Increased apical rotation in patients with severe aortic stenosis assessed by three-dimensional speckle tracking imaging

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Abstract

Background Two-dimensional (2D) speckle tracking imaging (STI) is a non-invasive method used to assess subtle changes in left ventricular (LV) function such as strain and rotational dynamics. However, 2D methodology is complicated by issues such as the out-of-plane problem inherent in short-axis imaging. In addition, circumferential rotation contributes to three-dimensional (3D) wall deformations and affects tracking accuracy. By using 3D-STI technique, we evaluated LV global longitudinal strain (GLS) and apical rotation in severe aortic stenosis (AS) patients with preserved LV ejection fraction (EF).

Methods LV GLS and apical rotation were evaluated using 3D-STI in 20 severe AS patients (79±8 years old; aortic valve area 0.7±0.2 cm^2) with preserved LVEF (68±7%). Data were compared with those of 11 hypertensive LV hypertrophy (LVH) patients (75±10 years old, EF=66±4%) and 12 controls (healthy individuals: 30±14 years old, EF=63±6%).

Results Compared with LVH patients, severe AS patients had significantly decreased values of GLS (-13.0 ± 2.4 vs. -10.4 ± 2.0%, $p = 0.008$). In contrast, LV rotation was significantly higher in AS than LVH patients (13.9 ± 3.0 vs.

10.8 ± 2.5°, $p = 0.007$). There was no significant difference in stroke volume index among three groups. In these three groups, severe AS patients had significantly decreased values of GLS (analysis of variance [ANOVA], $p < 0.001$) and increased LV rotation (ANOVA, $p < 0.001$).

Conclusions In severe AS patients, impaired GLS existed although LVEF was preserved. However, LV rotation was increased in patients with severe AS probably to maintain the LV stroke volume.

Key words: Aortic stenosis, Three-dimensional echocardiography, Speckle-tracking, Strain

Introduction

Aortic stenosis (AS) is the most common native valve heart disease. The therapeutic management of patients with AS depends on the hemodynamic severity of the stenosis and the presence of symptoms (angina, syncope, dyspnea), since the onset of symptoms and left ventricular (LV) systolic dysfunction determine a poor prognosis [1]. Once LV ejection fraction (EF) is decreased, outcome after surgical aortic valve replacement is worse [2], and it may thus be preferable to detect subclinical systolic LV dysfunction before LVEF becomes reduced. LV myocardial deformation measured by speckle-tracking echocardiography (STE) has emerged as a reliable measure of subtle LV systolic dysfunction. Global longitudinal strain (GLS) impairment is associated with symptoms, the likelihood of symptom recovery after aortic valve implantation, and overall survival [3-5]. Another parameter of myocardial deformation that can be measured by STE is apical rotation. Previous studies have shown apical rotation to be increased in patients with severe AS [6].

Currently available 2D STE methodology is complicated by its 2D imaging-based method. The out-of-plane problem inherent in short-axis

imaging is caused by longitudinal heart motion during the cardiac cycle. In addition, circumferential rotation contributes to three-dimensional (3D) wall deformations and affects tracking accuracy. 3D-STE technique can estimate LV regional circumferential, longitudinal, and radial strain components simultaneously [7, 8]. We evaluated LV global longitudinal strain (GLS) and apical rotation in severe aortic stenosis (AS) patients with preserved LV ejection fraction (EF) by using 3D-STI.

Methods

Study population

The study population comprised 20 patients with severe AS (defined by a valve area $\leq$ 1.0 cm^2 and a peak aortic jet velocity $\geq$ 4.0 m/s) [1], and 11 hypertensive patients with left ventricular hypertrophy (LVH) (defined by male > 115 g/m^2, female > 95 g/m^2) [9] and 12 controls subjects (healthy individuals), who gave their informed consent for the study. Exclusion criteria included mitral stenosis or moderate-to-severe mitral regurgitation, depressed LVEF (<50%), previous valve replacement, previous myocardial infarction and atrial fibrillation. This study protocol was approved by the

ethical committee of Shimane University Faculty of Medicine.

Echocardiography

All patients and control subjects underwent standard 2D echocardiographic study and 3D-STE (Artida ultrasound system, Toshiba Medical Systems Co, Tochigi, Japan). The LV internal dimensions at both end-diastole (LVDD) and end-systole (LVSD) were measured using 2D images from the parasternal long-axis acoustic window. Indexed LV mass (LVMI) was determined by using linear equations [9]. LV end-diastolic volume (EDV) and end-systolic volume (ESV) were measured using the biplane disk method. LVEF was calculated by the equation 100 × (EDV – ESV)/EDV. The transmitral flow velocity was recorded from the apical 4-chamber window by placing the sample volume at the level of the mitral valve leaflet chips. The peak early mitral inflow velocity (E), peak late mitral inflow velocity (A), E/A ratio, and deceleration time (DT) of the E wave were obtained. Tissue Doppler imaging of septal and lateral annulus motion of the LV was viewed to measure the early diastolic velocity (e'). The ratio between peak E and e' was calculated (E/e'). In patients with AS, the

maximal aortic valve (AV) velocity was recorded with the apical, right parasternal, or suprasternal multiple transducer positions, and AV area was calculated with the continuity equation through the use of LV outflow tract diameter and flow velocity. Peak and mean aortic pressure gradient (PG) were calculated using the Bernoulli equation. Stroke volume at the aortic annulus was measured in patients with AS and LVH. Right ventricular (RV) systolic pressure was calculated as the sum of transtricuspid gradient and right atrial pressure [10].

Full-volume ECG-gated 3D data sets were acquired from apical positions using a matrix array 2.5-MHz transducer (Fig. 1). To obtain these data sets, 4 or 6 sectors were scanned and automatically integrated into a wide-angle (70×70°) pyramidal data image covering the entire LV. Frame rate of each image was set at approximately 30 Hz. The images were analyzed with software (3D Wall Motion Tracking, Toshiba Medical Systems Co) specific for the analysis of data acquired by the Artida. 3D data sets were displayed as multiplanar reconstruction (MPR) images corresponding to apical 2-chamber and 4-chamber views and 3 short-axis levels, and measured GLS and apical rotation. Global strains were calculated

by averaging the peak systolic value of 16 segment measurements (6 LV basal, 6 mid, and 4 apical) of LS (Fig. 2). Apical rotation value was computed by the software for apical level as the mean of the segments within this level and expressed as the degree (°) of rotation around the LV center of cavity (Fig. 3). As viewed from the apex, counterclockwise rotation was expressed as a positive, and clockwise rotation as a negative value.

To determine the interobserver variability for strain and apical rotation, the analysis was repeated by a second observer (M.T.) who was blinded to the values obtained by the first observer (K.Y.). To determine the intraobserver variability, the analysis was repeated 1 month later by the same observer (K.Y.) in 10 randomly selected study patients.

Statistical analysis

Continuous data were expressed as means ± standard deviation (SD). Data obtained by 2D echocardiography and 3D-STE were compared among three groups (AS, LVH and controls) using one-way analysis of variance (ANOVA). In all statistical tests, values of $p < 0.05$ were considered to indicate statistical significance. Statistical analyses were performed using

SPSS Statistics for Macintosh, version 18.0 (SPSS, Inc.).

Results

The clinical characteristics and echocardiographic measurements are shown in Table 1. There were no significant differences in blood pressure and heart rate among the three groups. The patients with AS had a mean aortic valve area (AVA) of 0.7±0.2 cm^2 and a mean PG of 59±18 mmHg. The average age was 79±8 years and 40% were men. There were no patients with mild and moderate AS in hypertensive LVH group. LV mass index was larger in patients with AS compared to hypertensive LVH patients (141±38 vs. 134 ± 16 g/m^2). RV systolic pressure was also higher in patients with AS compared to hypertensive LVH patients (38±8 vs. 33±4 mmHg).

Compared to LVH patients, severe AS patients had significantly decreased values of GLS (-13.0 ± 2.4 vs. -10.4 ± 2.0%, $p = 0.008$). In contrast, apical rotation was significantly higher in AS patients than LVH patients (13.9 ± 3.0 vs. 10.8 ± 2.5°, $p = 0.007$). There was no significant difference in stroke volume index between these two groups. In the three groups including controls, severe AS patients had significantly decreased values of

GLS (ANOVA, $p<0.0001$) and increased apical rotation ($p<0.0001$) (Fig. 4). There was significant relationship between GLS and LV apical rotation ($p<0.0001$) (Fig. 5). LVEF was not significantly different among those groups.

In AS group, 10 patients (mean age; 77±8 years) were in New York Heart Association (NYHA) class I or II and 10 patients (mean age; 82±7 years were in NYHA class III or IV. There were no significant differences in GLS (-11.3±1.9 vs. -9.4±1.8 %, $p=0.156$) and LV apical rotation (13.7±2.7 vs. 14.1±3.5°, $p=0.780$) between NYHA class I or II group and NYHA class III or IV group.

In AS group, there were 9 patients with moderate to severe chronic kidney disease (estimated glomerular filtration rate <30 mL/min/1.73m^2 or hemodialysis). When we excluded AS patients with moderate to severe chronic kidney disease, there were no significant differences in hemoglobin (13.1±1.6 vs. 12.5±1.5 g/dL) and estimated glomerular filtration rate (72.7±21.5 vs. 72.4±14.8 mL/min/1.73m^2) between hypertensive LVH patients and AS patients (n=11). In these patients, AS patients had still significantly decreased values of GLS (-13.0±2.4 vs. -10.6±1.9%, p =

0.034) and higher apical rotation (13.5 ± 2.6 vs. 10.8 ± 2.5°, p = 0.023) compared to hypertensive LVH patients.

Interobserver and intraobserver variability

For the interobserver and intraobserver variability in GLS, intra-class correlation coefficients (ICCs) were 0.91 (95% confidence interval 0.36-0.99) and 0.95 (0.59-0.99), respectively. ICCs in apical rotation were 0.98 (0.84-0.99) and 0.98 (0.83-0.99), respectively.

Discussion

The present study demonstrated that patients with severe AS and preserved LVEF have decreased values of GLS and increased apical rotation compared with controls and hypertensive patients with LVH. In the normal heart, myocardial fiber helices in the subendocardial and subepicardial myocardial layers of the LV wall exert opposite torques. Torques caused by the subepicardial layers are larger than torques due to the subendocardial layers because of the longer arm of movement [11].

Age-related increases in LV apical rotation has been reported in healthy

subjects [12]. A transition from predominant basal function in infancy and childhood toward a gradual dominance of apical mechanical function was noted, which appears to reflect aging process of myocardium. Subendocardial ischemia has long been recognized as an early sign of the myocardium suffering from pressure overload caused by AS [13, 14]. Apical rotation was increased in AS patients, possibly because subendocardial ischemia diminishes the counteraction of the subendocardial myofibers. In our study patients, LVMI was slightly larger in AS compared to hypertensive LVH. Another potential mechanism for increased apical rotation in AS patients may be LV hypertrophy with an increased arm of force over which the subepicardial fibers work. Nevertheless, both mechanisms may be expected to lead to increased apical rotation.

In AS patients, GLS is a sensitive marker for the detection of subtle abnormalities in myocardial mechanics and may indicate pathology before event on conventional indices of LV function. Previous studies have indeed demonstrated that impairment in GLS can occur even in the setting of a preserved EF [15, 16]. Reduced GLS is associated with poor outcomes in patients with significant AS [4, 17]. Standard parameters do not analyze

subendocardial and subepicardial layers. High apical rotaion values in patients with AS showed a compensatory activity of subepicardial compared to subendocardial fibers, when the latter are influenced by the high values of after-load with worsening of longitudinal function.

The life expectancy in affluent countries has gradually increased, and the number of elderly patients with AS is increasing. However, approximately 30-40% of patients with severe AS are denied surgery because of high risk factors and comorbidities [18]. Transcatheter aortic valve implantation (TAVI), a less invasive technique than surgical aortic valve replacement, (AVR) appears to be a new option for elderly patients. In many patients, the development of symptoms is clear, but some asymptomatic patients are difficult to assess because of inactivity or under-reporting [19]. Exercise echocardiography may improve risk stratification and identify asymptomatic patients [20], but we sometimes experience difficulties in performing exercise studies in elderly patients. Although a watchful waiting approach is generally justified in asymptomatic patients with severe AS, the high event rate and the possibility of rapid deterioration in patients ≥80 years old, may justify consideration of early elective AVR or TAVI even when they are still

asymptomatic.

Clinical implications

At present, the best predictor for cardiac mortality in patients with AS is the development of symptoms. AS related symptoms may, however, be overlooked because of gradual changes in lifestyle, patients slowly adapt to the severity of AS. Early detection of myocardial fibrosis can possibly lead to the early identification of patients at risk for cardiac mortality. Decreased GLS and increased LV rotation assessed by 3D strain echocardiography could detect subtle LV subendocardial fibrosis in patients with severe AS. Further studies are needed to evaluate the role of apical rotation in deciding the timing of surgery.

Study limitations

This study was a single-center study that included a selected population of patients and the sample size was small. Further large number study patients are warranted. The accuracy of speckle-tracking imaging has been validated against sonomicrometry and tagged magnetic resonance imaging [21, 22].

However, the quality of tracking is dependent on the image quality and is vulnerable to dropouts of ultrasound data and reverberations. Due to a low inter-vendor agreement [23], 2-D strain data are not interchangeable when conducting a longitudinal follow-up or a cross-sectional assessment of LV function. In addition, significant variation in rotational deformation still exists and is evident when comparing healthy control groups across studies. The quantification of rotation can still provide valuable insight into myocardial function. The system and software from the same vendor should be used for a longitudinal follow-up in the same patients or a cross-sectional study.

Conclusions

In severe AS patients, impaired GLS existed although LVEF was preserved. However, LV rotation was increased in patients with severe AS probably to maintain the LV stroke volume.

Conflicts of interest

Maidar Tumenbayar, Kazuto Yamaguchi, Hiroyuki Yoshitomi, Akihiro Endo and Kazuaki Tanabe declare that they have no conflicts of interest.

Human rights statements

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later revisions.

Informed consent

Informed consent was obtained from all patients for being included in the study.

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Figure Legends

Fig. 1 Three-dimensional speckle tracking of the LV at end-diastole. The multiplanar reconstruction images correspond to the apical 2-chamber and 4-chamber views and 3 short-axis views at different levels.

Fig. 2 Measurement of LV global longitudinal strain (GLS) in a patient with severe AS. GLS was calculated by averaging the peak systolic values of 16 segment measurements (6 LV basal, 6 mid, and 4 apical segments).

Fig. 3 Measurement of apical rotation of the LV in a patient with severe AS. LV rotation value was computed by the software for apical, mid and basal levels of the LV as the mean of the segments within each levels. As viewed from the apex, counterclockwise rotation was expressed as a positive (blue), and clockwise rotation as a negative value (red).

Fig. 4 GLS and apical rotation in control group, LVH patients and AS patients. Patients with severe AS had significantly decreased values of GLS (ANOVA, $p < 0.0001$) and increased apical rotation ($p<0.0001$).

Fig.5 Relationship between GLS and LV apical rotation. There was significant relationship between decreased GLS and increased LV apical rotation ($p<0.0001$).

Table 1 Clinical characteristics and echocardiographic measurements

	Control (n=12)	LVH (n=11)	AS (n=20)	P (ANOVA)
Age, y	30±14	75±10	79±8	<0.0001
Heart rate, bpm	62±16	60±7	65±10	0.241
Systolic blood pressure, mmHg	119±8	134±12	129±23	0.157
Diastolic blood pressure, mmHg	69±8	79±13	71±15	0.146
Medications, n (%)				
Diuretics		1 (8)	8 (40)	0.031
Calcium antagonists		7 (58)	11 (55)	0.246
ACE inhibitors or ARBs		7 (58)	11 (55)	0.860
Beta blockers		2 (17)	2 (10)	0.619
Echocardiographic measurements				
LVDD, mm	49±4	47±6	45±5	0.05
LVSD, mm	33±5	19±5	27±5	0.008
LVEDV, mL	110±27	81±25	68±15	0.001
LVESV, mL	46±22	26±12	24±6	0.004
LVEF, %	63±6	66±4	68±7	ns

LVMI, g/m^2	79±14	134±16	141±38*	<0.0001
E/A	2.3±0.6	0.8±0.2	0.7±0.4	<0.0001
DT, msec	171±23	232±44	253±61	0.001
E/e’	6.9±1.0	12.7±4.4	18.5±9.1	<0.0001
RVSP, mmHg	28±1	33±4	38±8*	0.006
GLS, %	-16.8±1.2	-13.0±2.4	-10.4±2.0**	<0.0001
LV apical rotation, degree	6.3±1.6	10.8±2.5	13.9±3.0**	<0.0001
SVI, mL/m^2	55±9	47±9	51±12	ns

Values are mean ± standard deviation. *p<0.05 v.s. LVH, **p<0.001 v.s. LVH.

ACE angiotensin converting enzyme; *ARB* angiotensin II receptor blocker; *LVDD* left ventricular end-diastolic dimension; *LVSD* left ventricular end-systolic dimension; *LVEDV* left ventricular end-diastolic volume; *LVESV* left ventricular end-systolic volume; *LVEF* left ventricular ejection fraction; *LVMI* left ventricular mass index; *E/A* ratio of peak early mitral inflow velocity (E) and peak late mitral inflow velocity (A); *DT* deceleration time of the E wave; *E/e’* ratio of peak early mitral inflow velocity (E) and early diastolic velocity (e’); *RVSP* right ventricular systolic pressure; *GLS* global longitudinal strain; *SVI* stroke volume index