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Aortic Valve Replacement for Low-Flow/Low-Gradient Aortic Stenosis

Operative Risk Stratification and Long-Term Outcome: A European Multicenter Study

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Objectives We evaluated a large multicenter series of patients operated on for low-flow/low-gradient aortic stenosis (LF/LGAS) to stratify the operative risk, assess whether perioperative mortality has decreased over recent years, and analyze the post-operative outcome.

Background Although LF/LGAS is classically associated with a high operative risk, few data are available concerning the results of surgery in this setting.

Methods A total of 217 consecutive patients (168 men, 77%) with severe aortic stenosis (area <1 cm^2), low ejection fraction (EF) ($\leq$35%), and low mean gradient (MG) ($\leq$30 mm Hg) who underwent aortic valve replacement (AVR) between 1990 and 2005 were included.

Results Perioperative mortality was 16% and decreased dramatically from 20% in the 1990 to 1999 period to 10% in the 2000 to 2005 period. Higher European System for Cardiac Operative Risk Evaluation score (EuroSCORE), very low MG and EF, New York Heart Association functional class III or IV, history of congestive heart failure, and multivessel coronary artery disease (MVD) were associated with perioperative mortality. On multivariate analysis, very low preoperative MG and MVD were predictors of excess perioperative mortality. In the subgroup of patients with dobutamine stress echocardiography, the absence of contractile reserve was a strong predictor of perioperative mortality. Overall 5-year survival rate was 49 $\pm$ 4%. Lower MG, higher EuroSCORE, prior atrial fibrillation, and MVD were identified as independent predictors of overall long-term mortality.

Conclusions In view of the very poor prognosis of unoperated patients, the current operative risk, and the long-term outcome after surgery, AVR is the treatment of choice in the majority of cases of LF/LGAS. (J Am Coll Cardiol 2008;51: 1466–72) © 2008 by the American College of Cardiology Foundation

Patients with severe aortic stenosis (AS) and reduced left ventricular ejection fraction (LVEF) have a poor prognosis with conservative treatment. In addition, aortic valve replacement (AVR) in these patients is associated with a relatively high operative mortality (1,2). Operative risk is particularly high in patients with low pre-operative transvalvular mean gradient (MG) (3). Although American College of Cardiology/American Heart Association guidelines recently defined low-gradient AS as severe AS with an MG $\leq$30 mm Hg, low flow, and left ventricular dysfunction (4), the definition of "low-gradient" AS has varied from study to study (5). Few data are available concerning the results of surgery in patients with severe AS and a MG $\leq$30 mm Hg (3,6,7). Most published studies (5,8–10) have included patients with mean aortic transvalvular gradient between 30 and 40 mm Hg, who are known to be at lower operative risk (5). We therefore evaluated a large series of

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consecutive patients operated for AS with low gradient (≤30 mm Hg) to stratify the operative risk, assess whether the perioperative mortality decreased over the recent period, analyze the post-operative outcome, and determine the predictors of long-term mortality.

Methods

The study population consisted of 217 consecutive patients, 168 men (77%) and 49 women (23%), with symptomatic severe aortic stenosis (area <1 cm^2), low ejection fraction (EF) (≤35%), and low MG (≤30 mm Hg) who underwent aortic valve replacement between 1990 and 2005. Eleven centers were involved in this European study (Amiens, France; Bergamo, Italy; Bordeaux, France; Brest, France; Brussels, Belgium; Créteil, France; Lille, France; Rennes, France; Rouen, France; Saint Denis, France; and Strasbourg, France). Patients with significant aortic regurgitation, severe mitral regurgitation, or associated mitral surgery were excluded. Clinical, laboratory, and echocardiographic data are presented in Table 1. Pre-operative atrial fibrillation was defined as permanent or paroxystic atrial fibrillation before surgery. Patients with unstable hemodynamic status operated during the 4 days following admission were considered emergency cases. Clinical follow-up was completed in all patients, with a mean follow-up of 31 ± 21 months.

Echocardiography. Complete pre-operative echocardiography, including aortic valve area assessment, was performed in all patients (11). Left ventricular ejection fraction was estimated according to Simpson's rule (12) in 86% of patients and visually (13) in 14% of patients. Dobutamine stress echocardiography (DSE) was performed in 38% of patients (83 of 217) according to a previously described standard protocol (9,10). Contractile reserve was defined by an increase in stroke volume of ≥20% compared with the baseline value (9,10,14). All patients with contractile reserve had fixed AS, defined as an increase in valve area <0.3 cm^2 with a final valve area ≤1 cm^2 on DSE (9,10,14). Use of DSE for each patient was left to the discretion of the referring physicians in each center.

Coronary angiography. Pre-operative coronary angiography was performed in 98% of patients. Reduction of the normal diameter ≥50% was considered to define significant coronary artery stenosis in the left main coronary artery. A cutoff value of 70% was used for the right coronary, left anterior descending, and circumflex arteries. Multivessel coronary artery disease (MVD) was defined as significant stenoses on 2 or more vessels.

Calculation of the European System for Cardiac Operative Risk Evaluation (EuroSCORE). The standard EuroSCORE was calculated retrospectively for each patient using the calculator available online (15). Integrated risk factors in the EuroSCORE are patient-related, cardiac, and operation-related factors. Patient-related factors are age over 60 years, female gender, chronic pulmonary disease, extracardiac arterial disease, neurologic dysfunction, previous cardiac surgery, serum creatinine >200 μmol/l, active endocarditis, and critical pre-operative state. Cardiac factors are unstable angina, reduced LVEF, recent myocardial infarction, and pulmonary systolic pressure >60 mm Hg. Operation-related factors are emergency, other than isolated coronary surgery; thoracic aorta surgery; and surgery for post-infarct septal rupture.

Abbreviations and Acronyms

- **AS** = aortic stenosis
- **AVR** = aortic valve replacement
- **CAD** = coronary artery disease
- **DSE** = dobutamine stress echocardiography
- **EF** = ejection fraction
- **EuroSCORE** = European System for Cardiac Operative Risk Evaluation
- **HR** = hazard ratio
- **LF/LGAS** = low-flow/low-gradient aortic stenosis
- **LVEF** = left ventricular ejection fraction
- **MG** = mean gradient
- **MVD** = multivessel coronary artery disease
- **NYHA** = New York Heart Association
- **OR** = odds ratio

Mortality and clinical follow-up. Operative mortality was defined as death within 30 days after AVR (3,10). Overall mortality combined operative mortality and late mortality. The end points evaluated at follow-up were survival and New York Heart Association (NYHA) functional status. The NYHA functional status after surgery, obtained by direct patient examination or telephone interview, was available in 85% (156 of 183) of the patients who survived after AVR. Ejection fraction after AVR was evaluated by the referring physician and was available in 76% of the surviving patients after AVR.

Statistical analysis. Continuous variables are expressed as mean ± SD, and categorical variables are expressed as percentages. Comparisons between groups were performed using the chi-square test or the Fisher exact test (when needed) to analyze differences in categorical variables. The Student *t* test or Wilcoxon rank-sum test were used as appropriate for continuous variables. Changes in NYHA functional status over time were compared using the McNemar's test. The optimal cutoff value of EuroSCORE to predict operative mortality was determined by receiver-operating characteristic curve analysis. On multivariate analysis, the Cox proportional hazard model was used to study survival after AVR, and logistic regression was used to analyze operative mortality. All multivariate analyses were performed with $p < 0.05$ as the limit on univariate analysis for entering or removing variables. Survival curves were plotted using the Kaplan-Meier method and differences were tested with the log-rank test. A p value <0.05 was considered statistically significant.

Results

Pre-operative clinical, echocardiographic, and angiographic data from the 217 patients of the study are presented in Table 1. Pre-operatively, 79% (123 of 156) of patients were

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Table 1 Clinical Characteristics of the Population and Predictors of Perioperative Mortality on Univariate Analysis in the 217 Patients in the Study

	Total Population (n = 217)	Perioperative Period		p Value
		Alive* (n = 183)	Dead* (n = 34)	
Age (yrs)	71 ± 8	71 ± 9	72 ± 6	0.29
Men	168 (77%)	139 (76%)	29 (85%)	0.27
Stable angina	37 (17%)	33 (18%)	4 (12%)	0.46
Pre-operative NYHA functional class III to IV†	180 (83%)	147 (80%)	33 (97%)	0.013
History of congestive heart failure	195 (90%)	161 (88%)	34 (100%)	0.03
EuroSCORE (standard)	8.9 ± 2.7	8.7 ± 2.6	9.9 ± 3.1	0.02
EuroSCORE >10	59 (27%)	44 (24%)	15 (44%)	0.02
Diabetes mellitus	54 (25%)	44 (24%)	10 (29%)	0.48
Atrial fibrillation	58 (27%)	46 (25%)	12 (35%)	0.22
Prior myocardial infarction	49 (23%)	42 (23%)	7 (21%)	0.76
Multivessel coronary artery disease	61 (28%)	46 (25%)	15 (44%)	0.01
Aortic valve area (cm^2)	0.72 ± 0.15	0.72 ± 0.15	0.71 ± 0.17	0.62
Left ventricular ejection fraction (%)	28 ± 6	28 ± 5	26 ± 6	0.03
Mean transvalvular gradient (mm Hg)	25 ± 5	26 ± 5	22 ± 6	0.007
Mean transvalvular gradient ≤20 mm Hg	36 (17%)	26 (14%)	10 (29%)	0.03
Systolic pulmonary artery pressure (mm Hg)	47 ± 14	47 ± 14	47 ± 15	0.97
Left bundle-branch block	62 (29%)	54 (30%)	8 (24%)	0.66
Contractile reserve on dobutamine stress echocardiography*	62/83 (75%)	57/70 (81%)	5/13 (38%)	0.001
Aortic prosthesis size (mm)	23 ± 2	23 ± 2	24 ± 2	0.12
Aortic prosthesis type				
Mechanical	79 (36.5%)	68 (37%)	11 (32%)	
Bioprosthesis	137 (63%)	114 (62.5%)	23 (68%)	0.78
Aortic valve repair	1 (0.5%)	1 (0.5%)	0	
Coronary artery bypass graft	74 (34%)	58 (32%)	16 (47%)	0.08
Emergency AVR	27 (12%)	21 (11%)	6 (18%)	0.32
Cardiopulmonary bypass time (min) (n = 186)	105 ± 56	97 ± 38	151 ± 101	0.011
Cross-clamp time (min) (n = 187)	73 ± 34	69 ± 30	92 ± 47	0.024

*Dobutamine stress echocardiography was performed in 83 patients in the study; †pre-operative NYHA functional status under medical treatment.
AVR = aortic valve replacement; EuroSCORE = European System for Cardiac Operative Risk Evaluation; NYHA = New York Heart Association.

classified as NYHA functional class III or IV, compared with 16% (25 of 156) after AVR (p = 0.0001). The LVEF significantly improved from 28 ± 5% pre-operatively to 41 ± 13% after AVR (p = 0.0001).

Operative mortality. In the overall series, perioperative mortality was 16% (n = 34), related to cardiogenic shock in 79% (n = 27), septic shock in 9% (n = 3), stroke in 3% (n = 1), respiratory failure in 3% (n = 1), multiorgan failure in 3% (n = 1), and critical limb ischemia in 3% (n = 1). Longer cardiopulmonary bypass time and cross-clamp time were also associated with perioperative mortality. On univariate analysis, higher EuroSCORE, very low MG and EF, NYHA functional class III or IV, history of congestive heart failure, and MVD were associated with perioperative mortality (Table 1). These parameters were entered in the multivariate model for perioperative mortality. Pre-operative MG (odds ratio [OR] 0.89; 95% confidence interval [CI] 0.83 to 0.96; p = 0.02) and presence of MVD (OR 2.2; 95% CI 1.02 to 5.02; p = 0.045) were identified as independent predictors of perioperative mortality. Operative mortality was 40% in patients with a pre-operative MG ≤20 mm Hg and MVD, compared with 10% in patients without coronary artery disease (CAD) and with pre-operative MG >20 mm Hg (p = 0.02). Perioperative mortality was 25% when the EuroSCORE was >10, compared with 12% when the EuroSCORE was ≤10 (p = 0.02). Perioperative mortality was 15.5% in the subgroup of patients who underwent pre-operative DSE (n = 83) and reached 38% in patients without contractile reserve on DSE, compared with 8% in patients with contractile reserve. In the subgroup of patients who had DSE, multivariate analysis identified lack of contractile reserve (OR 4.4; 95% CI 1.1 to 17.5; p = 0.03) and MVD (OR 6; 95% CI 1.5 to 24; p = 0.01) as independent predictors of perioperative mortality. Patients who had DSE were more frequently women (32% vs. 16%; p = 0.006), had a lower rate of paroxysmal or permanent atrial fibrillation (18% vs. 32%; p = 0.023), had lower pre-operative EF (26 ± 6 vs. 29 ± 6; p = 0.002), and were less often operated in emergency (6% vs. 16%; p = 0.024).

Baseline characteristics of patients operated in the 1990 to 1999 era (n = 112) and in the 2000 to 2005 era (n = 105) are summarized in Table 2. Operative mortality was lower in the recent era (10% vs. 20%, p = 0.04). No significant differences were observed between the 2 groups for most pre-operative parameters. However, in the recent era, emergency AVR was more frequent (p = 0.04), prior myocardial

Table 2 Comparison of Patients Operated in the 1990 to 1999 Era and the 2000 to 2005 Era

	1990 to 1999 Era (n = 112)	2000 to 2005 Era (n = 105)	p Value
Age (yrs)	72 ± 8	71 ± 8	0.28
Men	86 (77%)	82 (78%)	0.82
Stable angina	19 (17%)	18 (17%)	0.95
Pre-operative NYHA functional class III to IV†	96 (86%)	84 (80%)	0.26
History of congestive heart failure	105 (94%)	90 (86%)	0.05
EuroSCORE	8.9 ± 2.5	9.2 ± 2.9	0.91
Diabetes	25 (22%)	29 (27%)	0.64
Atrial fibrillation	24 (21%)	34 (32%)	0.07
Prior myocardial infarction	20 (18%)	29 (28%)	0.09
Multivessel coronary artery disease	32 (29%)	29 (28%)	0.78
Aortic valve area (cm^2)	0.72 ± 0.15	0.71 ± 0.15	0.69
Left ventricular ejection fraction (%)	28 ± 6	28 ± 5	0.99
Mean transvalvular gradient (mm Hg)	25 ± 5	26 ± 5	0.32
Mean transvalvular gradient ≤20 mm Hg	20 (18%)	16 (15%)	0.60
Systolic pulmonary artery pressure (mm Hg)	47 ± 14	48 ± 14	0.99
Left bundle-branch block	30 (27%)	33 (31%)	0.31
Aortic prosthesis size (mm)	23 ± 2	23 ± 2	0.71
Aortic prosthesis type			
Mechanical	44 (39%)	35 (33%)	
Bioprosthesis	68 (60%)	70 (67%)	0.41
Aortic valve repair	1 (1%)	0	
Dobutamine stress hemodynamics*	46 (41%)	37 (35%)	0.38
CABG	40 (36%)	35 (33%)	0.75
Emergency AVR	9 (8%)	18 (17%)	0.04
Cardiopulmonary bypass time (min) (n = 186)	113 ± 62	98 ± 48	0.07
Cross-clamp time (min) (n = 187)	76 ± 35	69 ± 33	0.18
Cardiac shock as a cause of perioperative death	91% (21/23)	55% (6/11)	0.024
Perioperative mortality	22 (20%)	10 (10%)	0.04

*Dobutamine stress echocardiography was performed in 83 patients in the study; †pre-operative NYHA functional status under medical treatment. CABG = coronary artery bypass graft; other abbreviations as in Table 1.

infarction and atrial fibrillation tended to be more frequent, and cardiopulmonary bypass time tended to be shorter. Perioperative deaths related to cardiogenic shock were more frequent in the past era than in the current era (91% vs. 54%, p = 0.024).

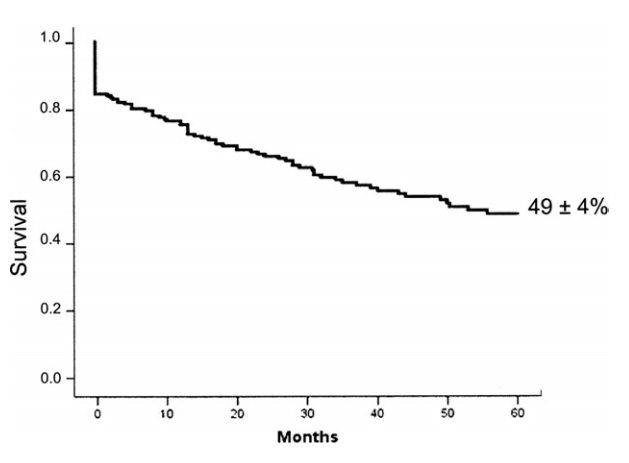

Figure 1 5-Year Overall Survival Curve in the Total Population

Survival after AVR. The overall 5-year survival rate in the total population was 49 ± 4% (Fig. 1). On univariate analysis, overall survival was significantly lower in patients with higher EuroSCORE, diabetes, prior AF, pre-operative MG ≤20 mm Hg, and MVD (Table 3, Fig. 2). These parameters were entered in the multivariate model for overall 5-year survival. Pre-operative MG (hazard ratio [HR] 0.95; 95% CI 0.91 to 0.99, p = 0.015), EuroSCORE (HR 1.13; 95% CI 1.04 to 1.23, p = 0.004), prior atrial fibrillation (HR 1.75; 95% CI 1.07 to 2.85; p = 0.025), and MVD (HR 1.85; 95% CI 1.05 to 2.72; p = 0.03) were identified as independent predictors of overall mortality.

Fifty-four patients died during follow up. Late deaths were due to cardiac causes in 19 of 43 patients (44%). Major bleeding was the cause of death in 21% (5 of 24) of the noncardiac causes.

Discussion

Operative risk in severe AS associated with LV dysfunction is known to be increased, particularly when mean transvalvular gradient is low. This retrospective multicenter study, the largest on low-flow/low-gradient AS (LF/LGAS) to

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Table 3 Predictors of Overall Mortality on Univariate Analysis in the 217 Patients in the Study

	Alive (n = 129)	Dead (n = 88)	p Value
Age (yrs)	71 ± 8	72 ± 8	0.24
Men	99 (77%)	69 (78%)	0.77
Angina	24 (19%)	13 (14%)	0.46
Pre-operative NYHA functional class I to II*	25 (19%)	12 (15%)	0.27
History of congestive heart failure	116 (90%)	79 (90%)	0.97
EuroSCORE	8.3 ± 5	9.7 ± 5	0.0001
Diabetes	25 (19%)	29 (33%)	0.03
Atrial fibrillation	30 (23%)	28 (32%)	0.049
Prior myocardial infarction	26 (20%)	23 (26%)	0.40
Multivessel coronary artery disease	28 (22%)	33 (38%)	0.005
Aortic valve area (cm^2)	0.72 ± 0.14	0.72 ± 0.16	0.98
Left ventricular ejection fraction (%)	28 ± 5	27 ± 6	0.06
Mean transvalvular gradient (mm Hg)	26 ± 4	24 ± 6	0.01
Mean transvalvular gradient ≤20 mm Hg	14 (11%)	22 (25%)	0.006
Systolic pulmonary artery pressure (mm Hg)	48 ± 13	47 ± 14	0.87
Left bundle-branch block	41 (32%)	21 (24%)	0.22
Aortic prosthesis size (mm)	23 ± 2	23 ± 2	0.60
Aortic prosthesis type			
Mechanical	51 (39.5%)	28 (32%)	0.26
Bioprosthesis	78 (60.5%)	59 (67%)	
Aortic valve repair	0	1 (1%)	
Coronary artery bypass graft	39 (30%)	35 (40%)	0.15
Emergency AVR	14 (11%)	13 (15%)	0.39

*Pre-operative NYHA functional status under medical treatment.
Abbreviations as in Table 1.

our knowledge, shows that operative mortality decreased from 20% to 10% over recent years. The presence of multivessel CAD, MG, and DSE results were identified as independent pre-operative predictors of perioperative mortality. Moreover, we found that pre-operative standard EuroSCORE was a useful tool for operative risk stratification. Long-term survival continued to be influenced by pre-operative MG, EuroSCORE, associated MVD, and atrial fibrillation.

Perioperative mortality (16%) in our series can be considered to be acceptable, as rates ranging from 11% to 21% have been reported in previous studies on patients with LF/LGAS (3,8). Pereira et al. (7) recently reported a lower operative mortality of 6% in a series of 68 patients. Systematic echocardiography in the setting of congestive heart failure might bring earlier diagnosis of significant AS before patients go into cardiogenic shock. Our study shows that operative mortality decreased dramatically from 20% to 10% in the recent era. This may be related to recent progress in cardiac surgery and perioperative care, leading to a lower incidence of left ventricular failure during the perioperative period. Moreover, the prevalence of cardiogenic shock as a cause of death was lower in the more recent period of our study. Perioperative risk can be clearly stratified. In our study, a EuroSCORE >10 identified a high-risk population of patients with a perioperative mortality of 25%, compared with 12% for a EuroSCORE ≤10. Connolly et al. (3) identified small prosthesis size as the only predictor of hospital mortality. In our study, we found that lower MG and presence of MVD were strong independent predictors of perioperative mortality. Moreover, Connolly et al. (3) reported a trend toward lower overall 5-year survival in patients with associated CAD compared to patients without CAD in a series of 52 patients. Our larger study demonstrated the major influence of MVD on operative mortality and long-term overall survival. Thus, in our series, the 5-year survival rate was 37% in patients with associated MVD, compared with 55% in patients without associated MVD ($p = 0.02$). Similarly, dobutamine stress hemodynamic results are a strong predictor of perioperative mortality in low-flow and very low-gradient AS (10). Pre-operative atrial fibrillation was found to influence overall survival, reflecting long-standing disease, which may be associated with more severe disease (16). In contrast, neither prior myocardial infarction nor small prosthesis size, as previously reported by others (3,17), were predictors of perioperative mortality in this study.

An improvement of functional class is frequently observed after AVR: 88% of patients in the series by Connolly et al. (2) and 76% of our patients improved their NYHA functional class by more than 1 class. As previously described (2,3,7,18), EF significantly improved after AVR owing to afterload mismatch correction (19). The 49% 5-year survival after AVR in our series was relatively high, compared with the 40% survival reported by Connolly et al. (3), including patients with a higher prevalence of CAD.

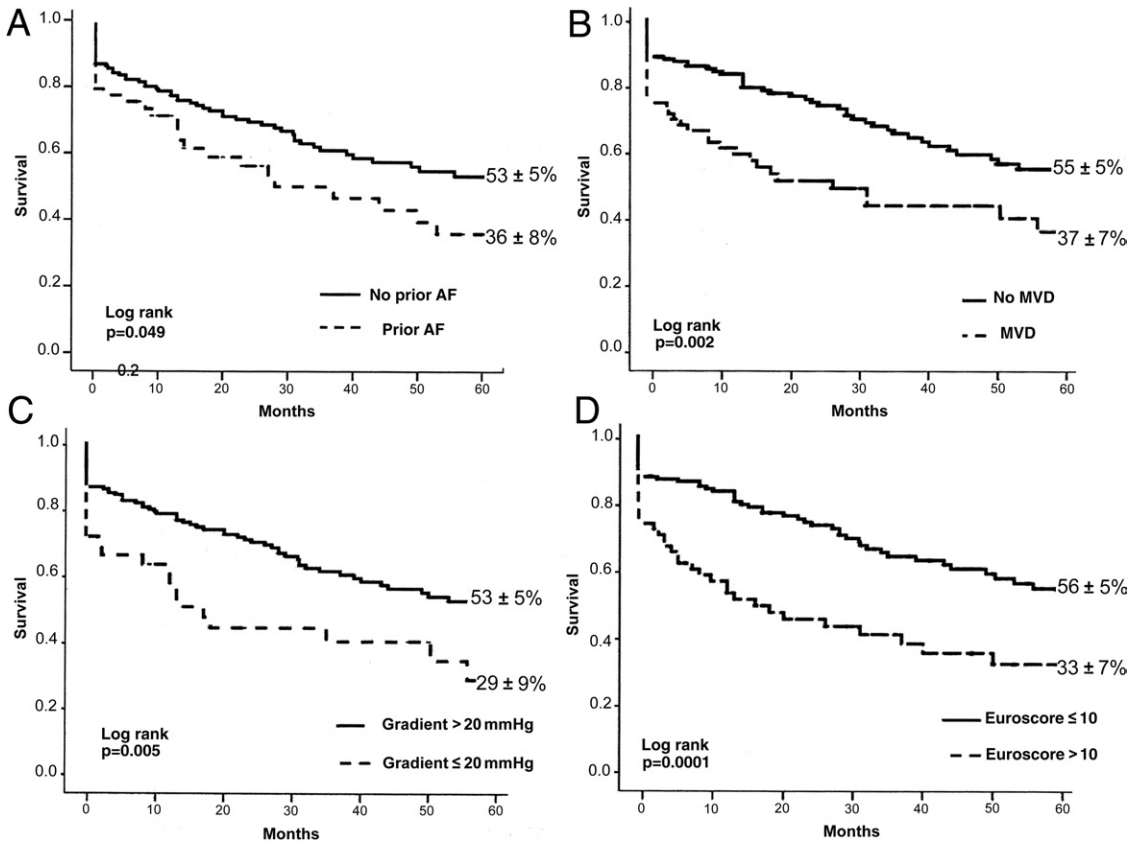

Figure 2 5-Year Overall Survival Curves

(A) Patients with and without prior atrial fibrillation, **(B)** patients with and without multivessel coronary artery disease, **(C)** patients with mean gradient ≤20 and >20 mm Hg, and **(D)** patients with pre-operative European System for Cardiac Operative Risk Evaluation score ≤10 and >10. AF = atrial fibrillation; MVD = multivessel coronary artery disease.

More than one-half of late deaths in the present study were due to noncardiac causes. Thus, in LF/LGAS, significant CAD and very low MG (≤20 mm Hg) are 2 major risk factors influencing both perioperative and long-term outcome.

Study limitations. This study was retrospective, but it included consecutive patients operated for LF/LGAS, according to the definition of American College of Cardiology/American Heart Association guidelines, in 11 European centers. The strength of this study is the large number of patients included in different centers, giving statistical power and avoiding single-center biases. No larger series of this type of patient has been published to date. Multivariate analyses in our study evaluated a relatively large number of potential predictors relative to the number of events. In view of the long inclusion period and the large number of centers, only 38% of patients in the study had DSE. As previously reported (9,10), the strong prognostic value of contractile reserve to assess the operative risk was demonstrated in this subgroup of patients. A more frequent use of DSE to stratify operative risk over recent years in our study might have been an explanation for the decrease in operative mortality in the recent period. However, the percentage of patients who had DSE was not significantly different during the 2 periods (35% in the 1990 to 1999 period vs. 41% in the 2000 to 2005 period; p = 0.38), similar to the proportion of patients without contractile reserve during DSE (11% in the 1990 to 1999 period vs. 10% in the 2000 to 2005 period; p = 0.48). We cannot assess in our series the prognosis of "pseudosevere AS," in which increase of transvalvular flow results in an increase in valve area to a nonsevere range (5), as patients who had this response to DSE were not referred for surgery in the different participating centers. However, we cannot exclude the probability that some patients of our series may not have had critical AS. Pre-operative NYHA functional status in our study was evaluated under optimal medical treatment. Seventeen percent (n = 37) of our patients were in pre-operative NYHA functional class II (no patients were in class I). Actually, pre-operative NYHA functional status was evaluated under optimal medical treatment (at least diuretics), and 90% of these 37 patients in pre-operative NYHA functional class II had a recent history of congestive heart failure. The prevalence of pre-operative NYHA functional classes I and II was 35% in the series reported by Pereira et al. (7) and 15% in the series of

Connolly et al. (3) and Powell et al. (17). Moreover, the prevalence of associated MVD in patients with less than pre-operative NYHA functional class III symptoms and in patients in NYHA functional class III or IV was comparable (30% vs. 28%, p = 0.79). Additionally, information on the recurrence of congestive heart failure after AVR was not available. These data would have been useful to assess the improvement of quality of life after AVR.

Conclusions

One of the main findings of this European multicenter study is a decrease in operative mortality over recent years in patients with LF/LGAS. Operative risk is now acceptable (i.e., around 10%) and may be stratified by taking into account the presence or absence of contractile reserve on DSE, presence of multivessel CAD, the value of pre-operative MG, and EuroSCORE. Finally, in view of the very poor prognosis of unoperated LF/LGAS, the current operative risk, and long-term outcome of operated patients, aortic valve replacement is the treatment of choice in the large majority of cases of LF/LGAS.

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REFERENCES

1. Vaquette B, Corbineau H, Laurent M, et al. Valve replacement in patients with critical aortic stenosis and depressed left ventricular function: predictors of operative risk, left ventricular function recovery, and long term outcome. Heart 2005;91:1324–9.
2. Connolly H, Oh J, Orszulak T, et al. Aortic valve replacement for aortic stenosis with left ventricular dysfunction. Prognostic indicators. Circulation 1997;95:2395–400.
3. 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.
4. Bonow RO, Carabello B, Chatterjee K, et al. ACC/AHA 2006 practice guidelines for the management of patients with valvular heart disease—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease). J Am Coll Cardiol 2006;48:598–675.
5. Nishimura RA, Grantham JA, Connolly HM, Schaff HV, Higano ST, Holmes DR Jr. Low-output, low-gradient aortic stenosis in patients with depressed left ventricular systolic function: the clinical utility of the dobutamine challenge in the catheterization laboratory. Circulation 2002;106:809–13.
6. Brogan W, Grayburn P, Lange R, Hilis L. Prognosis after valve replacement in patients with severe aortic stenosis and a low transvalvular pressure gradient. J Am Coll Cardiol 1993;21:1657–60.
7. Pereira JJ, Lauer MS, Bashir M, et al. Survival after aortic valve replacement for severe aortic stenosis with low transvalvular gradients and severe left ventricular dysfunction. J Am Coll Cardiol 2002;39:1356–63.
8. Blitz L, Gorman M, Herrmann H. Results of aortic valve replacement for aortic stenosis with relatively low transvalvular pressure gradients. Am J Cardiol 1998;81:358–62.
9. Monin JL, Monchi M, Gest V, Duval-Moulin AM, Dubois-Rande JL, Gueret P. Aortic stenosis with severe left ventricular dysfunction and low transvalvular pressure gradients: risk stratification by low-dose dobutamine echocardiography. J Am Coll Cardiol 2001;37:2101–7.
10. Monin JL, Quere JP, Monchi M, et al. Low-gradient aortic stenosis: operative risk stratification and predictors for long-term outcome: a multicenter study using dobutamine stress hemodynamics. Circulation 2003;108:319–24.
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. Schiller N, Shah P, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989;2:358–67.
13. Stamm RB, Carabello BA, Mayers DL, Martin RP. Two-dimensional echocardiographic measurement of left ventricular ejection fraction: prospective analysis of what constitutes an adequate determination. Am Heart J 1982;104:136–44.
14. Quere JP, Monin JL, Levy F, et al. Influence of pre-operative left ventricular contractile reserve on postoperative ejection fraction in low-gradient aortic stenosis. Circulation 2006;113:1738–44.
15. European System for Cardiac Operative Risk Evaluation. Available at: http://www.euroscore.org. Accessed January 2007.
16. Levy F, Garayalde E, Quere J, Ianetta-Peltier M, Peltier M, Tribouilloy C. Prognostic value of pre-operative atrial fibrillation in patients with aortic stenosis and low ejection fraction having aortic valve replacement. Am J Cardiol 2006;98:809–11.
17. Powell DE, Tunick PA, Rosenzweig BP, et al. Aortic valve replacement in patients with aortic stenosis and severe left ventricular dysfunction. Arch Intern Med 2000;160:1337–41.
18. Smith N, McAnulty J, Rahimtoola S. Severe aortic stenosis with impaired left ventricular function and clinical heart failure: results of valve replacement. Circulation 1978;58:255–64.
19. Ross J. Afterload mismatch in aortic and mitral valve disease: implications for surgical therapy. J Am Coll Cardiol 1985;5:811–2.