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Is there a relationship between aortic valve degeneration and left ventricle function?

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Degenerace aortální chlopně

SOUHRN

Cíl: Cílem naší studie bylo zkoumat případnou souvislost mezi degenerací aortální chlopně (aortic valve, AV) a funkcí levé komory srdeční (left ventricle, LV) a zda se taková souvislost následně projevuje na hodnotách biomarkerů.
Metody: Do studie bylo zařazeno 42 po sobě následujících pacientů s degenerativním postižením AV a 25 kontrolních jedinců. Aortální chlopně byly podle typu degenerace rozděleny na chlopně se stenotickými a sklerotickými změnami. U všech pacientů bylo před bicyklovou ergometrií v pozici pololeže a následně po ní provedeno vyšetření metodami dvoudimenzionální (2D) jícnové echokardiografie a 2D speckle tracking echokardiografie (STE). Sledovali jsme rovněž souvislost mezi sklerotickým postižením aorty a hodnoty biomarkerů, jako jsou galektin-3, troponin T stanovený metodou s vysokou citlivostí (high-sensitive [hs] troponin-T), C-reaktivní protein (CRP) a pro-BNP.
Výsledky: Celkový longitudinální strain (global longitudinal strain, GLS) LK byl při maximální zátěži a v době zotavování statisticky významně horší u pacientů s degenerovanou AV než u kontrol. Při bazální zátěži a maximální zátěži i v období zotavování byly u pacientů s degenerovanou AV – ve srovnání s kontrolami – statisticky významně více postižené i rezervoárová a konduitní funkce levé síně. Hodnoty CRP, hs-troponinu T a pro-BNP byly ve skupinách s degenerovanou AV statisticky významně vyšší než u kontrol. Hodnota LV GLS korelovala negativně s hodnotami CRP a E/e' při maximální zátěži i s průměrnými transvalvulárními tlakovými gradienty u AV v klidu a při maximální zátěži. Multivariační lineární regresní analýza prokázala, že hodnoty CRP a průměrné transvalvulární tlakové gradienty u AV při maximální zátěži jsou nezávislými prediktory LV GLS.
Závěry: Přes normální funkci LV nejenže dochází u pacientů s aortální sklerózou k významnému zhoršení LV GLS, tato změna je výraznější při maximální zátěži. Z výsledků naší studie lze usuzovat, že STE představuje spolehlivý nástroj pro časnou detekci poruchy funkce LV pacientů s aortální sklerózou.

Keywords:
Aortic valve degeneration

ABSTRACT

Purpose: The aim of the study was to explore the association between aortic valve (AV) degeneration and left ventricular (LV) functions and its relation with biomarkers.
Methods: Forty-two consecutive patients with degenerative AV disease and 25 controls were included. Degenerative AV were divided into stenotic and sclerotic valves. All patients underwent a two-dimensional (2D) transthoracic echocardiography and 2D speckle tracking echocardiography (STE) before and after semi-supine bicycle exercise test. We also evaluated the association between aortic sclerosis and biomarkers such as galactine-3, high-sensitive (hs) troponin-T, C-reactive protein (CRP) and pro-BNP.
Results: LV global longitudinal strain (GLS) was significantly impaired in degenerative AV patients than control at peak exercise and recovery period. Left atrial reservoir and conduit functions were also significantly impaired in degenerative AV patients than control at basal, peak exercise, and recovery period. CRP, hs-troponin T, and pro-BNP were significantly higher in degenerative valve groups than controls. LV-GLS was inversely correlated with CRP levels, E/e' at peak exercise, mean transvalvular aortic pressure gradients at rest and peak exercise. Multivariate linear regression analysis revealed that CRP levels and mean transvalvular aortic pressure gradients at peak exercise were independent predictors of LV-GLS at peak exercise.
Conclusions: Despite normal LV function, LV-GLS is not only significantly impaired in patients with aortic sclerosis but also the impairment is more pronounced during peak exercise. Results of the present study suggest that STE is a reliable tool in early detection on LV impairment in patients with aortic sclerosis.

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Introduction

Aortic valve (AV) degeneration is the most common cause of AV stenosis in the modern world. AV degeneration is characterized by an irregular increase in the thickness of the valve leaflets, commissures, or both in parasternal short axis view on transthoracic echocardiography (TTE) without great adjustment control. AV degeneration includes a wide range from valve sclerosis to severe valve stenosis. AV sclerosis is characterized by thickening, echogenicity, and calcification of the valve without a significant restriction of valve movements[1] and maximal transvalvular velocity of 1.5 to 2.5 m/s.[2,3] There is no specific finding for aortic sclerosis other than sound of systolic ejection murmur in aortic valve region. Aortic sclerosis is prevalent in 26% of the population under 65 years old and 48% of the population over 85 years old. Aortic degeneration is not only associated with age but also considered as a part of the atherosclerotic process.[4] It is still controversial whether the coronary artery risk factors such as age, hyperlipidemia, smoking, hypertension, and diabetes can also increase the risk of valve degeneration.[5] AV degeneration is essential for the cause of aortic stenosis (AS) and is also a risk factor for cardiovascular events (CV) as a part of the atherosclerotic process. Although early treatment of AV degeneration may suggest a reduction in AS and CV events, there is no comprehensive studies that demonstrate the relation between AV degeneration and CV events.

Transthoracic echocardiographic examination has an important role in the diagnosis of cardiac functions. However, it remains normal in the early stages of the aortic valve disease. Therefore, conventional echocardiographic techniques are inadequate when it comes to demonstrating subclinical forms of the disease. Two-dimensional (2D) speckle tracking echocardiography (STE) is an advanced method that provides an objective evaluation of left ventricular (LV) function.[6] Stress echocardiography might be superior to resting echocardiography in showing LV functions in patients with atherosclerotic CV disease. The aim of the study is to investigate the relation between AV degeneration and LV function by using 2D STE at rest and after stress test.

Methods

Study population

The study population consisted of 42 consecutive patients who were diagnosed with degenerative AV. The diagnosis of degenerative AV was performed based on an irregular thickening of the AV leaflets, commissures, or both at parasternal short axis image (characterized by bright echogenicity). Patients with degenerative AV were divided into two groups according to velocity of AV. While patients with AV velocity >2.5 m/s were accepted as stenotic AV group, patients with AV velocity ≤2.5 m/s and without valvular stenosis were accepted as sclerotic AV group. Twenty-five subjects without any valvular and/or flow velocity abnormality were enrolled in the study as control group. Patients who were diagnosed with a degenerative AV at the TTE, and voluntarily agreed to participate in the study were included.

Patients with rheumatic valve disease, bicuspid aortic valves, severe aortic stenosis: mean pressure gradient on aortic valve ≥40 mmHg, aortic valve area ≤1 cm^2, coronary artery disease (CAD), heart failure, previous history of syncope or angina, patients with LV wall motion abnormalities, abnormal heart rhythms (atrial fibrillation, atrial flutter, left branch block), moderate or severe valvular heart disease, patients who cannot do bicycle stress tests for psychological or orthopedic reasons, suboptimal image quality at the TTE, and patients who do not want to be involved in the study were excluded. Patients with symptoms at effort test (angina, dyspnea, syncope) and/or ECG and/or echocardiographic abnormalities of ischemia were excluded from the study. The investigation complied with the principles outlined in the Declaration of Helsinki. The study was approved by the local ethics committee, and all participants gave written informed consent.

Standard echocardiographic examination

All study population underwent a complete 2D transthoracic echocardiography with a commercially available echocardiography device (Vivid 7, GE Vingmed Ultrasound AS, Horten, Norway). Echocardiographic evaluation was performed by a single experienced cardiologist. Patients were positioned in the left lateral decubitus position. Data acquisition was performed with a 3.5-MHz transducer at a depth of 16 cm in the parasternal and apical views (standard parasternal short-axis from mid-ventricular level, apical long-axis, two-chamber and four-chamber images). The frame rate for gray-scale images is set to 44–82 frames/s. Echocardiographic images were obtained during breath hold, stored in cine loop format from three consecutive beats, and transferred to a workstation for further offline analysis. Conventional echocardiographic parameters were measured according to the guidelines of the American Society of Echocardiography.[7] E´ velocity was measured from the apical 4-chamber view with a 2- to 5-mm sample volume placed at the septal and lateral corner of the mitral annulus and mean E' value was calculated. Mitral annulus velocity was measured by Doppler tissue imaging using the pulsed wave Doppler mode.

Speckle tracking echocardiography

The atrial and ventricular functions were also assessed by STE with EchoPAC 6.1; GE Vingmed Ultrasound AS, Horton Norway program. All of the images were recorded with a rate of 55–90 frames/s to allow for reliable operation of the software. The speckles were tracked on the standard grayscale 2D images. Myocardial strain was calculated by measuring the change of the position of the speckles within a full myocardial segment during the cardiac cycle. The assessment of LV global longitudinal strain (GLS) was performed by applying 2D-STE to the apical two-, three-, and four-chamber views of the LV. LV was divided into six segments in each apical view. The value of LV-GLS was derived from the average of the six-segmental peak systolic longitudinal strain values from each apical view.

Left atrial (LA) endocardial border was manually traced in apical four-chamber view by composing the

six segments. After segmental tracking quality analysis and eventual manual adjustment, the strain curves were generated by the software for each atrial segment. The longitudinal LA wall deformation was assessed by measuring the peak values for strain during the contractile, reservoir, and conduit phases. The software used the QRS complex (R-R gating) as the initiation of the strain calculation. There are two peaks that correspond to the reservoir function (first peak between R wave and T wave) and atrial contractile function (starting on the P wave). The difference between reservoir strain and atrial contractile strain values reflects conduit function.

Exercise stress test

Exercise stress test was performed with GE E-Bike semi-supine ergometry using the standard stress protocol based on the guidelines in the American Society of Echocardiography guideline.[8] Test protocol was as: increasing workload by 25 watts in every 2 min and the maximal cycling test was performed until the symptom occurred.[9] 2D, TDI, and Doppler echocardiographic images were reported (apical four chambers, three chambers, two chambers, parasternal long- and short-axis views) at rest, peak exercise (immediately after the end of the effort or within the first 60–90 s) and 3 minutes of the recovery period. Patients were monitored during the test, and 12-lead ECG was recorded with Quinton 30146-001. ECG changes during the test were noted. Patient complaints (such as chest pain, shortness of breath, syncope) were registered during the stress. New onset stress-induced wall motion abnormalities were recorded. The blood pressure response to the effort test was noted. The exercise test was terminated early in patients with moderate to severe angina (3rd and 4th grade), syncope, pre-syncope, dizziness, or ST segment change in ECG (elevation or baseline ECG ≥2 mm horizontal or downslope depression), systolic blood pressure >250 mmHg, diastolic blood pressure >115 mmHg or with >10 mmHg decrease in systolic blood pressure.

Laboratory parameters

Blood samples (10 mL) were taken in one 10–12 hours fasting state and were placed in EDTA tubes. Quantitative assay of Galectin-3 was performed using the ELISA sandwich method. The serum CRP measurement was performed on an Imax 800 (Beckman Coulter, USA) instrument using a nephelometric method. Serum pro-BNP and sensitive troponin T levels were studied by an electrochemiluminescence method in Elecsys 2010 (Roche diagnostic, Germany).

Reproducibility

The analyses were repeated twice 1 day later by the same observer in order to assess intraobserver variability, which was calculated as the average difference between the 10 measurements taken. A second independent observer repeated the analyses for the assessment of interobserver variability, which was calculated as the absolute difference divided by the average of the two observations for 2D-STE parameters. The intraobserver and interobserver variability were 6% and 8%, respectively, in our study.

Statistical analysis

All statistical tests were performed with a commercially available software program (Statistical Package for the Social Sciences (SPSS) 11.0 for Windows, USA). Categorical variables were expressed as a percentage and compared with chi-square tests. Kolmogorov–Smirnow test was used to detect normality of numerical variables. Numerical variables were expressed as a mean±standard deviation. ANOVA (for parameters with parametric distribution) and Kruskal–Wallis (for parameters with nonparametric distribution) tests were used to compare numerical variables between the three groups. Pearson and Spearman correlation tests were used to perform correlation analysis. Linear regression analysis was performed to determinate the independent predictors of LV-GLS at peak exercise. A value of p <0.05 was considered statistically significant.

Results

Baseline demographic characteristics, clinical and laboratory parameters of groups were compared in Table 1. There was no difference in baseline clinical parameters and demographic characteristics between groups. While 2 patients had dyspnea and 4 patients had fatigue in patients with stenotic group, there were no symptoms in patients in sclerotic group and controls during exercise stress test. There were no ischemic ECG changes and new-onset LV wall motion abnormalities during exercise stress test. Among biochemical parameters, CRP, pro-BNP, and high sensitive troponin T levels were significantly higher in sclerotic and stenotic groups than control group. CRP level was higher in the sclerotic group than stenotic valve group (8.4±8 vs 5.6±4.1, p = 0.009) and high sensitive troponin T levels were significantly higher in the stenotic group than sclerotic and control groups (14.2±21 vs 7.7±7.2 and 3.8±1.3; p = 0.002). The galectin-3 level was higher in the stenotic group than in the control group and sclerotic group, but the difference was not significant between groups.

Transthoracic echocardiographic parameters of patients were compared before and after bicycle stress test in Table 2. LV ejection fraction (EF) was similar between groups. LA volume index was significantly higher in patients with stenotic group. While aortic root diameter was similar between groups, ascendant aortic diameter was significantly higher in stenotic group. Basal and peak exercise transvalvular aortic velocities were significantly higher in stenotic group. Basal and peak exercise E/e' ratio was also significantly higher in patients with stenotic group. 2D-STE parameters were compared in Table 3. While basal LV-GLS was similar between groups, peak exercise and recovery phase of LV-GLS were significantly impaired in patients with sclerotic and stenotic groups than controls. LA reservoir and conduit parameters were also significantly impaired in stenotic and sclerotic groups than controls.

Correlation analysis was performed between LV-GLS at peak exercise and some echocardiographic and laboratory parameters. CRP, E/e' ratio at peak exercise, mean transvalvular aortic pressure gradient at rest and at

Table 1 – Comparison of baseline demographic characteristics, clinical and laboratory parameters of groups

	Control (n = 25)	Sclerotic (n = 29)	Stenotic (n = 13)	*p*-value
Age (years)	51.8±9.2	54±6.7	57±6	0.2
Gender (male)	12 (48%)	10 (34%)	9 (69%)	0.11
Hypertension (n, %)	16 (64%)	21 (72%)	9 (69%)	0.8
Diabetes mellitus (n, %)	5 (20%)	6 (21%)	2 (15%)	0.92
Smoking (n, %)	6 (24%)	7 (24%)	2 (15%)	0.8
Glomerular filtration rate (ml/min)	126±63	101±27	112±36	0.33
Body mass index (kg/m²)	29±4.8	30±3.5	29±4.5	0.75
Low density lipoprotein (mg/dl)	119±23	122±33	109±27	0.33
High density lipoprotein (mg/dl)	42±9.8	45±12	44±10	0.38
Triglycerides (mg/dl)	143±51	159±54	137±62	0.24
C-reactive protein (mg/L)	3.6±2.5	8.4±8	5.6±4.1	**0.009**
pro-BNP (pg/mL)	62±43	148±121	178±158	**<0.001**
High sensitive troponin T (ng/L)	3.8±1.3	7.7±7.2	14.2±21	**0.002**
Galectine-3 (ng/ml)	0.64±0.28	0.65±0.37	0.78±0.4	0.51

Table 2 – Comparison of transthoracic echocardiographic parameters between groups

		Control (n = 25)	Sclerotic (n = 29)	Stenotic (n = 13)	*p*-value
Left atrial volume index (ml/m²)		31.5±10	36±9.4	46±16	**0.002**
Ejection fraction (%)		71.8±8	71.5±7.5	67±6.4	0.11
Aortic root diameter (mm)		28±3	27±4	29±5	0.48
Ascending aortic diameter (mm)		32±2.7	32±4.6	35±4.8	**0.04**
Interventricular septum thickness (mm)		10.3±1.0	10.4±1.1	11.8±2.0	**0.043**
Posterior wall thickness (mm)		9.7±0.9	9.6±0.8	10.6±1.3	**0.023**
Aortic velocity (m/s)	Basal	1.3±0.2	1.6±0.2	2.6±0.8	**<0.001**
	Peak	1.6±0.25	2±0.44	3.2±0.8	**<0.001**
	Recovery	1.24±0.23	1.5±0.23	2.6±0.8	<0.001
Mean transvalvular aortic pressure gradient (mmHg)	Basal	3.4±1.3	5±1.6	15±9.8	**<0.001**
	Peak	5.3±1.7	8.6±3.7	21.5±13.9	**<0.001**
	Recovery	3.5±1.2	4.9±1.8	15.8±10.7	**<0.001**
Mean mitral E velocity (m/s)	Basal	0.78±0.2	0.78±0.2	0.73±0.18	0.73
	Peak	1.2±0.23	1.4±1.9	1.0±0.21	**0.02**
Mean mitral A velocity (m/s)	Basal	0.79±0.2	0.77±0.2	0.81±0.2	0.75
	Peak	1.1±0.2	1.3±1.7	1.0±0.24	0.49
Mean e' velocity (cm/sn)	Basal	10.4±3.1	10.3±3.8	6.7±2	**0.001**
	Peak	14.5±3.1	12.2±3.6	9.1±2.5	**<0.001**
Mean a' velocity (cm/s)	Basal	9.9±3.6	8.8±3.3	9.2±1.7	0.60
	Peak	10±3.6	9.3±3	9.6±2.5	0.87
E/e' ratio	Basal	7.9±2.4	8.6±3	11±3.8	**0.037**
	Peak	8.1±1.3	8.7±2.9	17±20	**<0.001**

peak exercise were significantly correlated with LV-GLS at peak exercise (Table 4). Linear regression analysis was performed to determinate the independent predictors of LV-GLS at peak exercise. CRP and mean transvalvular aortic pressure gradient at peak exercise were independent predictors of LV-GLS (Table 5).

Table 3 – Comparison of speckle tracking echocardiographic parameters between groups

		Control (n = 25)	Sclerotic (n = 29)	Stenotic (n = 13)	*p*-value
Left ventricular global longitudinal strain (%)	Basal	–19.8±2.9	–18±3.9	–18±2.8	0.11
	Peak	–22.9±2.3	–18.7±3.2	–19.3±3.2	<0.001
	Recovery	–21.3±2.7	–18.4±3.1	–19.4±2.8	0.005
Left atrial reservoir function	Basal	28.8±10.4	21.3±7.1	21.3±8.3	**0.007**
	Peak	38±17	24.6±11	25.8±7.6	**0.003**
	Recovery	31.8±17	21±7.7	22.5±9.6	**0.03**
Left atrial conduit function	Basal	14.4±4.7	11.2±3.9	10.5±4.1	**0.02**
	Peak	19.2±6.6	13.8±5.3	13.7±5	**0.005**
	Recovery	15.2±7	10.9±3.1	10.9±4.7	0.05

Table 4 – Correlation analysis of LV-GLS at peak exercise with echocardiographic and laboratory parameters

	r	*p*
C-reactive protein (mg/L)	–0.38	**0.002**
High sensitive troponin T (ng/L)	–0.24	0.06
E/e' at peak exercise	–0.3	**0.03**
Mean transvalvular aortic pressure gradient at rest	–0.32	**0.009**
Mean transvalvular aortic pressure gradient at peak exercise	–0.3	**0.01**

LV-GLS – left ventricular global longitudinal strain.

Table 5 – Linear regression analysis for determination of the independent predictors of LV GLS at peak exercise

	Beta	*p*
C-reactive protein	–437	**<0.001**
E/e' at peak exercise	–0.15	0.21
Mean transvalvular aortic pressure gradient at peak exercise	–0.286	**0.023**
Age	–0.016	0.89

LV-GLS – left ventricular global longitudinal strain.

Discussion

Atherosclerosis is an active process that affects the whole body. As a sign of atherosclerosis, degeneration can affect not only the aortic valves, but affects also the left ventricle. Increased afterload causes LA dilatation and dysfunction, and it is a poor predictor of prognosis in patients with AS.[10] In our study, although LAVI was significantly higher in patients with aortic stenosis, it was found to be high in all degenerative valves compared to the control group. LV hypertrophy causes a decrease in the LV compliance and diastolic dysfunction in severe AS.[11] In severe AS, the increase in LV pressure causes wall tension, and LV hypertrophy develops as a compensator to reduce this wall tension.[11–13] In our study, E/e' was significantly higher in stenotic valves than the sclerotic and control groups. Factors such as age, hypertension, and diabetes mellitus may also affect the outcome of patients with degenerative AV. Due to the fact that there is a close relationship between AV degeneration and systemic atherosclerosis, the likelihood of AV degeneration without those risk factors is rare.

Left ventricular functions may impair before AS develops in patients with degenerative AV disease. Left ventricle contractile reserve can be measured with 2D-STE. 2D-STE reveals early LV dysfunction better than LVEF.[14] The autopsy studies revealed that although LVEF was normal, LV strain values decreased in AS patients with AS with myocardial fibrosis.[15] Evaluation of LV functions by 2D-STE can be useful in the selection of an appropriate time for AV replacement and follow-up of patients with asymptomatic severe AS.[16] Systemic endothelial dysfunction develops in aortic valve sclerosis,[17] and studies show impaired coronary flow reserve to be a result of endothelial dysfunction.[18] Considering that degenerative changes affect the myocardium beyond the valve, we performed 2D speckle tracking and LV strain measurements in all patients with degenerative AV patients. 2D-STE was performed only in patients with AS in the previous studies. In our study, we also included patients with sclerotic valves.

Stress echocardiography is a screening method that allows dynamic assessment of heart functions. In our study, all degenerative AV patients underwent bicyclic stress test. We wanted to demonstrate the LV dysfunction which may be masked at resting echocardiography. In our study, LV-GLS was similar between groups at resting period. However, at the peak exercise and recovery period, the LV-GLS was significantly lower in degenerative valves than the control group. In a previous study, Lech et al. demonstrated that patients with asymptomatic severe AS had lower change in GLS during exercise when compared to controls without statistical significance[19] Our study is the first study to evaluate LV function by stress test in patients with sclerotic AV. We showed that LV dysfunction in the early stage of the degenerative valve is not detectable at rest. However, it was apparent at exercise. In our study, we demonstrated that LV-GLS at peak exercise was significantly correlated with mean transvalvular aortic pressure gradient at rest and peak exercise. Our results suggest that measurement of LV-GLS is a load dependent parameter to evaluation of LV function. Left atrial reservoir and conduit functions were also significantly impaired in degenerative AV patients than control at basal, peak exercise, and recovery period.

Inflammation is more active in the early stages of degenerative AV disease. In a study by Skowasch et al., it has

been found that CRP is also secreted from degenerative AV tissue and CRP levels are further increased in severe valve stenosis.[20] In other studies, CRP levels were associated with the severity of AS and were found to decrease within six months after valve replacement.[21] In studies conducted by Novaro et al., they showed that CRP level was not involved in the development and progression of AV degeneration and the critical factors of AV degeneration were age, male sex, hypertension, coronary artery disease and renal failure.[22] Galante et al. first determined that the increase in CRP levels in degenerative AV patients was not related to AV velocity or AV area. In our study, CRP level was significantly higher in patients with sclerotic AV group than controls and stenotic group. Insufficient number of patients in stenotic group may be a reason of lower CRP level in stenotic group than sclerotic group. The high level of CRP in degenerative valves compared with the control group could suggest that degeneration is the result of active inflammation such as atherosclerosis, and control of CRP levels may be used in the future for degenerative valve treatment. Previous studies demonstrated that statin treatment reduced CRP levels and decreased degenerative valve progression as a pleiotropic effect. However, it should not be forgotten that patients were also under treatment with several drugs such as ACE inhibitors, acetylsalicylic acid, and beta-blockers in these studies.[23–28]

In our study, the level of pro-BNP was high in the degenerative AV group compared with the control group. As we know, in patients with severe AS, the level of pro-BNP increased as a result of LV hypertrophy and diastolic dysfunction.[29,30] pro-BNP levels increased more significantly in severe AS than sclerotic valves as in other studies.[31,32] In our research, pro-BNP levels were high in the sclerotic group. In these patients, the LV diastolic function parameter (E/e') is within its reasonable limits. High levels of pro-BNP in degenerative valves without stenosis also suggest that degeneration is a systemic disease that affects LV function at the early stage of AV degeneration without significant stenosis. High sensitive troponin T helps to detect low levels of troponin elevation as a consequence of myocardial injury due to high sensitivity. High sensitive troponin T increases not only in acute coronary syndrome but also in conditions such as sepsis, heart failure, aortic stenosis. In our study, the level of high sensitive troponin T increased significantly in degenerative valves compared to the control group. Troponin level was in the normal ranges in sclerotic valves group. In previous studies, increased troponin level was associated with LV hypertrophy and impairment of LV systolic function in patients with moderate and severe AS.[33,34] Troponin T was not studied in sclerotic valves in previous studies. In our study, it was higher in the stenotic valve than in the control group, even in the normal ranges of sclerotic valves. We think that the cause of this elevation was the development of LV necrosis at the subclinical level as a result of degeneration.

Galectin-3 is a new prognostic marker of fibrosis, fibroblast proliferation, and scar tissue development.[35,36] In a previous study, de Boer et al. demonstrated that galectin-3 levels also increase in AS.[37] There has been no study about the association between degenerative AV and galectine-3 levels so far. We evaluated the level of galectin-3 in sclerotic AVs as an early sign of fibrosis. Although there was no significant difference between the control group and degenerative valve group, galectin-3 level gradually increased in sclerotic valve and stenotic valves groups compared to the control group. The lack of significant differences between the groups in our study may be due to the small number of patients.

Study limitations

The most important limitation of our study is the small number of patients. Large sample studies are crucial for verification of data. Reassessment of stress echocardiography and prospective follow-up of patients in the study is essential for evaluation of prognosis and progression of LV dysfunction. The indexes of LV systolic performance (as LVEF and LV-GLS) are load dependent, particularly on afterload. One possible component of the worse LV--GLS at stress in sclerotic and stenotic groups could be attributable to increased afterload. Therefore, it would be better if we include the blood pressure response in the evaluation, and also the response to stress of aortic transvalvular pressure gradient. Many factors affect LV function, apart from AV degeneration. Therefore, a more homogeneous patient population is needed.

Conclusion

Our study shows that LV and LA function may be affected at the early stage of degenerative AV disease. Stress echocardiography and 2D-STE can successfully demonstrate the impairment of LV function in early stage of the disease. Clinicians should give more attention to improve the evaluation and treatment of these patients in order to try to decrease their disease progression.

Conflict of interest

The authors declare no potential conflict of interest.

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