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Original article

Prognostic value of global left ventricular strain for conservatively treated patients with symptomatic aortic stenosis

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ABSTRACT

Aims: Impaired left ventricular (LV) strain is associated with an increased risk of cardiac events in asymptomatic severe aortic stenosis (AS). We aimed to evaluate the prognostic value of global LV strain in conservatively treated patients with symptomatic AS.

Methods and results: This cohort study retrospectively reviewed symptomatic AS patients who were treated conservatively or surgically between July 2007 and April 2010. We measured their global longitudinal strain (GLS) and global circumferential strain (GCS). Clinical events were defined as readmission for heart failure or all-cause death for 2 years. GLS and GCS could predict a worse outcome in the conservatively treated group at cut-offs of =−16.5% (77% sensitivity and 67% specificity) and =−22.2% (92% sensitivity and 83% specificity), respectively. By univariate Cox regression analysis, age, logistic EuroSCORE, aortic valve area, GLS, and GCS were significant predictors. When adjusted for age, logistic EuroSCORE, and aortic valve area, impaired GLS and GCS were independently associated with a higher risk of clinical events.

Conclusion: In conservatively treated patients with symptomatic AS, impaired GLS and GCS were associated with an increased risk of cardiac events during a 2-year follow-up. Global LV strain may help to define a higher risk subset; therefore, a larger and prospective observation study would be necessary.

Introduction

Previous studies have demonstrated that patients with severe aortic stenosis (AS) and a preserved left ventricular (LV) ejection fraction have impaired global longitudinal strain (GLS), and that the impairment of GLS improves after aortic valve replacement [1–5]. In patients with asymptomatic severe AS, impaired GLS was reported to be associated with a poor prognosis [6]. Clinically, up to 30% of patients with symptomatic AS are treated conservatively [7–9]. The role of strain parameters in the prognosis of symptomatic AS patients who are treated conservatively remains unclear. Accordingly, the aims of this study were to assess global LV strain in patients with symptomatic AS and a preserved LV ejection fraction who were treated conservatively, and to evaluate the prognostic value of strain parameters in these patients.

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Methods

Patients

This cohort study retrospectively reviewed symptomatic AS patients who were treated conservatively or surgically between July 2007 and April 2010. Patients were excluded from the analysis if they were not in sinus rhythm or had a LV ejection fraction <50%. Patients with a previous valve replacement, severe aortic or mitral regurgitation, and unsuitable two-dimensional imaging quality for speckle-tracking analysis were also excluded from the study. Patients were included after their first symptomatic presentation of angina, dyspnea, or both. Patients who did not undergo aortic valve replacement were conservatively treated patients [10]. The predominant reasons included high estimated surgical risk and patient refusal. If patients were not managed surgically, medications including aspirin (35%), statin (19%), beta-blocker (26%), and renin–angiotensin system blocker (48%) were given. The study group consisted of 31 conservatively treated patients who met these criteria; these patients were divided into 2 subgroups according to the occurrence of clinical events (patients with or without clinical events within 2 years). The clinical events were defined as all-cause death or readmission for heart failure, which were

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determined by evaluation of medical records. Additionally, we enrolled a control (surgical) group of 31 patients who met the above criteria but were treated with aortic valve replacement for the comparison of clinical outcome with the conservatively treated group. All echocardiographic measurements were performed by an experienced research personnel blinded to other clinical characteristics.

The study complies with the Declaration of Helsinki. The research protocol was approved by the local Institutional Review Board.

Echocardiography

Conventional 2-dimensional echocardiography was performed using commercially available equipment (Vivid 7, GE, Horten, Norway) with a 3.5-MHz transducer. LV ejection fraction was determined by the biplane Simpson's method. LV mass was calculated using the formula proposed by Devereux et al. [11], and was corrected by body surface area to derive the LV mass index. Measurements of LV diastolic filling included the mitral early (E)-velocity, mitral late (A)-velocity, and the E/A ratio [10]. In addition, tissue Doppler echocardiography was performed with the peak early diastolic velocity (E') measured at the basal septal segment in the apical 4-chamber view and the E/E' ratio was calculated [12]. The maximum transaortic pressure gradient was calculated using the Bernoulli equation, and mean transaortic pressure gradient was calculated by averaging the instantaneous gradients over the ejection period on the continuous-wave Doppler recordings [13]. The aortic valve area (AVA) was calculated with the continuity equation as previously described [14–17].

Strain analysis

Two-dimensional speckle-tracking strain analysis was performed offline by using a commercially available program (EchoPAC version 110.0, GE) [18–20]. The frame rate for this study was between 50 and 80 Hz. Longitudinal strain was obtained from the apical 4-chamber, 2-chamber, and long-axis views in an 18-segment LV model [21,22]. Circumferential strain was calculated from the parasternal short-axis view in the basal-, mid-, and apical-LV levels. If 2 or more segments were inadequately tracked, we excluded the data because the images were not useable for speckle-tracking analysis [19]. Three patients (2 conservatively treated; 1 surgically treated) were excluded from the analysis due to inadequate imaging quality. Subsequently, peak longitudinal strain and peak circumferential strain of all 18 LV segments were averaged to assess the GLS and global circumferential strain (GCS).

Statistical analysis

Data are presented as mean ± standard deviation or as a count (percentage). Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) statistical software, version 18 for Windows. To compare each parameter between the groups, the chi-square test and Fisher's exact test were used for categorical variables, as appropriate, and the 2-sample t test and Mann–Whitney U-test were used for continuous variables. A Cox proportional hazards model was used for multivariate analysis to investigate which prognostic factors identified using univariate analysis were significantly associated with clinical events. Receiver operating characteristic curve (ROC) analysis was used to determine the optimal cut-off value of strain parameters for the prediction of clinical events. Event-free survival between the groups and subgroups was compared using a log-rank test, and representative Kaplan–Meier survival curves were constructed. The effect of different variables on event-free survival was investigated using the Cox proportional hazard model. For all analyses, a p-value <0.05 was considered statistically significant.

Results

Baseline characteristics

Baseline characteristics for the study patients are shown in Table 1. The mean age was 70.2 ± 12.4 years and approximately half of the patients were male. No significant differences were found in age, gender, risk factors of coronary artery disease, percentage of coronary artery disease, LV mass, and LV ejection fraction between the conservatively treated group and the surgical control group. There were significant differences in logistic EuroSCORE, maximal transaortic pressure gradient, mean transaortic pressure gradient, and AVA between the 2 groups. In the conservatively treated group, the GLS and GLS rate were −16.1 ± 3.2% and $-0.86 \pm 0.20\ s^{-1}$, respectively; the GCS and GCS rate were −22.7 ± 5.2% and $-1.32 \pm 0.38\ s^{-1}$, respectively.

Clinical events and event-free survival

Four patients (6%) were admitted for heart failure and 12 patients (19%) died during the follow-up period. The cause of death

Table 1
Baseline characteristics.

	Total (n = 62)	Conservatively treated (n = 31)	AVR (n = 31)	p-Value
Age (years)	70.2 ± 12.4	72.9 ± 14.5	67.4 ± 9.2	0.08
Male, n (%)	30 (48)	15 (48)	15 (48)	1.00
Hypertension, n (%)	35 (56)	16 (52)	19 (61)	0.44
Dyslipidemia, n (%)	13 (21)	4 (13)	9 (29)	0.12
Smoking, n (%)	8 (13)	4 (13)	4 (13)	1.00
Diabetes mellitus, n (%)	16 (26)	10 (32)	6 (19)	0.25
Coronary artery disease, n (%)	12 (19)	5 (16)	7 (23)	0.52
Logistic EuroSCORE	10.4 ± 10.7	14.3 ± 12.1	6.5 ± 7.5	0.003
LV ejection fraction (%)	72.1 ± 9.1	71.4 ± 8.7	72.8 ± 9.7	0.53
LV mass index (g/m^2)	172.9 ± 67.9	171.6 ± 66.1	174.2 ± 71.0	0.89
Maximal PG (mmHg)	66.8 ± 23.9	56.1 ± 20.6	77.4 ± 22.3	0.001
Mean PG (mmHg)	39.3 ± 18.2	32.5 ± 13.5	53.5 ± 18.7	0.001
E/A	0.88 ± 0.23	0.99 ± 0.53	0.86 ± 0.39	0.29
E/E'	20.3 ± 7.0	21.7 ± 7.6	18.8 ± 6.1	0.11
Aortic valve area (cm^2)	0.88 ± 0.23	0.95 ± 0.21	0.81 ± 0.23	0.01
Death	12 (19)	9 (29)	3 (10)	0.12
Readmission for heart failure	4 (11)	4 (13)	0 (0)	0.32

AVR, aortic valve replacement; E/A, the ratio between early diastolic mitral inflow velocity and late inflow velocity; E/E', the ratio between early diastolic inflow velocity and early diastolic tissue velocity; LV, left ventricular; PG, pressure gradient.