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FOCUS ISSUE: VALVULAR HEART DISEASE

CME

Outcome After Aortic Valve Replacement for Low-Flow/Low-Gradient Aortic Stenosis Without Contractile Reserve on Dobutamine Stress Echocardiography

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Objectives This study investigated whether aortic valve replacement (AVR) is associated with improved survival in patients with severe low-flow/low-gradient aortic stenosis (LF/LGAS) without contractile reserve (CR) on dobutamine stress echocardiography (DSE).

Background Patients with LF/LGAS without CR have a high mortality rate with conservative therapy. The benefit of AVR in this subset of patients remains controversial.

Methods Eighty-one consecutive patients with symptomatic calcified LF/LGAS (valve area ≤1 cm^2, left ventricular ejection fraction ≤40%, mean pressure gradient [MPG] ≤40 mm Hg) without CR on DSE were enrolled. Absence of CR was defined as the absence of increase in stroke volume of ≥20% compared with the baseline value. Multivariable analysis and propensity scores were used to compare survival according to whether or not AVR was performed (n = 55).

Results Five-year survival was higher in AVR patients compared with medically managed patients (54 ± 7% vs. 13 ± 7%, p = 0.001) despite a high operative mortality of 22% (n = 12). An AVR was independently associated with lower 5-year mortality (adjusted hazard ratio from 0.16 to 5.21 varying with time [95% confidence interval: 0.12–3.16 to 0.21–8.50], p = 0.00026). In 42 propensity-matched patients, 5-year survival was markedly improved by AVR (65 ± 11% vs. 11 ± 7%, p = 0.019). Associated bypass surgery (p = 0.007) and MPG ≤20 mm Hg (p = 0.035) were independently predictive of operative mortality. Late survival after AVR (excluding operative death) was 69 ± 8% at 5 years.

Conclusions In patients with LF/LGAS without CR on DSE, AVR is associated with better outcome compared with medical management. Surgery should not be withheld from this subset of patients solely on the basis of lack of CR on DSE. (J Am Coll Cardiol 2009;53:1865–73) © 2009 by the American College of Cardiology Foundation

Patients with severe low-flow/low-gradient aortic stenosis (LF/LGAS) have a poor prognosis with conservative treatment. In the setting of LF/LGAS, operative risk can be stratified using dobutamine stress echocardiography (DSE) (1–3). According to recent studies, patients with left ventricular contractile reserve (CR) on DSE (i.e., an increase in stroke volume under dobutamine infusion of ≥20% compared with the baseline value) have a relatively low operative mortality, about 5% to 7% (2,3). Therefore, patients with

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Abbreviations and Acronyms

AS = aortic stenosis
AVR = aortic valve replacement
CABG = coronary artery bypass graft surgery
CAD = coronary artery disease
CR = contractile reserve
DSE = dobutamine stress echocardiography
EuroSCORE = European System for Cardiac Operative Risk Evaluation
LF/LGAS = low-flow/low-gradient aortic stenosis
LVEF = left ventricular ejection fraction
MPG = mean transaortic pressure gradient
NYHA = New York Heart Association

severe LF/LGAS and CR have an acceptable operative risk, and aortic valve replacement (AVR) improves long-term survival and functional status in most cases (2–4).

Conversely, patients without CR have a high operative mortality, about 30% in a recent series (2). Because of this high reported operative risk, many clinicians consider that the absence of CR on DSE represents a contraindication for AVR. However, actual surgical experience in LF/LGAS without CR on DSE is limited, because very few data on AVR patients have been reported (2,3). Moreover, the prognosis with medical management is extremely poor and a trend toward better survival with AVR was observed in a small series (2). We recently reported that patients without CR who survive the perioperative period improve their functional status in more than 90% of cases and show an increase in left ventricular ejection fraction (LVEF) by >10% in more than 60% of cases (5). Accordingly, the recent American College of Cardiology/American Heart Association guidelines state that some patients without CR could benefit from AVR (1). This European multicenter registry, focusing on a series of consecutive LF/LGAS patients without CR on DSE prospectively enrolled in 10 centers between 1991 and 2006, was retrospectively analyzed to compare survival after AVR and on conservative management and to identify predictors of perioperative mortality and long-term outcome.

Methods

Study sample. Eighty-one patients with low-flow/low-gradient (mean transaortic pressure gradient [MPG] ≤40 mm Hg, LVEF ≤40%) symptomatic calcified AS (aortic valve area ≤1 cm^2) without CR on DSE were prospectively enrolled in 10 centers (Amiens, France; Argenteuil, France; Bordeaux, France; Brest, France; Brussels, Belgium; Créteil, France; Lorient, France; Reims, France; Rennes, France; and Strasbourg, France). The study population was divided into 2 groups according to whether or not aortic valve surgery was performed (AVR group, n = 55; and medical group, n = 26). In patients treated with AVR, the severity of AS was assessed by visual inspection of the valve at the time of surgery. The degree of calcification and commissural fusion was described and the stiffness of each leaflet was assessed in situ to confirm the severity of AS. Preliminary data from this registry were previously published (2,4–6). Forty-four patients from these series (with extended follow-up) were included in the present report. The study was approved by local institutional review boards or ethics committees, in accordance with institutional policies, national legal requirements, and the revised Helsinki declaration. Informed consent was obtained from each patient before any study procedures.

Echocardiography. All patients underwent a comprehensive Doppler echocardiographic study using commercially available ultrasound systems. The echocardiographic severity of aortic valve calcification was graded qualitatively as previously proposed by Rosenhek et al. (7), and grades 3 (multiple large calcium deposits) and 4 (extensive calcification of all cusps) were considered to be significant valve calcification. Left ventricular outflow tract diameter was assumed to be constant at different flow states, and the baseline value was used to calculate stroke volume at baseline and during dobutamine infusion according to standard formulae (8). Transaortic gradients were calculated using the simplified Bernoulli equation (9). Aortic valve area was calculated by the continuity equation (10). The LVEF was calculated in all patients at inclusion. Dobutamine echocardiographic studies were evaluated off-line in each center by a single experienced echocardiographer. Details of the DSE have been described previously (2,3,5,11). Briefly, after baseline measurements, a dobutamine infusion was started at 5 μg/kg body weight/min, and titrated upward to a maximum dose of 20 μg/kg/min. Absence of CR during DSE was classically defined as the absence of increase in stroke volume of ≥20% compared with the baseline value (2,3,5,11).

Coronary angiography. Pre-operative coronary angiography was performed in all patients. Reduction of the normal diameter ≥50% was considered to define significant coronary artery disease (CAD) in the left main coronary artery. A cutoff value of 70% was used for the right coronary, left anterior descending, and circumflex arteries. Multivessel CAD was defined as the presence of 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 (12). Risk factors integrated in the EuroSCORE are patient-, cardiac-, and operation-related factors. Patient-related factors are: age >60 years, female sex, chronic pulmonary disease, extracardiac arterial disease, neurological dysfunction, previous cardiac surgery, serum creatinine >200 μmol/l, active endocarditis, and critical pre-operative state. Cardiac-related factors are unstable angina, reduced LVEF, recent myocardial infarction, and pulmonary systolic pressure >60 mm Hg. Operation-related factors are: emergency surgery other than isolated coronary artery bypass surgery, thoracic aorta surgery, and surgery for post-infarct septal rupture.

Clinical decision and follow-up. Clinical decisions for each patient were left to the discretion of the referring