.40 ± 0.14*	0.011

*Significant difference ($p < 0.05$) versus PAVI. †Significant difference ($p < 0.05$) versus SAVR-ST. ‡Matched variables.
LVEF = left ventricular ejection fraction; PAVI = percutaneous aortic valve implantation; SAVR-SL = surgical aortic valve replacement–stentless valve; SAVR-ST = surgical aortic valve replacement–stented valve.

Table 2 Distribution of Label Prosthesis Size According to Type of Aortic Bioprosthesis

Prosthesis Size (mm)	PAVI	SAVR-ST	SAVR-SL
19	—	9 (18)	—
21	—	20 (40)	17 (34)
23	18 (36)	16 (32)	18 (36)
25	—	5 (10)	13 (26)
26	32 (64)	—	—
27	—	—	2 (4)

Values are n (%).
Abbreviations as in Table 1.

occurrence and degree of AR after PAVI. The valve size/aortic annulus diameter ratio was 1.25 ± 0.14 in cases with no or trivial AR compared with 1.24 ± 0.09 in cases with mild or moderate AR (p = 0.79).

No significant differences in LVEF were observed among groups at hospital discharge, but LVEF improved in the PAVI group compared with baseline values (ΔLVEF: 5 ± 10%, p < 0.001), whereas it remained similar to baseline in the SAVR-ST (ΔLVEF: 1 ± 8%, p = 0.39) and SAVR-SL (−1 ± 13%, p = 0.82) groups (p = 0.01 for comparison between groups) (Fig. 2). The LVEF data grouped according to baseline LVEF are shown in Table 5. The increase in LVEF was more pronounced in the 45 patients with reduced LVEF (≤50%) at baseline compared with the 105 patients with normal LVEF (>50%) at baseline (p < 0.001 for comparison between low and normal LVEF patients in all groups).

Doppler echocardiographic data at 6 to 12 months of follow-up are shown in Table 3. There were no significant changes in mean transvalvular gradient, EOA, and EOAi between hospital discharge and 6 to 12 months of follow-up in the PAVI and SAVR-ST groups (p > 0.15 for all variables in both groups), whereas mean transvalvular gradient and EOA exhibited a significant reduction and increase, respectively, in the SAVR-SL group compared with the values at discharge (Δ mean gradient: −4 ± 4 mm Hg, p < 0.001; ΔEOA: +0.18 ± 0.36 cm^2, p = 0.002; and ΔEOAi: +0.1 ± 0.21 cm^2/m^2, p = 0.003). At follow-up, transvalvular gradient was higher and EOA and EOAi were smaller in the SAVR-ST group than in the PAVI and SAVR-SL groups, and no significant differences were observed regarding these variables between the PAVI and SAVR-SL groups. However, the incidence of severe PPM remained higher (p = 0.007) in the SAVR-ST (28%) and SAVR-SL (20%) groups than in the PAVI group (6%).

The incidence and degree of AR remained similar to those at hospital discharge in the 3 groups, with higher incidence of mild AR in the PAVI group (46%) compared with the SAVR-ST (10%) and SAVR-SL (16%) groups (p < 0.001) (Table 4). There were no differences between

Table 4 Aortic Regurgitation Data at Discharge and at Follow-Up Grouped According to Type of Aortic Bioprosthesis

	PAVI	SAVR-ST	SAVR-SL	p Value
Aortic regurgitation at discharge				
None	6 (12)	31 (62)*	33 (66)*	<0.0001
Trivial	19 (38)	14 (28)	11 (22)	
Mild	21 (42)	5 (10)*	6 (12)*	
Moderate	4 (8)	0 (0)	0 (0)	
Severe	0 (0)	0 (0)	0 (0)	
Aortic regurgitation at follow-up				
None	11 (22)	26 (52)*	33 (66)*	<0.0001
Trivial	13 (26)	18 (36)	9 (18)	
Mild	23 (46)	5 (10)*	8 (16)*	
Moderate	3 (6)	1 (2)	0 (0)	
Severe	0 (0)	0 (0)	0 (0)	

Values are n (%). *Significant difference (p < 0.05) versus PAVI.
Abbreviations as in Table 1.

Table 3 Doppler Echocardiographic Data According to Type of Aortic Bioprosthesis

	PAVI	SAVR-ST	SAVR-SL	p Value
LVEF, %				
Discharge	59 ± 12*	56 ± 11	55 ± 14	0.053
Follow-up	59 ± 17	62 ± 18	60 ± 16	0.255
Mean transaortic gradient, mm Hg				
Discharge	10 ± 4*	13 ± 5*†	14 ± 6*†	<0.001
Follow-up	10 ± 4*	13 ± 5*†	9 ± 4*‡§	<0.001
Effective orifice area, cm^2				
Discharge	1.61 ± 0.40*	1.29 ± 0.25*†	1.38 ± 0.38*†	<0.0001
Follow-up	1.50 ± 0.36*	1.33 ± 0.28*†	1.57 ± 0.49*‡§	0.001
Indexed effective orifice area, cm^2/m^2				
Discharge	0.90 ± 0.26*	0.76 ± 0.16*†	0.80 ± 0.21*†	0.003
Follow-up	0.87 ± 0.18*	0.78 ± 0.17*†	0.90 ± 0.27‡§	0.019
Severe prosthesis-patient mismatch, n (%)				
Discharge	5 (11)	13 (26)†	14 (28)†	0.042
Follow-up	3 (6)	14 (28)†	10 (20)†	0.007

The p values presented refer to the intergroup comparisons. *Significant difference (p < 0.05) versus baseline. †Significant difference (p < 0.05) versus PAVI. ‡Significant difference (p < 0.05) versus SAVR-ST. §Significant difference (p < 0.05) versus discharge.
Abbreviations as in Table 1.

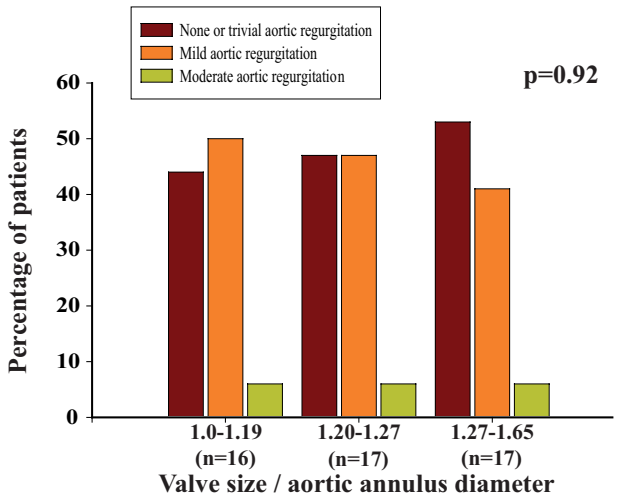

Figure 1 **Prosthesis Oversizing and Aortic Regurgitation**

Incidence and degree of aortic regurgitation at hospital discharge in the percutaneous aortic valve implantation (PAVI) patients grouped according to the degree of prosthesis oversizing with respect to the aortic annulus diameter. **Red bars** = no or trivial aortic regurgitation; **orange bars** = mild aortic regurgitation; **green bars** = moderate regurgitation.

groups regarding LVEF values at follow-up. The LVEF remained similar to that at hospital discharge in the PAVI group ($p = 0.10$), whereas it increased by 5 ± 10% ($p < 0.001$) and 4 ± 9% ($p = 0.004$) in the SAVR-ST and SAVR-SL groups, respectively, between hospital discharge and follow-up (Fig. 2). The increase in LVEF was higher in the group of 45 patients with low LVEF at baseline compared with the group of 105 patients with baseline LVEF within normal values ($p < 0.001$). Table 5 summarizes the changes in LVEF between baseline, hospital discharge, and follow-up in low and normal LVEF patients in the 3 aortic bioprosthesis groups.

Small aortic annulus size subgroup. Table 6 and Figure 3 show the data of EOAi and incidence of severe PPM in the 3 bioprosthesis groups according to the size of the patient's aortic annulus. Compared with the SAVR-ST and SAVR-SL groups, PAVI was associated with a larger EOAi and a lower incidence of severe PPM at discharge and at follow-up in the subset of patients with aortic annulus diameter ≤20 mm, whereas no differences in the incidence of severe PPM were observed between groups in patients with aortic annulus >20 mm. In the latter subset of patients, the SAVR-SL valve was associated with a larger EOAi at follow-up compared with the PAVI and SAVR-ST groups.

Discussion

The results of this study showed that PAVI with the Cribier-Edwards or Edwards SAPIEN valve was associated with lower transprosthetic gradients and higher EOAs early after the procedure compared with SAVR with the Magna (stented) and Freestyle (stentless) valves. At midterm follow-up there were no changes in the hemodynamic parameters of percutaneously implanted valves, which continued to provide a better hemodynamic performance than surgically implanted stented valves. The superior hemodynamic results obtained with PAVI translated into a significant reduction in the incidence of severe PPM at discharge (11%) and at midterm follow-up (6%) compared with the stented (discharge: 26%; midterm: 28%) and stentless (discharge: 28%; midterm: 20%) surgical valves. PAVI was associated with a marked reduction of severe PPM in patients with a small (≤20 mm) aortic annulus; whereas in patients with a larger annulus, the overall incidence of PPM was, as expected, much lower, with no significant differences between PAVI and SAVR groups. Furthermore, although no differences were observed between PAVI and SAVR patients in LVEF values at midterm follow-up, only patients who had undergone PAVI exhibited a significant early (between baseline and hospital discharge) increase in LVEF, and this effect was more pronounced in patients with low LVEF at baseline. Finally, the occurrence of any degree of AR was more common after PAVI (88%) than after SAVR (46%) early after the procedure. However, the degree of residual AR was trivial or mild in the vast majority (91%) of PAVI patients, with no cases of severe AR, and it remained stable at midterm follow-up.

Prosthesis-patient mismatch. Several studies have recognized the high prognostic relevance of achieving an optimal hemodynamic result after aortic valve replacement (1–3,13–16). The presence of severe PPM has been associ-

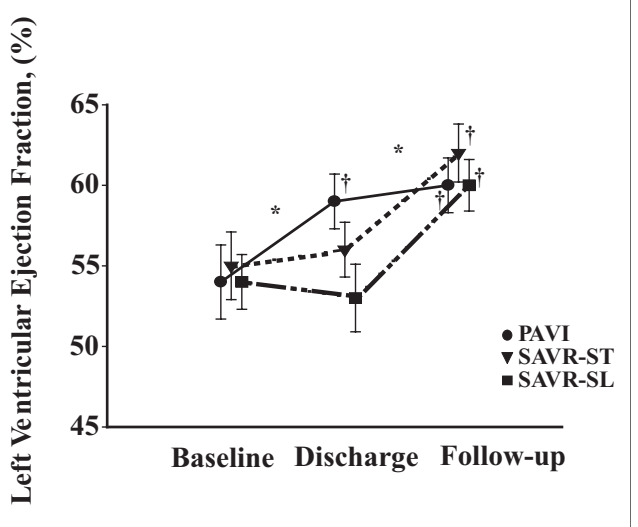

Figure 2 **LVEF After Aortic Valve Implantation**

Changes in left ventricular ejection fraction (LVEF) after aortic valve implantation in the 3 aortic bioprosthesis groups: percutaneous aortic valve implantation (PAVI) **(circles)**; surgical aortic valve replacement–stentless valve (SAVR-SL) **(squares)**; and surgical aortic valve replacement–stented valve (SAVR-ST) **(triangles)**. Error bars represent standard errors of the estimate. *LVEF different in PAVI groups versus other groups ($p < 0.05$). †LVEF different from baseline group ($p < 0.005$).

JACC Vol. 53, No. 20, 2009
May 19, 2009:1883–91

Table 5 LVEF Data Grouped According to Baseline LVEF (≤50% or >50%) and Type of Bioprosthesis

	LVEF at Baseline ≤50%				LVEF at Baseline >50%			
	PAVI (n = 15)	SAVR-ST (n = 15)	SAVR-SL (n = 15)	p Value	PAVI (n = 35)	SAVR-ST (n = 35)	SAVR-SL (n = 35)	p Value
Baseline, %								
LVEF	33 ± 12	34 ± 10	36 ± 10	0.529	63 ± 5	63 ± 5	63 ± 5	0.800
Discharge, %								
LVEF	48 ± 11*	42 ± 11	41 ± 15	0.110	64 ± 6	61 ± 7	59 ± 11	0.062
ΔLVEF	15 ± 8	8 ± 7†	5 ± 14†	0.014	1 ± 6	−2 ± 7	−4 ± 11	0.114
Follow-up, %								
LVEF	53 ± 13*	53 ± 17*‡	51 ± 15*	0.848	63 ± 7	64 ± 7	64 ± 10‡	0.089
ΔLVEF	20 ± 13	19 ± 16	15 ± 18	0.921	0 ± 7	1 ± 8	1 ± 11	0.473

The p values presented refer to the intergroup comparisons. *Significant difference ($p < 0.05$) versus baseline. †Significant difference ($p < 0.05$) from PAVI. ‡Significant difference ($p < 0.05$) versus discharge.

ΔLVEF = variation of left ventricular ejection fraction from baseline; other abbreviations as in Table 1.

ated with lesser improvement in the functional capacity of the patients (13), lesser regression of LV hypertrophy (14), higher rates of cardiac failure (16), and higher rates of perioperative and long-term mortality (2,3,15,16) after SAVR. The Magna and Freestyle valves are among the most commonly used stented and stentless bioprostheses for SAVR, and the results of valve hemodynamic performance observed in the present study for these 2 types of bioprosthesis were consistent with those of previous studies (17–20), although the aortic annulus and bioprosthesis size were smaller in the present study. Previous studies have also reported that the hemodynamic performance of stentless bioprostheses is generally superior, and accordingly, the prevalence/severity of PPM is lower compared with stented bioprostheses (18,20,21). However, the implantation of a stentless bioprosthesis is more complex and requires longer cardiopulmonary bypass time. The superior hemodynamic performance of stentless bioprostheses has been attributed to better sizing (namely, ability to implant a larger valve in a given aortic annulus), better preservation of the systolic expansion of the aortic root and annulus, and continued improvement of valve hemodynamics in the 3 to 6 months after operation (16,17). That explains why the hemodynamic performance of the SAVR-SL valve became superior to that of the SAVR-ST valve and equivalent to that of the PAVI valves after 6 to 12 months. Nonetheless, the results of the present study showed that the incidence of severe PPM remains high with both stented and stentless bioprostheses among patients with a small aortic annulus. Lopez et al. (22) reported a high rate (58%) of severe PPM among patients with a small aortic root undergoing SAVR with the Freestyle stentless bioprosthesis, and that was associated with high (>30%) perioperative mortality. Interestingly, the results of the present study reveal that the post-operative improvement in the valve hemodynamic performance that is observed with stentless bioprostheses essentially occurs in patients with a medium or large aortic annulus, whereas it is minimal or absent in patients with a small aortic annulus, who are precisely those at highest risk for severe PPM. This observation may explain why the rate of severe PPM remained higher in the SAVR-SL group than in the PAVI group at 6 to 12 months of follow-up despite significant improvement in the mean values of EOA and gradients in the SAVR-SL group between hospital discharge and follow-up.

With the balloon-expandable Cribier-Edwards or Edwards SAPIEN valve, PAVI was associated with excellent hemodynamic results, with a mean residual transprosthetic

Table 6 Indexed Effective Orifice Area and Incidence of Severe Patient-Prosthesis Mismatch Grouped According to Aortic Annulus Size and Type of Bioprosthesis

	Annulus Size ≤20 mm				Annulus Size >20 mm			
	PAVI (n = 28)	SAVR-ST (n = 28)	SAVR-SL (n = 28)	p Value	PAVI (n = 22)	SAVR-ST (n = 22)	SAVR-SL (n = 22)	p Value
Discharge								
Indexed effective orifice area, cm^2/m^2	0.87 ± 0.27	0.74 ± 0.17*	0.71 ± 0.15*	0.032	0.94 ± 0.26†	0.78 ± 0.15	0.92 ± 0.22	0.033
Severe patient-prosthesis mismatch, n (%)	2 (7)	8 (29)*	10 (36)*	0.049	3 (14)	5 (23)	4 (18)	0.583
Mean gradient, mm Hg	9 ± 4	14 ± 5*	16 ± 6*	<0.0001	10 ± 5	11 ± 4	11 ± 4	0.902
Follow-up								
Indexed effective orifice area, cm^2/m^2	0.87 ± 0.19	0.75 ± 0.2*	0.77 ± 0.18*	0.190	0.88 ± 0.17†	0.79 ± 0.13	1.08 ± 0.27*†‡	0.002
Severe patient-prosthesis mismatch, n (%)	2 (7)	9 (32)*	9 (32)*	0.007	1 (5)	5 (23)	1 (5)‡	0.574
Mean gradient, mm Hg	9 ± 4	14 ± 5*	11 ± 4†‡	0.004	10 ± 4†	12 ± 4	7 ± 4*†‡	0.004

*Significant difference ($p < 0.05$) versus PAVI. †Significant difference ($p < 0.05$) versus SAVR-ST. ‡Significant difference ($p < 0.05$) versus discharge.

Abbreviations as in Table 1.

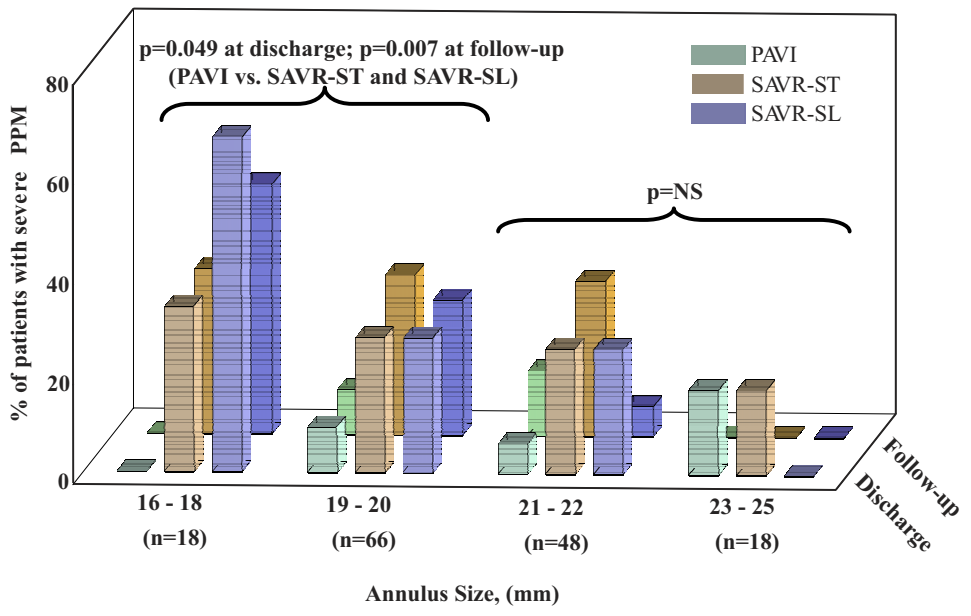

Figure 3 Prosthesis-Patient Mismatch

Incidence of severe prosthesis-patient mismatch (PPM) in the 3 aortic bioprosthesis groups at hospital discharge and at follow-up according to the aortic annulus size: percutaneous aortic valve implantation (PAVI) **(green bars)**; surgical aortic valve replacement–stentless valve (SAVR-SL) **(blue bars)**; and surgical aortic valve replacement–stented valve (SAVR-ST) **(brown bars)**.

gradient of 10 mm Hg and a mean EOA >1.5 cm^2. Importantly, these results were maintained without significant changes at 6 to 12 months of follow-up. Several studies have reported similar hemodynamic results with PAVI, with transprosthetic gradients ≤11 mm Hg and EOAs >1.5 cm^2, and no significant changes in the hemodynamic parameters up to 2-year follow-up (4–9). The present study was the first to evaluate the incidence of PPM after PAVI and to compare these data with those of surgically implanted bioprostheses. The results of this study showed a very low incidence of severe PPM, which was much lower than that observed with surgically implanted stented or stentless valves. Importantly, this superiority of PAVI in terms of reduction of PPM was limited to patients with a small aortic annulus in whom the incidence of severe PPM after PAVI was as low as 7%, compared with a 32% rate after SAVR. Whereas valve sizing during SAVR is limited by the dimensions of the aortic annulus, PAVI is systematically performed with an oversized valve, leading to some distension of the aortic annulus to accommodate the valve during balloon expansion. These findings suggest that expanding the bioprosthesis against a severely calcified native valve (10) does not appear to be a major limiting factor to PAVI and its hemodynamic outcome. Moreover, although the PAVI valves are stented valves, the stent is much thinner than that of the stented valves used for SAVR, and it therefore causes minimal obstruction to blood flow. Hence, our findings suggest that, compared with SAVR, PAVI provides better results in terms of valve EOA, transprosthetic gradient, and prevention of PPM, especially for patients with a small aortic annulus. Recent studies have reported that severe PPM has less impact on clinical outcomes in elderly patients compared with younger ones (23,24); and, conversely, it has been shown that the clinical impact of PPM is much more pronounced in patients with pre-existing LV systolic dysfunction irrespective of age (3,24). Hence, it remains uncertain whether or not the lower incidence of severe PPM associated with PAVI will translate into significantly better clinical outcomes for this population, which includes a high proportion of both elderly patients and patients with reduced LVEF. Future prospective randomized studies such as the ongoing PARTNER (Placement of Aortic Transcatheter Valves) trial will provide an opportunity to address this question.

Improvement in LVEF. Consistent with the results of the present study, Cribier et al. (4) and Webb et al. (5) have previously reported that PAVI was associated with a significant increase in LVEF (+5%) as early as 1 week after the procedure, and that this improvement was even greater (+15%) among patients with low LVEF before the intervention (4). The present study further showed that this early improvement was greater than that observed after SAVR, especially in patients with LVEF ≤50%. Both the better hemodynamic results leading to a lower LV afterload and the avoidance of cardiopulmonary bypass in the PAVI group might have been involved in this early improvement in LVEF that was not observed with SAVR (13,25). Future studies are needed to determine whether this early and faster

recovery of LV systolic function increase associated with PAVI translates into a reduction of the high perioperative mortality generally observed in the high-risk group of patients with severe aortic stenosis and low LVEF undergoing SAVR.

AR. PAVI has been associated with a high rate of paravalvular prosthetic regurgitation, with an incidence ranging from 65% to 85% (4–8), which is much higher than that observed after SAVR (26,27). The presence of the severely calcified native valve between the percutaneously implanted bioprosthesis and the aortic annulus probably precludes a complete sealing of the paravalvular space, and thereby leads to some degree of AR in most cases. Interestingly, the present study showed that greater oversizing of the percutaneous valve with respect to the aortic annulus was not associated with lesser incidence and severity of AR (Fig. 1), suggesting that other mechanisms such as the degree of valve calcification or leaflet-commissural deformation of the native valve (10) might be more important than the amount of valve-aortic annulus stretching by the stent of the percutaneous bioprosthesis. Importantly, and also in accordance with the results of the present study, the vast majority of paravalvular leaks after PAVI were trivial or mild, with an incidence of moderate AR ranging from 0% to 26% and an incidence of severe AR ranging from 0% to 10% (4–9). Furthermore, the degree of paravalvular AR generally remains stable or even improves slightly over time (4–8), as was also seen in the present study. Also, the presence of mild-to-moderate paravalvular leaks after PAVI has not been associated with any clinical consequences at midterm (1- to 2-year) follow-up (4–8). Rallidis et al. (26) showed that paraprosthetic regurgitation occurred in up to 48% of the patients after SAVR. Most of these paravalvular leaks were trivial or mild and did not progress or have any significant impact on clinical outcomes at 5-year follow-up. Furthermore, it has been well demonstrated that the presence of mild-to-moderate AR is usually well tolerated for a long time (28). Larger studies with clinical end points and long-term follow-up will have to determine the degree of progression and potential clinical consequences associated with these paravalvular leaks after PAVI. Also, future research efforts should focus on improving this valve technology to further reduce the occurrence of paravalvular leaks. In the meantime, given the uncertainty about the progression rate of the paravalvular leaks and about the durability of the percutaneously implanted prosthetic valves in the long-term, these valves should be used with caution in the patients who have a long life expectancy.

Study limitations. This study included a series of patients who underwent PAVI reaching the 6 to 12 months of follow-up and excluded patients who died during the perioperative period or within the few months after the procedure and those with incomplete follow-up data. This patient selection might have partially biased the results regarding PAVI, but this might have also occurred to the same extent with SAVR patients. Also, no clinical data regarding patients' functional capacity and quality of life were included in the study. The reason was that all patients who underwent PAVI were considered nonoperable or at very high surgical risk, implying that they were older and had more comorbidities than patients who underwent SAVR. Considering these significant baseline differences between groups, we think that comparing clinical data such as functional class between PAVI and SAVR patients might have been misleading. The follow-up period was relatively short, and future studies with longer follow-up should be carried out to determine whether the hemodynamic performance of percutaneous valves remains stable at long-term follow-up. Finally, this was a case-control study, and although the data had been prospectively gathered in all patients, future prospective randomized studies such as the PARTNER trial, which compares PAVI to SAVR, will have to confirm these results.

Acknowledgments

The authors thank Jacinthe Aubé, Jocelyn Beauchemin, and Stéphanie Dionne for data collection and technical assistance, and Serge Simard for statistical analysis.

Reprint requests and correspondence: Dr. Josep Rodés-Cabau, Quebec Heart & Lung Institute/Laval Hospital, 2725 Chemin Ste-Foy, Québec City, Quebec G1V 4G5, Canada. E-mail: josep.rodes@criucpq.ulaval.ca.

REFERENCES

1. Pibarot P, Dumesnil JG. Prosthesis-patient mismatch: definition, clinical impact, and prevention. Heart 2006;92:10224–9.
2. Blais C, Dumesnil JG, Baillot R, Simard S, Doyle D, Pibarot P. Impact of prosthesis-patient mismatch on short-term mortality after aortic valve replacement. Circulation 2003;108:983–8.
3. Mohty D, Malouf JF, Girard SE, Schaff HV, Grill DE, Enriquez-Sarano ME. Impact of prosthesis-patient mismatch on long-term survival in patients with small St. Jude Medical mechanical prostheses in the aortic position. Circulation 2006;113:420–6.
4. 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.
5. 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.
6. Walther T, Simon P, Dewey T, et al. Transapical minimally invasive aortic valve implantation. Multicentre experience. Circulation 2007; 116:I240–5.
7. Rodés-Cabau J, Dumont E, DelaRochellière 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.
8. Svensson LG, Dewey T, Kapadia S, et al. United States feasibility study of transcatheter insertion of a stented aortic valve by the left ventricular apex. Ann Thorac Surg 2008;86:46–55.
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. Zegdi R, Ciobotaru V, Noghin M, et al. Is it reasonable to treat all calcified stenotic aortic valves with a valved stent? Results from a human anatomic study in adults. J Am Coll Cardiol 2008;51:579–84.

11. Zoghbi WA, Enriquez-Sarano M, Foster M, et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 2003;16:777–802.
12. Perry GJ, Helmcke F, Nanda NC, Byard C, Soto B. Evaluation of aortic insufficiency by Doppler color flow mapping. J Am Coll Cardiol 1987;9:952–9.
13. Pibarot P, Dumesnil JG, Lemieux M, Cartier P, Metras J, Durand LG. Impact of prosthesis-patient mismatch on hemodynamic and symptomatic status, morbidity and mortality after aortic valve replacement with a bioprosthetic heart valve. J Heart Valve Dis 1998;7:211–8.
14. Tasca G, Brunelli F, Cirillo M. Impact of valve prosthesis-patient mismatch on left ventricular mass regression following aortic valve replacement. Ann Thorac Surg 2005;79:505–10.
15. Rao V, Jamieson WRE, Ivanov J, Armstrong S, David TE. Prosthesis-patient mismatch affects survival following aortic valve replacement. Circulation 2000;102:III5–9.
16. Tasca G, Mhagna Z, Perotti S, et al. Impact of prosthesis-patient mismatch on cardiac events and mortality after aortic valve replacement in patients with pure aortic stenosis. Circulation 2006;113:570–6.
17. Dumesnil JG, Leblanc MH, Cartier PC, et al. Hemodynamic features of the Freestyle aortic bioprosthesis compared with stented bioprosthesis. Ann Thorac Surg 1998;66 Suppl:130–3.
18. Pibarot P, Dumesnil JG, Jobin J, Cartier P, Honos G, Durand LG. Hemodynamic and physical performance during maximal exercise in patients with aortic bioprosthesis valve. Comparison of stentless versus stented bioprosthesis. J Am Coll Cardiol 1999;34:1609–17.
19. Perez de Arenaza D, Lees B, Flather M, et al. Randomized comparison of stentless versus stented valves for aortic stenosis. Effects on left ventricular mass. Circulation 2005;112:2696–702.
20. Ali A, Halstead JC, Cafferty F, et al. Are stentless valves superior to modern stented valves? A prospective randomized trial. Circulation 2006;114:I535–40.
21. Pibarot P, Dumesnil JG, Cartier PC, Metras J, Lemieux M. Patient-prosthesis mismatch can be predicted at the time of operation. Ann Thorac Surg 2001;71 Suppl:265–8.
22. Lopez S, Mathieu P, Pibarot P, et al. Does the use of stentless aortic valves in subcoronary position prevent patient-prosthesis mismatch for small aortic annulus? J Card Surg 2008;23:331–5.
23. Moon MR, Pasque MK, Munfakh NA, et al. Prosthesis-patient mismatch after aortic valve replacement: impact of age and body size on late survival. Ann Thorac Surg 2006;81:481–8.
24. Mothy D, Dumesnil JG, Echahidi N, et al. Impact of prosthesis-patient mismatch on long-term survival after aortic valve replacement. J Am Coll Cardiol 2009;53:39–47.
25. Selvanayagam JB, Petersen SE, Francis JM, et al. Effects of off-pump versus on-pump coronary surgery on reversible and irreversible myocardial injury: a randomized trial using cardiovascular magnetic resonance imaging and biochemical markers. Circulation 2004;109:345–50.
26. Rallidis LS, Moyssakis IE, Ikonomidis I, Nihoyannopoulos P. Natural history of early paraprosthetic regurgitation: a five-year follow-up. Am Heart J 1999;138:351–7.
27. O'Rourke DJ, Palac RT, Malenka DJ, Marrin CA, Arbuckle BE, Plehn JF. Outcome of mild periprosthetic regurgitation detected by intraoperative transesophageal echocardiography. J Am Coll Cardiol 2001;38:163–6.
28. Goldbarg SH, Halperin JL. Aortic regurgitation: disease progression and management. Nat Clin Pract Cardiovasc Med 2008;5:269–79.

Key Words: aortic stenosis ■ heart valve prosthesis ■ percutaneous aortic valve implantation ■ aortic valve replacement ■ bioprosthesis ■ hemodynamics.