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Incremental Prognostic Utility of Left Ventricular Global Longitudinal Strain in Asymptomatic Patients With Significant Chronic Aortic Regurgitation and Preserved Left Ventricular Ejection Fraction

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ABSTRACT

OBJECTIVES We sought to examine the prognostic utility of left ventricular (LV) global longitudinal strain (GLS) in asymptomatic patients with ≥III+ aortic regurgitation (AR), an indexed LV end-systolic dimension of <2.5 cm/m^2, and preserved left ventricular ejection fraction (LVEF).

BACKGROUND Management of asymptomatic patients with severe chronic AR and preserved LVEF is challenging and is typically based on LV dimensions.

METHODS We studied 1,063 such patients (53 ± 16 years; 77% men) seen between 2003 and 2010 (excluding those with symptoms, obstructive coronary artery disease, acute AR/dissection, aortic/mitral stenosis, more than moderate mitral regurgitation, and previous cardiac surgery). Society of Thoracic Surgeons (STS) score was calculated. The primary endpoint was mortality. Average resting LV-GLS was measured offline on 2-, 3-, and 4-chamber views using Velocity Vector Imaging (Siemens, Malvern, Pennsylvania).

RESULTS Mean STS score, LVEF, LV-GLS, and right ventricular systolic pressure were 4.4 ± 5.0%, 57.0 ± 4.0%, −19.5 ± 0.2%, and 31.0 ± 9.0 mm Hg, respectively. In total, 671 patients (63%) underwent aortic valve surgery at a median of 42 days after the initial evaluation. At 6.8 ± 3.0 years, 146 patients (14%) had died. On multivariable Cox survival analysis, LV-GLS (hazard ratio [HR]: 1.11), STS score (HR: 1.51), indexed LV end-systolic dimension (HR: 0.50), right ventricular systolic pressure (HR: 1.33), and aortic valve surgery (HR: 0.35) were associated with longer term mortality (all $p < 0.001$). Sequential addition of LV-GLS and aortic valve surgery improved the C-statistic for longer term mortality for the clinical model (STS score + right ventricular systolic pressure + indexed LV end-systolic dimension) from 0.61 (95% confidence interval [CI]: 0.51 to 0.72) to 0.67 (95% CI: 0.54 to 0.87) and to 0.77 (95% CI: 0.63 to 0.90), respectively ($p < 0.001$ for both). A significantly higher proportion (log-rank $p = 0.01$) of patients with LV-GLS worse than median (−19.5%) died versus those with an LV-GLS better than median (86 of 513 [17%] vs. 60 of 550 [11%]). The risk of death at 5 years significantly increased with an LV-GLS of worse than −19%.

CONCLUSIONS In asymptomatic patients with ≥III+ chronic AR and preserved LVEF, worsening LV-GLS was associated with longer term mortality, providing incremental prognostic value and improved reclassification. (J Am Coll Cardiol Img 2017;■:■–■) © 2017 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

AR = aortic regurgitation

AV = aortic valve

iLVESD = indexed left ventricular end-systolic dimension

LV = left ventricular

LVEF = left ventricular ejection fraction

LV-GLS = left ventricular global longitudinal strain

RVSP = right ventricular systolic pressure

STS = Society of Thoracic Surgeons

Chronic severe aortic regurgitation (AR) imposes significant volume and pressure overload on the left ventricle (LV), with resultant compensatory (but eventually detrimental) changes in the myocardium (1,2). Such patients typically remain asymptomatic for a long time, but once there is a decrease in the left ventricular ejection fraction (LVEF) and the development of heart failure, survival decreases significantly in the absence of corrective surgery. Hence, the current guidelines recommend aortic valve (AV) surgery in severe AR once symptoms occur or when the LVEF is depressed LVEF as a class I indication (3). However, the management of asymptomatic patients with severe chronic AR and preserved LVEF is challenging and hitherto has been based on LV dimensions with ongoing controversy regarding appropriate timing of AV surgery (3).

Current guidelines recommend that AV surgery (Class II indication) be considered in asymptomatic patients with preserved LVEF, when there is evidence of a significantly dilated LV (3). However, these recommendations were derived mostly from small studies, performed >2 decades ago at a time when surgical mortality and morbidity were higher than what is seen today (4-7). The natural history for many such patients may not be as benign (approximately 0.2% per year) as reported previously; with a recent report suggesting an annual mortality rate of 2.2% per year (4-8). With significant improvements in diagnostic techniques and emergence of advanced surgical techniques, surgical morbidity and mortality have decreased considerably, suggesting that there is a need to reassess surgical thresholds in such patients (9,10). Hence, there is also an increasing recognition and an impetus to identify predisposed individuals (asymptomatic or early symptoms) who are at an increased risk for adverse outcomes, despite preserved LV function. We have recently demonstrated that at a high-volume experienced center, asymptomatic/minimal symptomatic patients with ≥III+ AR and preserved LVEF demonstrate significantly improved longer term survival after AV surgery, which approximates that of a normal age- and sex-matched U.S. population (11). Furthermore, non-operated patients with indexed left ventricular end-systolic dimensions (iLVESDs) of ≤2.0 cm/m^2 had an excellent 5-year survival; however, the risk of death significantly and continuously increased once iLVESD was >2 cm/m^2. In addition, multiple smaller reports have evaluated the potentially incremental prognostic role of newer echocardiographic indices like LV global longitudinal strain (LV-GLS), tissue Doppler and torsion in patients with chronic severe AR (12-18). We hypothesized that LV-GLS could provide incremental prognostic utility in asymptomatic patients with ≥III+ AR. The aim of our study was to examine the incremental prognostic utility of LV-GLS for the primary endpoint of death in a contemporary group of asymptomatic patients with ≥III+ AR, iLVESD <2.5 cm/m^2, and preserved LVEF.

METHODS

This observational cohort study included 1,063 asymptomatic patients with ≥III+ chronic AR, preserved LVEF (≥50%), and iLVESD <2.5 cm/m^2, who were evaluated at our center between January 2003 and December 2010, out of an original database of 4,176 patients. To be included, at the time of initial encounter, all patients were evaluated clinically by a cardiologist experienced in managing valvular heart disease, including a thorough history, physical examination, laboratory evaluation, and echocardiography (including stress echocardiography in selected patients with unclear symptom status), and the lack of symptoms was ascertained. All patients had echocardiogram and cardiology evaluation within 30 days of each other (>90% on the same day). The breakdown of final study population, after the application of various exclusion criteria, is shown in **Figure 1**. We also excluded 103 patients in whom LV-GLS values were not recorded for multiple reasons (atrial fibrillation, septal wall motion abnormality due to pacemaker/bundle branch block, or suboptimal tracking due to poor acoustic windows).

Baseline characteristics were recorded prospectively in the electronic medical record at the time of initial medical encounter and manually extracted for the current study. We recorded type of AV surgery (repair vs. replacement, type of valve prosthesis) and the need for concomitant aortic surgery (including the valve-sparing David procedure, Bentall procedure, and supra-coronary ascending aortic grafting). The decision to operate was made by consensus between cardiologists and cardiothoracic surgeons, after discussion of risks, benefits, and alternatives with the patients. Society of Thoracic Surgeons (STS) score was calculated.

ECHOCARDIOGRAPHY DATA. All patients underwent comprehensive baseline echocardiograms using commercial instruments (Philips Medical Systems, Bothell, Washington; Siemens Medical Solutions Inc., Malvern, Pennsylvania; General Electric, Milwaukee, Wisconsin). The LV ejection fraction, indexed LV dimensions, and left atrial area were measured at rest