JACC: CARDIOVASCULAR IMAGING
PUBLISHED BY ELSEVIER
VOL. 9, NO. 7, 2016
ISSN 1936-878X/$36.00
http://dx.doi.org/10.1016/j.jcmg.2015.09.026

Discordant Grading of Aortic Stenosis Severity

Echocardiographic Predictors of Survival Benefit Associated With Aortic Valve Replacement

Maxime Berthelot-Richer, MD, MSc, Philippe Pibarot, DVM, PhD, Romain Capoulade, PhD, Jean G. Dumesnil, MD, Abdellaziz Dahou, MD, Christophe Thebault, MD, Florent Le Ven, MD, Marie-Annick Clavel, DVM, PhD

ABSTRACT

OBJECTIVES This study sought to assess the survival benefit associated with aortic valve replacement (AVR) according to different strata of echocardiographic parameters of aortic stenosis (AS) severity, and especially in patients with an aortic valve area (AVA) comprised between 0.8 cm^2 and 1 cm^2.

BACKGROUND Discordant findings between AVA (≤1.0 cm^2) and mean gradient (MG) (<40 mm Hg) raise uncertainty regarding the actual severity of AS. Some studies suggested that the AVA threshold value to define severe AS should be decreased to 0.8 cm^2 to reconcile these discordances.

METHODS A total of 1,710 patients with documented moderate to severe AS by Doppler echocardiography were separated into 4 strata of AS severity based alternatively on AVA, indexed AVA, MG, or peak aortic jet velocity (V_{peak}). We compared the survival rates of medically versus surgically treated patients. To eliminate covariate differences that may lead to biased estimates of treatment effect, a propensity matching with a greedy 5-to-1 digit-matching algorithm was used.

RESULTS Mean AVA was 0.9 ± 0.3 cm^2, mean MG 33 ± 18 mm Hg, and mean V_{peak} 3.6 ± 0.9 m/s. A total of 1,030 (60%) patients underwent AVR within 3 months following echocardiographic evaluation. During a mean follow-up of 4.4 ± 3.0 years there were 469 deaths. Patients with an AVA between 0.8 cm^2 and 1.0 cm^2 had a significant observed survival benefit with AVR (hazard ratio: 0.37 [95% confidence interval: 0.21 to 0.63]; $p = 0.0002$). AVR was also associated with improved survival in patients with MG between 25 mm Hg and 40 mm Hg or V_{peak} between 3 m/s and 4 m/s, but only in patients with concomitant AVA ≤1 cm^2 ($p = 0.001$ vs. $p = 0.46$ in patients with AVA >1 cm^2).

CONCLUSIONS These results do not support decreasing the AVA threshold value for severity to 0.8 cm^2 and they confirm that AVR is associated with improved survival in a substantial number of patients with discordant aortic grading. (J Am Coll Cardiol Img 2016;9:797–805) © 2016 by the American College of Cardiology Foundation.

According to American and European guidelines (1-3), severe aortic stenosis (AS) is defined by several echocardiographic criteria including aortic valve area (AVA) ≤1 cm^2, indexed AVA (AVAi) ≤0.6 cm^2/m^2, mean gradient (MG) ≥40 mm Hg, and peak aortic jet velocity (V_{peak}) ≥4 m/s. However, up to 30% of patients with AS present with discordant echocardiographic parameters of AS severity. The most frequent discordant grading pattern is an AVA ≤1 cm^2 and/or AVAi ≤0.6 cm^2/m^2 (indicating a severe disease) with an MG <40 mm Hg and/or V_{peak} <4 m/s (rather consistent with a moderate disease) (4-7). In that situation, uncertainty remains regarding the actual AS severity and whether or not to refer the symptomatic patient to aortic valve replacement (AVR).

Although discordance (i.e., small AVA/AVAi but low MG/V_{peak}) in severe low-flow AS, with or without

From the Institut Universitaire de Cardiologie et de Pneumologie de Québec/Québec Heart & Lung Institute, Laval University, Québec, Canada. All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received April 13, 2015; revised manuscript received September 7, 2015, accepted September 10, 2015.

JACC: CARDIOVASCULAR IMAGING, VOL. 9, NO. 7, 2016
JULY 2016:797–805

ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

AVA = aortic valve area

AVAi = indexed AVA

AVR = aortic valve replacement

CABG = coronary arteries bypass graft

CI = confidence interval

LV = left ventricular

MG = mean gradient

V_{peak} = peak aortic jet velocity

preserved ejection fraction, is accepted, the possibility of discordance in severe AS with normal flow is highly controverted. Nevertheless, discordant echocardiographic grading of AS severity in a normal flow patient may be related to multiple factors including measurement errors (3,8), small body size, reduced arterial compliance (7,9), or inherent discordance between AVA/AVAi and MG/V_{peak} cutpoints used for the definition of severe AS (5). With regards to the latter factor, it has been demonstrated that, from a hemodynamic standpoint, an MG of 40 mm Hg does not correspond to an AVA of 1.0 cm² but rather to an AVA of 0.8 cm² (5). Hence, to reconcile the AVA/AVAi and MG/V_{peak} criteria to define severe AS, some authors have proposed to lower the AVA cutpoint from 1.0 to 0.8 cm² (5,10,11). However, survival studies have reported that an AVA ≤1.0 cm² is the most powerful and sensitive predictor of death (12).

SEE PAGE 806

Furthermore, AVR is associated with better survival in symptomatic patients with AVA ≤1.0 cm² and low MG (<40 mm Hg) (6,13,14). However, no previous study has assessed the benefit of AVR according to the different echocardiographic criteria proposed in the literature. The primary objective of this study was thus to assess the survival benefit associated with surgical AVR according to different strata of echocardiographic parameters of AS severity. The secondary objective was to assess the survival benefit associated with AVR in patients with discordant aortic grading and normal flow.

METHODS

POPULATION. All adult patients who underwent a comprehensive Doppler echocardiographic examination for moderate to severe aortic valve stenosis (AVA ≤1.5 cm²) at our center between 2000 and 2012 were eligible for this study. Patients with a history of rheumatic valve disease or endocarditis, life-threatening comorbid conditions at diagnosis, more than mild aortic regurgitation (i.e., vena contracta ≥3 mm, regurgitant volume ≥30 cc, regurgitant fraction ≥30%, and/or regurgitant effective orifice area ≥0.1 cm²) (15), mild mitral stenosis (mitral valve area ≤1.5 cm² or MG ≥5 mm Hg) (3), and/or mild mitral regurgitation (vena contracta ≥3 mm, regurgitant volume ≥30 cc, regurgitant fraction ≥30% or regurgitant effective orifice area ≥0.2 cm²) (16), or any other valve disease or prior valve replacement were excluded.

We also excluded patients who underwent any concomitant intervention except coronary artery bypass graft (CABG) at the time of AVR (including aortic root replacement, mitral annuloplasty, and so forth); and patients who underwent transcatheter AVR because the aim of this study was to assess the benefit of surgical AVR. Clinical, Doppler echocardiographic, and operative data were prospectively collected in consecutive patients and were retrospectively analyzed.

DOPPLER ECHOCARDIOGRAPHIC MEASUREMENTS. Left ventricular (LV) dimensions, mass, and left ventricular ejection fraction (LVEF) were measured according to recommendations of the American Society of Echocardiography (17). Measurement of the LV outflow tract, V_{peak}, and time velocity integrals allowed calculation of stroke volume, MG by modified Bernoulli formula, and AVA by the continuity equation. AVA and stroke volume were indexed to body surface area. Normal LV function and flow was defined as LVEF ≥50% and stroke volume index >35 ml/m². To minimize measurement error as a potential cause of discordance, we excluded suboptimal echocardiograms.

THERAPEUTIC MANAGEMENT AND OUTCOMES. All patients who underwent AVR within 3 months after baseline echocardiographic evaluation were classified in the AVR treatment group. In all patients of this group, the decision to refer the patient to AVR was decided by the treating physician before or at the time of echocardiographic evaluation. Patients who did not undergo AVR (n = 627) or who underwent AVR >3 months (n = 53 with medical mean follow-up of 4.4 ± 3.0 years) after echocardiographic evaluation were classified in the medical treatment group. In patients with delayed AVR (i.e., >3 months), only medical follow-up was taken into account (i.e., follow-up was censored at that time of AVR). Mortality data were obtained from the Institut National de la Statistique du Québec. The follow-up data were complete for all patients.

STATISTICAL ANALYSES. Results are expressed as mean ± SD or percentages. Differences between groups were analyzed with the use of the 2-sided Student *t* test for continuous variables, with the Wilcoxon rank sum test for ordinal variables and the chi-square test of Fisher exact test for categorical variables as appropriate.

We grouped patients into strata according to their levels of echocardiographic parameters. Numbers of strata were decided to have sufficient statistical power for the multivariate survival analysis. Each echocardiographic parameter (AVA, AVAi, MG, and