

# Aortic Stenosis With Severe Left Ventricular Dysfunction and Low Transvalvular Pressure Gradients

## Risk Stratification by Low-Dose Dobutamine Echocardiography

Jean-Luc Monin, MD,\* Mehran Monchi, MD,† Virginie Gest, MD,\* Anne-Marie Duval-Moulin, MD,\* Jean-Luc Dubois-Rande, MD, PhD,\* Pascal Gueret, MD, FACC\*

Créteil, France and Liège, Belgium

- OBJECTIVES** We sought to assess risk stratification by using dobutamine stress echocardiography (DSE) in patients with aortic stenosis (AS) and severe left ventricular (LV) dysfunction.
- BACKGROUND** Few data are available on risk stratification for valve replacement in patients with AS, LV dysfunction and low transvalvular gradients.
- METHODS** Low-dose DSE was performed in 45 patients (16 women and 29 men; median [quartile range] age in years: 75 [69 to 79]; left ventricular ejection fraction: 0.29 [0.23 to 0.32]; aortic valve area [cm<sup>2</sup>]: 0.7 [0.5 to 0.8]; mean transaortic gradient [mm Hg]: 26 [21 to 33]). Patients were classified into two groups: group I (n = 32, LV contractile reserve on DSE) and group II (n = 13, no contractile reserve). Valve replacement was performed in 24 and 6 patients in groups I and II, respectively.
- RESULTS** Perioperative mortality was 8% in group I and 50% in group II (p = 0.014). Survival at five years after the operation was 88% in group I. Compared with medical therapy, valve surgery was associated with better long-term survival in group I (hazard ratio for death [HR-D] 0.13, 95% confidence interval [CI] 0.002 to 0.49) and reduced survival in group II (HR-D 19.6, 95% CI 2.7 to 142). The effect of valve surgery on survival remained significant in both groups after adjustment for age, diabetes, respiratory disease and hypertension. Medical therapy had the same effect in both groups.
- CONCLUSIONS** In patients with AS, LV dysfunction and low transvalvular gradients, contractile reserve on DSE is associated with a low operative risk and good long-term prognosis after valve surgery. In contrast, operative mortality remains high in the absence of contractile reserve. (J Am Coll Cardiol 2001;37:2101-7) © 2001 by the American College of Cardiology

Valve replacement is the only effective treatment for patients with severe aortic stenosis (AS) and congestive heart failure (1), although perioperative mortality is increased in case of left ventricular (LV) dysfunction (2) and low transvalvular pressure gradients (3-5). In previous studies, operative mortality in the setting of low transvalvular gradients has been reported to be as high as 33% (4), with no clinical or hemodynamic variables to stratify operative risk (4,6). Furthermore, some patients may have LV dysfunction due to primary cardiomyopathy, with only moderate AS, and may not benefit from valve surgery (3). Dobutamine stress echocardiography (DSE) has been proposed in patients with AS and low pressure gradients (7) to calculate the aortic valve area (AVA) at two different flow states, in order to identify the patients who are likely to benefit from valve replacement. However, the study of deFilippi et al. (7) was limited by a small sample size, due to the infrequent occurrence of these conditions in a clinical setting. The

present study aimed to assess risk stratification by DSE in a larger group of patients with severe AS, LV dysfunction and low transvalvular gradients.

## METHODS

**Patient selection.** Patients were prospectively enrolled between April 1994 and June 2000 if they had severe native AS, defined by AVA  $\leq 1$  cm<sup>2</sup> (8) with severe LV systolic dysfunction (left ventricular ejection fraction [LVEF]  $\leq 30\%$ ) or a mean (transaortic) pressure gradient (MPG)  $\leq 40$  mm Hg. Exclusion criteria were atrial fibrillation, more than mild aortic regurgitation and severe comorbidities. Forty-eight patients met the inclusion criteria, two of whom were excluded for atrial fibrillation and one for cardiac amyloidosis. Thus, 45 patients form the basis of this report. The study protocol was approved by the Review Board of our institution; informed consent was obtained from all patients before the investigations.

**Doppler echocardiography.** A complete Doppler echocardiographic study was performed with commercially available equipment (128 XP-10c or Sequoia C 256, Acuson, Mountainview, California). Left ventricular outflow track

From the \*Fédération de Cardiologie, Hôpital Henri Mondor, Créteil, France; and †University Hospital Sart Tilman, Liège, Belgium. This study was supported in part by a grant from the Fédération Française de Cardiologie.

Manuscript received November 12, 2000; revised manuscript received March 1, 2001, accepted March 22, 2001.

**Abbreviations and Acronyms**

AS	= aortic stenosis
AVA	= aortic valve area
CABG	= coronary artery bypass graft surgery
CAD	= coronary artery disease
DSE	= dobutamine stress echocardiography
LV	= left ventricle or ventricular
LVEF	= left ventricular ejection fraction
LVOT	= left ventricular outflow tract
MPG	= mean pressure gradient
NYHA	= New York Heart Association
SV	= stroke volume

(LVOT) velocities were recorded in the apical view: the Doppler sample volume was located just below the aortic valve and advanced as close as possible before spectral broadening. Special care was taken to maintain the sample volume location throughout the stress hemodynamic study. Stroke volume (SV) was calculated according to standard formulae (9). Transaortic flow was recorded with continuous wave Doppler using a multiwindow approach (9); transaortic gradients were calculated using the simplified Bernoulli equation (10). Aortic valve area was calculated by the continuity equation (11). Aortic valve resistance was calculated according to the standard formula (12). For each Doppler measurement, high-quality tracings were obtained and three to five cycles were averaged, avoiding post-extrasystolic beats. Cine loops were stored in the apical four-chamber and two-chamber views for LVEF calculation.

**Dobutamine stress hemodynamic study.** After the baseline study, a dobutamine infusion was begun at 5  $\mu\text{g}/\text{kg}$  body weight per min, titrated upward in steps of 2.5  $\mu\text{g}/\text{kg}$  per min every 5 min up to a maximal dose of 20  $\mu\text{g}/\text{kg}$  per min. The dobutamine infusion was stopped when the maximal dose or heart rate acceleration  $\geq 10$  beats/min was reached. Systemic blood pressure and the 12-lead electrocardiogram were monitored throughout the test. Bi-apical cine loops, LVOT and transaortic Doppler tracings were stored at the end of each step; the dose increment was delayed until all recordings were considered optimal. The maximal transaortic velocities were recorded in the apical view in all but one patient in whom the right parasternal approach was used.

**Clinical decisions and follow-up.** The final therapeutic decision for each individual patient was left to the discretion of the referring physicians, who had knowledge of the results of DSE. Clinical data at follow-up were obtained in all patients at a median interval of 24 months (range 8 to 39) by direct patient examination or telephone interview by the referring physician. A complete Doppler echocardiographic study was obtained 12 months (range 6 to 26) after valve surgery in 18 of the 21 surviving patients, including measurement of LVEF in 16 patients. Evaluated end points at follow-up were survival, New York Heart Association (NYHA) functional class and echocardiographically demonstrated LVEF.

**Data analysis.** The stress hemodynamic studies were evaluated off-line by a single experienced echocardiographer (V.G.) who had no knowledge of the clinical data, using the software of the echocardiographic equipment to calculate gradients, SV, AVA, valve resistance and LVEF by the bi-plane Simpson's rule (13). When image quality was inadequate, LVEF was not assessed. According to a reported mean variability in LVOT Doppler measurements of 5% to 7.5% (14-16), LV contractile reserve on DSE was defined by an increase in SV of  $\geq 20\%$ . Patients were classified into two groups according to the presence (group I) or absence (group II) of contractile reserve on DSE. The follow-up studies were evaluated in separate sessions by the same observer.

**Statistical analysis.** Continuous data are presented as median values and corresponding 25th and 75th percentiles. Dichotomous data are presented as percentages. Statistical analysis was performed using nonparametric statistical tests. The chi-square test or Fisher exact test was applied for dichotomous and categorical data. The Mann-Whitney *U* test was used to compare numeric data of the two groups. The relative risk of postoperative death was determined using the standard formula. Survival was represented by Kaplan-Meier curves. A Cox proportional hazards analysis was performed to assess the independent influence of valve surgery on survival in each group, with and without adjustments for baseline age, diabetes, hypertension and chronic obstructive pulmonary disease.

Two-tailed *p* values  $< 0.05$  were considered statistically significant. Analyses were done on a personal computer using Stata software (version 5.0 for Windows, Stata Corp., College Station, Texas).

## RESULTS

**Clinical characteristics.** For the whole group, baseline characteristics included age (years: 75 [69 to 79]), LVEF 0.29 (0.23 to 0.32), cardiac index (l/min per  $\text{m}^2$ : 1.9 [1.6 to 2.2]), AVA ( $\text{cm}^2$ : 0.7 [0.5 to 0.8]), indexed AVA ( $\text{cm}^2/\text{m}^2$ : 0.4 [0.3 to 0.4]), MPG (mm Hg: 26 [21 to 33]) and valve resistance ( $\text{dynes}\cdot\text{cm}^{-5}$ : 227 [191 to 304]). Coronary angiography was performed in 37 patients and showed no significant coronary artery disease (CAD) in 18 patients; one-, two- or three-vessel disease was present in three, six and six patients, respectively; and four patients had previous patent coronary artery bypass graft surgery (CABG).

The baseline clinical and hemodynamic characteristics by group are presented in Table 1. Patients were slightly older in group II than in group I ( $p = 0.04$ ), otherwise there were no group differences in gender ratio, comorbidities, NYHA functional class, associated CAD, medical treatment or baseline hemodynamic data. At the time of their first evaluation, all patients presented with symptoms of congestive heart failure; associated symptoms were angina in two patients and syncope in two other patients.

**Table 1.** Baseline Clinical and Hemodynamic Data by Group

Variable	Group I (n = 32)	Group II (n = 13)	p Value
Age (yrs)	74 (64-78)	79 (73-82)	0.04
Gender (M/F)	19/13	10/3	0.26
NYHA functional class (I/II/III/IV)	0/6/18/8	0/4/7/2	0.61
CAD (1/2/3-vessel)	2/3/3	1/3/3	0.15
Previous AMI	7 (22%)	2 (15%)	0.69
Systemic hypertension	10 (31%)	3 (23%)	0.58
Diabetes mellitus	6 (19%)	1 (8%)	0.35
Renal disease	1 (3%)	3 (23%)	0.12
Respiratory disease	2 (6%)	2 (15%)	0.33
Diuretics	23 (62%)	9 (69%)	0.81
ACE inhibitors	14 (44%)	3 (23%)	0.25
Heart rate (beats/min)	76 (69-87)	82 (72-90)	0.33
SBP (mm Hg)	106 (95-119)	96 (86-117)	0.24
SV (ml)	43 (34-52)	46 (31-49)	0.98
LVEF	0.29 (0.23-0.35)	0.28 (0.20-0.30)	0.44
CI (l/min per m <sup>2</sup> )	1.9 (1.6-2.1)	2.1 (1.7-2.5)	0.73
AVA (cm <sup>2</sup> )	0.7 (0.5-0.8)	0.7 (0.6-0.8)	0.84
Indexed AVA (cm <sup>2</sup> /m <sup>2</sup> )	0.4 (0.3-0.4)	0.4 (0.3-0.4)	0.51
MPG (mm Hg)	26 (21-34)	30 (22-33)	0.80
Resistance (dynes·s·cm <sup>-5</sup> )	223 (183-288)	249 (190-322)	0.53

Data are presented as the median value (25th-75th percentiles) or number (%) of patients.

ACE = angiotensin-converting enzyme; AMI = acute myocardial infarction; AVA = aortic valve area; CAD = coronary artery disease; CI = cardiac index; LVEF = left ventricular ejection fraction; M/F = male/female; MPG = mean pressure gradient; NYHA = New York Heart Association; SBP = systolic blood pressure; SV = stroke volume.

**Dobutamine stress hemodynamic studies.** Data from the DSE studies are listed in Table 2. There were no group differences in dobutamine peak dose, peak heart rate or peak blood pressure. All studies were terminated for attainment of a maximal dose or heart rate acceleration  $\geq 10$  beats/min. The mean duration of the DSE studies was 29 min (range 22 to 37). The test was well tolerated in all patients, with no sustained arrhythmia, no sign of ischemia and no fall in blood pressure. Premature ventricular or atrial contractions occurred in seven patients.

**Changes in Doppler echocardiographic indexes with dobutamine.** As predefined, group I was characterized by an increase in SV concordant with an increase in LVEF on

DSE ( $p < 0.001$  vs. baseline). In contrast, there was no significant change in LVEF with dobutamine in group II ( $p = 0.11$  vs. baseline).

In group I, MPG and AVA increased significantly ( $p < 0.0001$  and  $p < 0.001$ , respectively, vs. baseline). In eight patients in group I, AVA remained stable, whereas AVA increased by 0.1, 0.2, 0.3 and 0.4 cm<sup>2</sup> in 14, 5, 3 and 2 patients, respectively. Thus, final AVA was 1 cm<sup>2</sup> in three patients, whereas it remained  $< 1$  cm<sup>2</sup> in one patient (despite an increase in AVA by 0.4 cm<sup>2</sup>). Only one patient in the whole group had a final AVA  $> 1$  cm<sup>2</sup>, which increased from 0.9 to 1.3 cm<sup>2</sup>. Valve resistance did not change significantly in group I ( $p = 0.07$  vs. baseline).

**Table 2.** Data From the Dobutamine Stress Echocardiographic Studies by Group

Variable	Group I (n = 32)	Group II (n = 13)	p Value
Dobutamine peak dose ( $\mu\text{g}/\text{kg}$ per min)	8 (7.5-10)	12.5 (7.5-14)	0.07
$\Delta$ Heart rate (beats/min)	10 (5-13)	12 (8-14)	0.11
Peak SBP (mm Hg)	118 (103-132)	102 (89-132)	0.37
Peak SV (ml)	59 (48-70)	49 (35-52)	0.02
$\Delta$ SV (%)	34 (29-53)	8 (7-13)	0.0001
Peak LVEF	0.40 (0.32-0.49)	0.31 (0.20-0.35)	0.007
$\Delta$ LVEF	0.12 (0.07-0.13)	0.03 (0.02-0.05)	0.0001
Peak CI	2.8 (2.6-3.3)	2.7 (2.2-3.2)	0.47
$\Delta$ CI (%)	49 (42-74)	24 (18-37)	0.0001
Peak AVA (cm <sup>2</sup> )	0.8 (0.6-0.9)	0.8 (0.5-0.8)	0.18
$\Delta$ AVA (%)	17 (8-29)	5 (-3-8)	0.006
Peak MPG (mm Hg)	41 (32-51)	30 (24-41)	0.13
$\Delta$ MPG (%)	38 (31-45)	20 (14-30)	0.0002
Peak resistance (dynes·s·cm <sup>-5</sup> )	251 (194-307)	244 (187-352)	0.83
$\Delta$ Resistance (%)	9 (-6-20)	8 (-4-24)	0.88

Data are expressed as peak dose values, variation ( $\Delta$ ) from baseline (international units) or percent variation ( $\Delta$ ) from baseline. Abbreviations as in Table 1.

In group II, MPG also increased, although less than that in group I. In contrast, there was no significant change in AVA ( $p = 0.15$  vs. baseline) or valve resistance ( $p = 0.24$  vs. baseline) in this group.

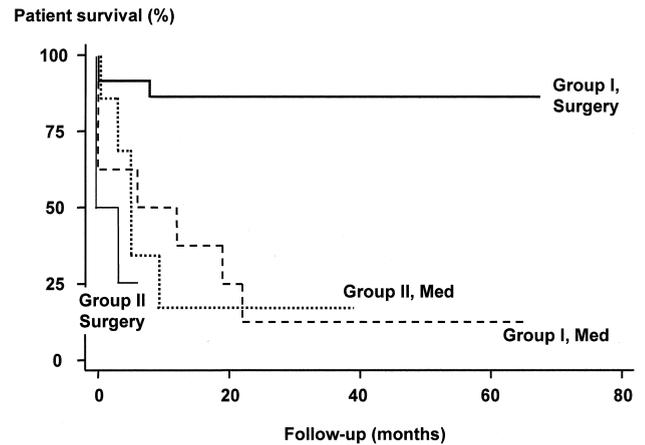
**Clinical outcomes. THERAPEUTIC DECISIONS.** In group I, valve replacement was performed in 24 patients, with concomitant CABG in eight patients; surgical inspection of the valve showed marked leaflet calcification and severely reduced leaflet mobility in all patients. The remaining eight patients in group I were treated medically for the following reasons: patient refusal for the operation ( $n = 3$ ), older age and comorbidities ( $n = 2$ ) and AVA considered outside the severe range by the referring physician ( $n = 3$ ). In group II, six patients underwent valve replacement (including four with concomitant CABG), whereas seven patients were treated medically due to patient refusal ( $n = 2$ ), age and comorbidities ( $n = 4$ ) and AVA considered outside the severe range ( $n = 1$ ).

**PERIOPERATIVE MORTALITY.** Perioperative (30-day) mortality was 8% in group I (2 of 24 patients) and 50% in group II (3 of 6 patients). The five deaths were caused by pump failure in all patients: three patients could not be weaned from cardiopulmonary bypass and the two other patients died two and three days, respectively, after valve surgery. The relative risk of perioperative death was 6.0 in group II (95% confidence interval 1.3 to 28;  $p = 0.014$ ). Coronary artery bypass graft surgery was not associated with a higher perioperative mortality in group II ( $p = 0.4$ ).

**LONG-TERM SURVIVAL.** In group I, one other patient died of a mesenteric infarction three months after valve surgery. Among the eight patients in group I who were treated medically, seven died of sudden death ( $n = 2$ ), end-stage heart failure ( $n = 4$ ) or respiratory disease ( $n = 1$ ). Among the five patients in group I with an increase in AVA of  $\geq 0.3 \text{ cm}^2$  on DSE who were treated medically, four died at a median interval of 12 months (two from sudden death and two from congestive heart failure). In these four patients, valve replacement was not performed due to patient refusal in two and AVA considered outside the severe range in two; coronary angiography had shown no significant disease in one patient and two-vessel disease in one and was not performed in the two remaining patients. The only patient from group I to be alive at five years of follow-up, with medical therapy, had a final AVA of  $1.3 \text{ cm}^2$  on DSE, normal coronary arteries and cardiomyopathy due to alcohol abuse, which improved with medical treatment.

In group II, one patient died three months after valve replacement from heart failure. Of the seven patients who were treated medically, five died at five months (3 to 6) of follow-up due to sudden death ( $n = 1$ ), heart failure ( $n = 2$ ) or respiratory disease ( $n = 2$ ).

**PREDICTORS OF SURVIVAL.** Figure 1 shows the Kaplan-Meier survival estimates by group and treatment strategy (medical therapy or valve surgery).



**Figure 1.** Kaplan-Meier survival curves by group and treatment. Med = medical therapy.

Survival at five years was 88% (21 of 24 patients) in group I patients who underwent valve surgery. There was no significant difference in survival of medically treated patients between group I and II ( $p = 0.64$ ). The Cox proportional hazard analysis indicated that survival duration was improved by valve surgery in group I. In contrast, group II patients had a better survival with medical therapy (Table 3).

Survival duration with medical therapy was comparable in both groups. After adjustment for age, diabetes, systemic hypertension and chronic obstructive pulmonary disease, survival remained improved by valve surgery in group I, but not in group II, whereas medical treatment had the same effect in both groups (Table 4).

**POSTOPERATIVE FUNCTIONAL IMPROVEMENT AND LVEF.** Among the 21 patients in group I who survived after valve replacement, marked functional improvement was noted (Fig. 2): 17 patients were initially in NYHA functional class III/IV as compared with only one patient in class III at follow-up ( $p = 0.001$  vs. baseline). In addition, LVEF improved in these patients, from 0.29 (0.23 to 0.35) to 0.44 (0.36 to 0.46) ( $p < 0.0001$  vs. baseline) (Fig. 3). In the two patients from group II who survived after valve surgery, NYHA functional class improved moderately in one case (from IV to III), whereas the other patient remained in class III.

**Table 3.** Cox Proportional Hazard Analysis of the Effect of Surgical Treatment on Survival Duration in the Two Groups

	Hazard Ratio for Death	p Value	95% Confidence Interval
Group 1, medical therapy	1.0	Reference	
Group 2, medical therapy	1.19	0.77	0.37-3.7
Group 1, valve surgery	0.13	0.003	0.002-0.49
Group 2, valve surgery	19.6	0.003	2.7-142

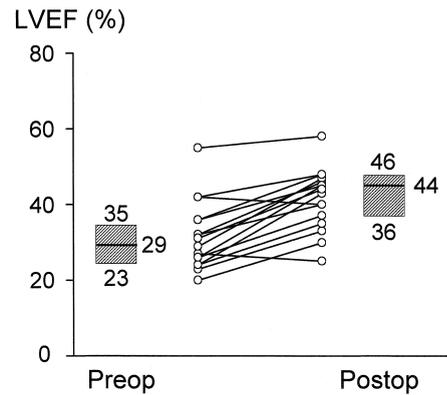
**Table 4.** Cox Proportional Hazard Analysis of the Effect of Surgical Treatment on Survival Duration in the Two Groups After Adjustment for Baseline Age, Diabetes, Hypertension and Chronic Obstructive Pulmonary Disease

	Hazard Ratio for Death	p Value	95% Confidence Interval
Group 1, medical therapy	1.0	Reference	
Group 2, medical therapy	1.07	0.916	0.32-3.5
Group 1, valve surgery	0.13	0.015	0.02-0.67
Group 2, valve surgery	31.7	0.002	3.4-295

**DISCUSSION**

The rare subset of patients with AS, severe LV dysfunction and low transvalvular pressure gradients represents a common medical challenge given their dismal spontaneous prognosis and their high operative risk. Furthermore, some of them may have primary cardiomyopathy and nonsevere AS and may not benefit from valve replacement (3,4). Therefore, new diagnostic methods are needed to accurately assess the severity of AS and to select the patients who are likely to benefit from valve surgery. The present study confirms the feasibility and safety of low-dose DSE in these patients and demonstrates that in case of contractile reserve, operative mortality is low and long-term outcome is improved by valve surgery. In contrast, in our series, the patients without contractile reserve had a high perioperative mortality and valve surgery did not improve their long-term survival.

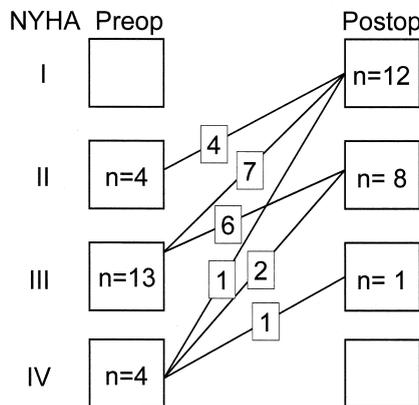
**Risk stratification by dobutamine echocardiography.** In previous studies, perioperative mortality after valve replacement in patients with AS and LV dysfunction has been reported to be between 11% and 33% (4,6,14). Blitz et al. (14) reported a perioperative mortality rate of 11% in a series of 52 patients with AS and moderate LV dysfunction (mean LVEF  $0.48 \pm 0.20$ ). The preoperative data from our



**Figure 3.** Left ventricular ejection fractions (LVEF) before (preop) and after (postop) valve replacement in group I patients. Open circles represent individual patient data (n = 16); solid horizontal lines indicate median values; and hatched boxes indicate quartiles.

patients indicate more severely impaired LV function, comparable to the series of Brogan et al. (4) and Connolly et al. (6), who reported perioperative mortality rates of 33% and 21%, respectively. In the present study, a contractile reserve on DSE was associated with a perioperative mortality rate of 8%, dramatically decreased compared with the aforementioned studies (4,6). This difference in mortality, compared with the rates reported previously, could partly be due to improved surgical and anesthesia technique over time. Nevertheless, the striking difference in operative mortality between the patients with and those without contractile reserve in our study supports the idea that DSE is useful to stratify operative risk. Of note, previous studies failed to identify any preoperative variables to stratify operative risk (4,6); the only predictor of surgical mortality was a postoperative variable (small-size aortic prosthesis) reported by Connolly et al. (6). Moreover, LV contractile reserve was associated with 88% survival five years after valve replacement, thus predictive of long-term outcome, whereas in previous studies, long-term survival was only influenced by the absence of CAD (14).

**Changes in Doppler indexes and valve area with dobutamine.** We found an increase in AVA and MPG in group I of 17% and 58%, respectively, whereas valve resistance increased by only 9%; these results are concordant with previous reports (15-17) and support the fact that valve resistance is less flow-dependent than AVA. deFilippi et al. (7) defined relative AS by an increase in AVA  $\geq 0.3 \text{ cm}^2$  on DSE and reported a favorable mid-term outcome with medical therapy in five such patients. Of note, all five of these patients had a final AVA  $>1 \text{ cm}^2$  and were considered as having primary cardiomyopathy associated with moderate AS (7). Five patients from our series also had an increase in AVA  $\geq 0.3 \text{ cm}^2$  on DSE, but only one patient had a final AVA clearly outside the severe range ( $>1 \text{ cm}^2$ ); the four remaining patients had a poor outcome with medical therapy. We cannot determine whether LV dysfunction in these four patients was due to primary cardiomyopathy or significant AS, given their final AVA borderline to the



**Figure 2.** Preoperative and postoperative New York Heart Association (NYHA) functional classes of the 21 patients in group I who survived after valve replacement.

severe range (8). Our data, added to those of deFilippi et al. (7), suggest that relative AS should be defined by an increase in AVA  $\geq 0.3$  cm<sup>2</sup> and a final AVA  $> 1$  cm<sup>2</sup> on DSE; this setting was very infrequent in our series (1 in 45 patients).

**Justification for a low-dose protocol.** Previous studies in patients with AS (7,15,16,18,19) have used higher doses of dobutamine and attained up to 85% of the maximal predicted heart rate (18). This raises the issue of inducing myocardial ischemia in patients with frequently associated CAD (5,7,18). Pop et al. (19) reported numerous side effects of DSE by aiming at 80% of the maximal predicted heart rate. Furthermore, Lin et al. (18) reported a decrease in LVEF at a mean dose of  $27 \pm 11$   $\mu\text{g}/\text{kg}$  per min in patients with associated CAD.

The goal of inotropic stimulation is to optimize LVEF by recruitment of contractile reserve, without inducing ischemia; in our experience, this can be achieved without a significant acceleration in heart rate (20). Therefore, we defined an increase in heart rate  $\geq 10$  beats/min as an end point for test termination. Nevertheless, we observed significant increases in SV, cardiac output and LVEF that clearly separated the patients with from those without contractile reserve, concordant with LVEF changes in each group. Given the simplicity and good reproducibility of Doppler LVOT measurements (21-23), we found that a 20% increase in SV was a reliable cut point to assess LV contractile reserve in patients with AS and LV dysfunction.

**Postoperative improvement in LVEF.** Median LVEF improved in group I patients after valve replacement, from 0.29 to 0.44. This improvement compares favorably with the mean increase of  $10 \pm 14$  ejection fraction units after valve replacement reported by Connolly et al. (6). Although modest, this increase in LVEF is important for patients with severely impaired LV function and is probably related to their improved survival and functional status, like in other patients with cardiomyopathy (24).

**Study limitations.** The relatively small number of patients included in this study reflects the infrequent occurrence of AS with low transvalvular gradients in clinical practice. These patients represented 5% of all patients referred to our laboratory for evaluation of AS during the enrollment period; a similar prevalence has been reported by others (6,14). To the best of our knowledge, no larger study of DSE in such patients has been published to date.

Furthermore, the subgroup of patients without contractile reserve (group II) who underwent valve surgery represents only six patients. Nevertheless, operative mortality in these patients was significantly higher than that in group I, and valve surgery did not improve their long-term survival. Thus, our data support the idea that DSE may be valuable for risk stratification, although no definitive conclusions can be drawn from this small subgroup, especially for therapeutic implications.

Very few patients from our series underwent complete cardiac catheterization, so we cannot compare invasive and noninvasive data on cardiac output, gradients or valve area.

Nevertheless, Doppler echocardiographic measurements of valve gradients and valve area in patients with AS have been largely validated (11,21,25-27) and are widely recognized as reliable (8).

Patients from this series were not randomized for treatment, because it seemed unethical given the dismal spontaneous prognosis in this group. From an ethical standpoint, it seemed that therapeutic decisions for each individual patient had to be made by the referring physicians according to current practice guidelines.

**Conclusions.** The present study confirms the feasibility and safety of low-dose DSE in patients with severe AS, LV dysfunction and low transvalvular pressure gradients. Our results demonstrate that the presence of contractile reserve on DSE is associated with a low operative risk and a good long-term prognosis, whereas operative mortality remains high in the absence of contractile reserve. Larger prospective studies are needed to confirm the prognostic value of DSE in these patients.

---

**Reprint requests and correspondence:** Dr. J. L. Monin, Fédération de Cardiologie, Hôpital Henri Mondor, 51 Avenue De Lattre de Tassigny, 94010 Créteil, France. E-mail: jean-luc.monin@hmn.ap.hop.paris.fr.

---

## REFERENCES

1. Ross J Jr., Braunwald E. Aortic stenosis. *Circulation* 1968;38:61-7.
2. Smith N, McAnulty JH, Rahimtoola SH. Severe aortic stenosis with impaired left ventricular function and clinical heart failure: results of valve replacement. *Circulation* 1978;58:255-64.
3. Carabello BA, Green LH, Grossman W, et al. Hemodynamic determinants of prognosis of aortic valve replacement in critical aortic stenosis and advanced congestive heart failure. *Circulation* 1980;62:42-8.
4. Brogan WC 3rd, Grayburn PA, Lange RA, Hillis LD. Prognosis after valve replacement in patients with severe aortic stenosis and a low transvalvular pressure gradient. *J Am Coll Cardiol* 1993;21:1657-60.
5. Connolly HM, Oh JK, Orszulak TA, et al. Aortic valve replacement for aortic stenosis with severe left ventricular dysfunction: prognostic indicators. *Circulation* 1997;95:2395-400.
6. Connolly HM, Oh JK, Schaff HV, et al. Severe aortic stenosis with low transvalvular gradient and severe left ventricular dysfunction: result of aortic valve replacement in 52 patients. *Circulation* 2000;101:1940-6.
7. deFilippi CR, Willett DL, Brickner ME, et al. Usefulness of dobutamine echocardiography in distinguishing severe from nonsevere valvular aortic stenosis in patients with depressed left ventricular function and low transvalvular gradients. *Am J Cardiol* 1995;75:191-4.
8. Bonow RO, Corabello B, de Leon AC, 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 (Committee on Management of Patients with Valvular Heart Disease). *J Am Coll Cardiol* 1998;32:1486-588.
9. Nishimura RA, Miller FA Jr., Callahan MJ, et al. Doppler echocardiography: theory, instrumentation, technique, and application. *Mayo Clin Proc* 1985;60:321-43.
10. Currie PJ, Seward JB, Reeder GS, et al. Continuous-wave Doppler echocardiographic assessment of severity of calcific aortic stenosis: a simultaneous Doppler-catheter correlative study in 100 adult patients. *Circulation* 1985;71:1162-9.
11. Skjaerpe T, Hegrenaes L, Hatle L. Noninvasive estimation of valve

- area in patients with aortic stenosis by Doppler ultrasound and two-dimensional echocardiography. *Circulation* 1985;72:810-8.
12. Cannon JD Jr., Zile MR, Crawford FA Jr., Carabello BA. Aortic valve resistance as an adjunct to the Gorlin formula in assessing the severity of aortic stenosis in symptomatic patients. *J Am Coll Cardiol* 1992; 20:1517-23.
  13. Schiller NB, Shah PM, Crawford M, et al., the American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr* 1989;2:358-67.
  14. Blitz LR, Gorman M, Herrmann HC. Results of aortic valve replacement for aortic stenosis with relatively low transvalvular pressure gradients. *Am J Cardiol* 1998;81:358-62.
  15. Blitz LR, Herrmann HC. Hemodynamic assessment of patients with low-flow, low-gradient valvular aortic stenosis. *Am J Cardiol* 1996;78: 657-61.
  16. Bermejo J, Garcia-Fernandez MA, Torrecilla EG, et al. Effects of dobutamine on Doppler echocardiographic indexes of aortic stenosis. *J Am Coll Cardiol* 1996;28:1206-13.
  17. Casale PN, Palacios IF, Abascal VM, et al. Effects of dobutamine on Gorlin and continuity equation valve areas and valve resistance in valvular aortic stenosis. *Am J Cardiol* 1992;70:1175-9.
  18. Lin SS, Roger VL, Pascoe R, et al. Dobutamine stress Doppler hemodynamics in patients with aortic stenosis: feasibility, safety, and surgical correlations. *Am Heart J* 1998;136:1010-6.
  19. Pop C, Metz D, Tassan-Mangina S, et al. Apport de l'échographie-Doppler sous dobutamine dans le rétrécissement aortique serré avec dysfonction ventriculaire gauche. *Arch Mal Coeur Vaiss* 1999;92: 1487-93.
  20. Monin JL, Garot J, Scherrer-Crosbie M, et al. Prediction of functional recovery of viable myocardium after delayed revascularization in postinfarction patients: accuracy of dobutamine stress echocardiography and influence of long-term vessel patency. *J Am Coll Cardiol* 1999;34:1012-9.
  21. Otto CM, Pearlman AS, Comess KA, et al. Determination of the stenotic aortic valve area in adults using Doppler echocardiography. *J Am Coll Cardiol* 1986;7:509-17.
  22. Otto CM, Pearlman AS, Gardner CL. Hemodynamic progression of aortic stenosis in adults assessed by Doppler echocardiography. *J Am Coll Cardiol* 1989;13:545-50.
  23. Perakis AC, Montarello JK, Rosenthal E, et al. In vitro measurement of stenotic human aortic valve orifice area in a pulsatile flow model: validation of the continuity equation. *Eur Heart J* 1990;11:492-9.
  24. Rahimtoola SH. Severe aortic stenosis with low systolic gradient: the good and bad news. *Circulation* 2000;101:1892-4.
  25. Zoghbi WA, Farmer KL, Soto JG, et al. Accurate noninvasive quantification of stenotic aortic valve area by Doppler echocardiography. *Circulation* 1986;73:452-9.
  26. Oh JK, Taliercio CP, Holmes DR Jr., et al. Prediction of the severity of aortic stenosis by Doppler aortic valve area determination: prospective Doppler-catheterization correlation in 100 patients. *J Am Coll Cardiol* 1988;11:1227-34.
  27. Otto CM, Pearlman AS, Gardner CL, et al. Experimental validation of Doppler echocardiographic measurement of volume flow through the stenotic aortic valve. *Circulation* 1988;78:435-41.