INCREMENTAL ROLE OF LEFT ATRIAL FUNCTIONAL ASSESSMENT IN SEVERE AORTIC STENOSIS

Úloha hodnotenia funkcie ľavej predsiene pri diagnostike závažnej aortálnej stenózy

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Abstract
Objectives: Severe symptomatic aortic stenosis is associated with a worse prognosis. The aim of our study was to determine the relationship between functional parameters of the left atrium (LA) and standard clinical and echocardiographic parameters in patients with severe symptomatic aortic stenosis, and to determine their role in the diagnostic algorithm of patients with severe aortic stenosis at the same time.
Methodology: 70 patients with confirmed severe symptomatic aortic stenosis were retrospectively included in the study. The values of LA deformations (LASr, LASct, LAScd) were determined by the "speckle tracking" method of echocardiography. Based on the ratio of the LA volume indexed to the body surface (LAVI) and measured using the Doppler tissue imaging (echocardiography) (DTI) in the area of the septal edge of the mitral annulus, the left atrium coupling index (LACI) was determined. We monitored the correlation of functional parameters of the left atrium with standard clinical and echocardiographic parameters of aortic stenosis.
Results: LACI values were statistically significantly positively correlated with the progression of symptoms, expressed by NYHA functional class ($p = 0.0004$) and negatively correlated with LV ejection fraction ($r = -0.66$; $p = 0.0004$), mean and peak flow gradient through the aortic valve ($r = -0.62$; $p = 0.0009$ and $r = -0.58$; $p = 0.002$, respectively). Moreover, the LASct value was correlated with the mean flow gradient across the aortic valve ($r = 0.55$; $p = 0.048$). A statistically significant relationship with other selected clinical and echocardiographic parameters was not proven.
Conclusion: Among the selected functional parameters of the left atrium, only LACI is significantly correlated with the progression of symptoms and the decrease of the systolic function of the left ventricle in the group of patients with severe symptomatic aortic stenosis. This parameter has potential in the prediction of clinical changes and could be included in the diagnostic algorithm of patients with severe aortic stenosis in the future (tab. 3, fig. 3, lit. 18). Text in PDF www.lekarsky.herba.sk.
KEY WORDS: aortic stenosis, symptoms, echocardiography, left atrial function, deformation.
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Abstrakt
Ciele: Závažná symptomatická aortálna stenóza sa spája s horšou prognózou. Cieľom našej práce bolo určiť vzťah medzi funkčnými parametrami ľavej predsiene a štandardnými klinickými a echokardiografickými parametrami u pacientov so závažnou symptomatickou aortálnou stenózou. Zároveň stanoviť ich úlohu v diagnostickom algoritme pacientov so závažnou aortálnou stenózou.
Metódy: Do štúdie bolo retrospektívne zaradených 70 pacientov s potvrdenou závažnou symptomatickou aortálnou stenózou. Hodnoty deformácií ľavej predsiene (LASr, LASct, LAScd) boli stanovené metódou “speckle tracking” echokardiografie. Na základe pomeru hodnoty objemu ľavej predsiene indexovanej na povrch tela (LAVI) a meranej pomocou tkanivovej dopplerovskej echokardiografie (DTI) v oblasti septálneho okraja mitrálneho anulu bol určený “coupling” index ľavej predsiene (LACI). Sledovali sme koreláciu funkčných parametrov ľavej predsiene so štandardnými klinickými a echokardiografickými parametrami aortálnej stenózy.
Výsledky: Hodnoty LACI štatisticky významne pozitívne korelovali s progresiou symptómov, vyjadrených funkčnou triedou NYHA ($p = 0.0004$) a negatívne korelovali s ejekčnou frakciou ĽK ($r = -0.66$; $p = 0.0004$), stredným a vrcholovým gradientom prietoku cez aortálnu chlopňu ($r = -0.62$; $p = 0.0009$ and $r = -0.58$; $p = 0.002$, v tomto poradí). Navyše hodnota LASct korelovala so stredným gradientom prietoku cez aortálnu chlopňu ($r = 0.55$; $p = 0.048$). Nebol dokázaný štatisticky významný vzťah k ostatným vybraným klinickým a echokardiografickým parametrom.
Záver: Spomedzi zvolených funkčných parametrov ľavej predsiene iba LACI významne koreluje s progresiou symptómov a poklesom systolickej funkcie ľavej komory v skupine pacientov so závažnou symptomatickou aortálnou stenózou. Tento parameter má potenciál v predikcii klinických zmien a v budúcnosti by mohol byť zahrnutý do diagnostického algoritmu pacientov so závažnou aortálnou stenózou (*tab. 3, obr. 3, lit. 18). Text v PDF www.lekarsky.herba.sk.*
KĽÚČOVÉ SLOVÁ: aortálna stenóza, symptómy, echokardiografia, funkcia ľavej predsiene, deformácia.

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Introduction

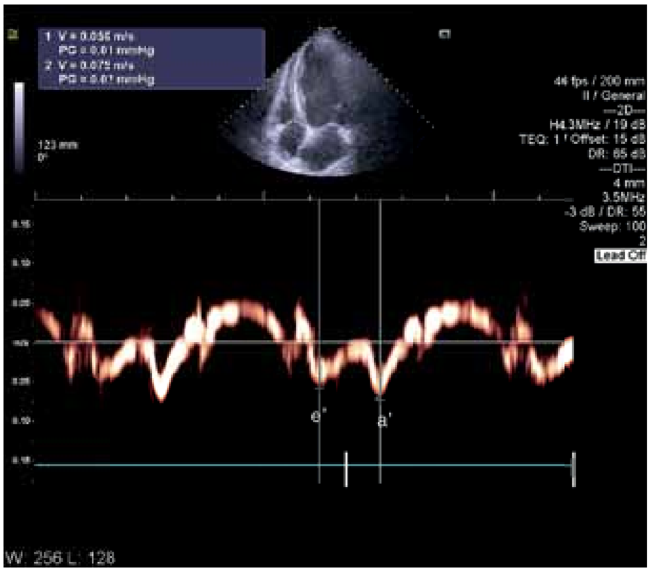
Aortic stenosis (AS) is the most common valvular disease in Europe and is associated with increased morbidity and mortality. Due to aging of the population, its prevalence is increasing rapidly (1). The progression of AS severity leads to an increase in afterload, hypertrophy and fibrosis of the left ventricle (LV) and subsequently to its systolic and/or diastolic dysfunction (2). Proper timing of aortic valve replacement, either surgically or transcatheter, is very important. In addition to echocardiographic and laboratory parameters, patient symptomatology is also decisive. Structural changes however, may occur before symptoms appear or LV systolic dysfunction, so it is crucial to find a sensitive marker to detect changes at an early stage of the disease. Functional changes of the LA in severe AS are significantly associated with increased incidence of heart failure, mortality and the need for aortic valve replacement (3). To the best of our knowledge, no article has been published that would establish the role of all atrial functional parameters including LACI in the diagnostic algorithm of patients with severe AS. Therefore, we focused on the correlation of LA functional parameters (along with LACI) with standard clinical and echocardiographic parameters and their diagnostic potential in a group of patients with severe AS.

Materials and methodology

Patients included in the study were hospitalized at the 1st Department of Cardiology at the East Slovak Institute of Cardiovascular Diseases in the period from January 2017 to December 2022. Each individual underwent a 2D TTE and TEE examination, performed by Siemens ultrasound system ACUSON SC2000. Inclusion criteria were: 1. age above 18 years; 2. confirmed severe symptomatic aortic stenosis; 3. sinus rhythm; 4. recorded echocardiographic values of LAVI and DTI a´. Exclusion criteria included: atrial fibrillation, uncontrolled arterial hypertension, at least moderate mitral stenosis or regurgitation, at least moderate aortic regurgitation, primary tricuspid regurgitation, infiltrative disease (such as amyloidosis, hemochromatosis, sarcoidosis) hypertrophic cardiomyopathy, previous aortic valve replacement and poor acoustic window. We compiled a list of the main clinical and echocardiographic parameters evaluating the degree of severity of AS. Symptoms were evaluated based on the New York Heart Association (NYHA) Functional Classification. The incidence of angina pectoris and syncope was reported. Echocardiographic variables were analyzed retrospectively offline from archived recordings. Measurements were done by an experienced echocardiographer. The ejection fraction (EF) of the left ventricle (LV), volume of the LV at the end of diastole (EDV) and systole (ESV) were obtained by the modified Simpson´s method. LV mass and its indexed value (indexed to the body surface area in m2) was calculated using the Devereux formula et al. The diastolic function of the LV was determined by recording mitral inflow using pulsed-wave Doppler. The peak velocity of the E wave (early filling wave), the deceleration time of the E wave, and the peak velocity of the A wave (the late filling wave given by atrial contraction) were measured.

Myocardial velocity in the region of the septal edge of the mitral annulus in ventricular systole (Sm), in early ventricular diastole (e´) and in the late phase of diastole (at the time of atrial contraction, a´) was determined by DTI (Fig. 1).

Figure 1. Evaluation of myocardial velocity in the region of the septal edge of the mitral annulus in early ventricular diastole (e´) **and in the late phase of diastole** (at the time of atrial contraction: a´) **determined by tissue doppler imaging.**



The E/e´ ratio was calculated as an indicator of LV filling pressure. Left atrial volume was obtained using the Simpson method from the apical four-chamber and two-chamber projections and subsequently indexed to body surface area (LAVI). Based on the ratio of LAVI and DTI a´, measured in the region of the septal edge of the mitral annulus, LACI was determined: LACI = LAVI/DTI a´. LA strain was determined using speckle tracking echocardiography from focused four and two chamber views, with the region of interest delineated by the LA endocardial border. LA strain was reported according to the reservoir, conduit and contractile phases of the LA cycle (Fig. 2a, 2b). Aortic orifice area (AVA) was calculated based on the continuity equation and indexed to body surface area. We determined the maximum flow velocity through the aortic valve (Vmax), peak gradient (PG), mean gradient (MG), stroke volume (SV) and its indexed value per body surface (SVi). Values were averaged from three heart cycles.

The research was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD). The normality of the distribution of individual parameters was determined by the Shapiro – Wilk test, their mutual correlations by the Pearson test. Selected LA parameters correlation with categorical variables that capture more than two categories, were analyzed using ANOVA. All analyzes were performed using two-tailed tests at the 5 % significance level ($p < 0.05$ values were considered statistically significant). All statistical calculations were performed in RStudio, version 2021.09.1.

Figure 2a. Evaluation of left atrial reservoir strain by speckle tracking echocardiography.

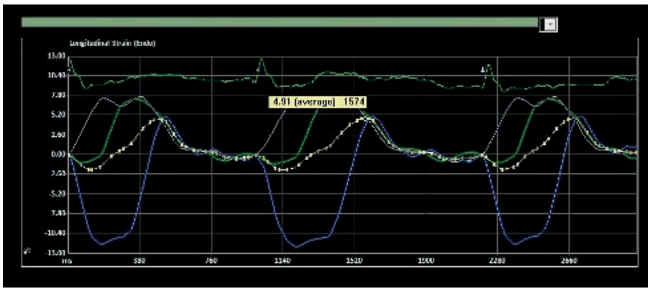
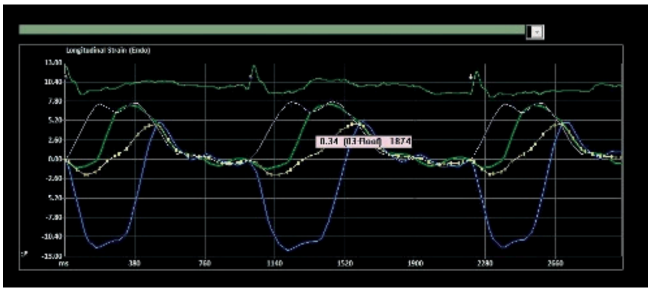


Figure 2b. Evaluation of left atrial contractile strain by speckle tracking echocardiography.



Results

A total of 70 patients with severe symptomatic AS were included in the study. The average age of the entire cohort was 76.87 ± 8.42 years. 50 % of patients were male. Among the selected LA functional parameters, only LACI values were statistically significantly positively correlated with symptom progression by NYHA functional class ($p = 0.0004$) and negatively correlated with a LV ejection fraction ($r = −0.66$; $p = 0.0004$), mean and peak aortic valve gradient ($r = −0.62$; $p = 0.0009$ and $r = −0.58$; $p = 0.002$, respectively). Also for LASr and LAScd there is statistically significant difference between mean values and NYHA classes, however, we cannot stated any correlation. We can only declare that their mean values in the NYHA class II is significantly higher than in NYHA class III and IV. Figure 3 and Table 1 show the mean LACI, LASr, LASct and LAScd values for each NYHA class.

Table 1. Mean values of LACI, LASr, LASct and LAScd in NYHA classes.

	NYHA I	**NYHA II**	**NYHA III**	**NYHA IV**	**p**
LACI	-	5	8,92	13	0,0004
LASr	-	26,56	9,94	12,05	0,034
LASct	-	11,51	4,06	5,59	0,17
LAScd	-	15,04	5,87	6,49	0,049

LACI – left atrial coupling index; LASr – left atrial reservoir strain; LASct – left arial contractile strain; LAScd – left atrial conduit strain; NYHA (I, II, III, IV) – New York Heart Association (class I, II, III, IV)

Moreover, LASct values correlated with mean aortic valve gradient ($r = 0.55$; $p = 0.048$). There was no statistically significant relationship between other LA functional parameters and selected clinical or echocardiographic parameters. Baseline clinical and echocardiographic variables and their association with selected LA functional parameters are presented in Tables 2 and 3.

Table 2. Clinical variables and their association with LACI, LASr, LASct, LAScd.

	Mean ± SD	**LASr**		**LASct**		**LAScd**	
		r	p	r	p	r	p
Age	76.87 ± 8.42	0.1483558	0.64540964	0.21415099	0.50391199	0.05867727	0.85625977
Male (%)	50.00	−0.3095332	0.30341174	−0.5067247	0.07719302	−0.0619781	0.84058891
CAD (%)	63.64	0.0420331	0.90233951	−0.0432949	0.89942058	0.12371281	0.71705490
IM (%)	22.73	−0.1951165	0.56533633	−0.1446658	0.67128328	−0.2167758	0.52201112
CABG (%)	27.27	0.5260147	0.09650488	0.36240419	0.27338695	0.61233953	0.04521923
PCI (%)	22.73	−0.1604641	0.63741412	−0.4056276	0.21581766	0.12101897	0.72300414
ADCHSZ (%)	27.27	−0.1053951	0.75777172	−0.1719548	0.61316070	−0.0180688	0.95794806
DM PAD (%)	9.09	−0.18406389	0.58797400	−0.0300207	0.93017896	−0.3157245	0.34424719
DM IT (%)	4.55	−0.32084012	0.33605195	−0.3452947	0.29832777	−0.2441169	0.46943101
DLP (%)	90.91	0.18406389	0.58797400	0.0300207	0.93017896	0.31572453	0.34424719
CMP (%)	13.64	−0.32084012	0.33605195	−0.3452947	0.29832777	−0.2441169	0.46943101
PAOO (%)	18.18	−0.45819975	0.15638850	−0.3981681	0.22519227	−0.4478494	0.16717357
Syncope (%)	22.73	0.08188990	0.81082729	0.2241923	0.50750780	−0.0800703	0.81496717

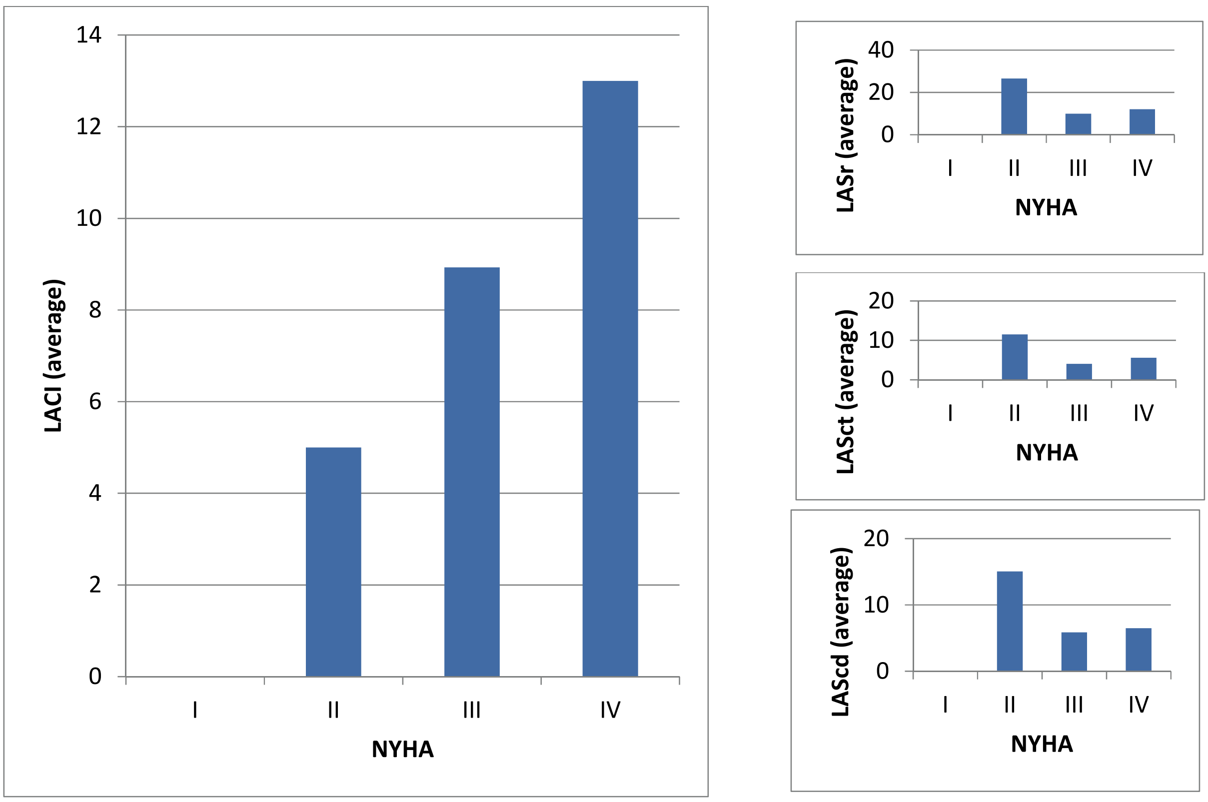
CAD – coronary artery disease; IM – myocardial infarction; CABG – coronary artery bypass graft; PCI – percutaneous coronary intervention; ADCHSZ – acute heart failure; DM PAD – diabetes mellitus treated with oral antidiabetic drugs; DM IT – diabetes mellitus treated with insulin therapy; DLP – dyslipidemia; CMP – stroke; PAOO – peripheral arterial occlusive disease; LACI – left atrial coupling index; LASr – left atrial reservoir strain; LASct – left arial contractile strain; LAScd – left atrial conduit strain

Table 3. Echocardiographic parameters and their association with LACI, LASr, LASct, LAScd.

	Mean ± SD	LACI		LASr		LASct	
		r	p-value	r	p-value	r	*p-value*
EF LV	50.37 ± 10.46	-0.6636643	0.0004067914	0.37793813	0.20293167	0.270382	0.37161299
MG	48.07 ± 19.88	-0.6297357	0.0009754446	0.53282850	0.06081621	0.556999	0.04799800
PG	79.72 ± 31.23	-0.5803826	0.0029463348	0.44482534	0.12774393	0.487291	0.09122003
AVA	0.64 ± 0.165	0.2250009	0.2904836916	-0.04553587	0.88256888	-0.261361	0.38839273
AVAi	0.34 ± 0.087	0.2769855	0.1900874847	-0.11631027	0.70513656	-0.165106	0.58985917
SV 2D	67.00 ± 21.62	-0.3084344	0.1625446269	0.44812304	0.14401275	0.368941	0.23792901
SVI 2D	35.64 ± 9.83	-0.3028349	0.1707081140	0.42953679	0.16345448	0.446797	0.14534833

LACI – left atrial coupling index; LASr – left atrial reservoir strain; LASct – left arial contractile strain; LAScd – left atrial conduit strain; EF LV – left ventricular ejection fraction; MG – mean transaortic gradient; PG – peak transaortic gradient; AVA – aortic valve area; AVAi – aortic valve area indexed to body surface area; SV 2D – stroke volume measured in two dimensional imaging; SVi 2D – value of stroke volume indexed to LACI – left atrial coupling index; LASr – left atrial reservoir strain; LASct – left arial contractile strain; LAScd – left atrial conduit strain; EF LV – left ventricular ejection fraction; MG – mean transaortic gradient; PG – peak transaortic gradient; AVA – aortic valve area; AVAi – aortic valve area indexed to body surface area; SV 2D – stroke volume measured in two dimensional imaging; SVi 2D – value of stroke volume indexed to body surface area

Figure 3. Mean values of LACI, LASr, LASct and LAScd in NYHA classes. LACI – left atrial coupling index; LASr – left atrial reservoir strain; LASct – left arial contractile strain; LAScd – left atrial conduit strain; NYHA (I, II, III, IV) – New York Heart Association (class I, II, III, IV).



Discussion

The prognostic value of LA deformational parameters in various diseases is known, which, according to the latest publications, also includes AS (3 – 5). LACI is a new parameter of LA function, which is calculated based on the ratio of the LAVI and a' (measured by DTI in the region of the septal edge of the mitral annulus). It has been confirmed that LACI is an important prognostic parameter in patients with HF and reduced LV systolic function to be used in clinical practice. A LACI value ≥ 6 was associated with higher mortality. At the same time, LACI was significantly correlated with the degree of severity of secondary mitral regurgitation. Integrating this parameter into the standard echocardiographic protocol can refine the prediction of the patient's prognosis and thus the intensification of the treatment procedure (6 – 8). The results of our study prove that LACI represents a new prospective echocardiographic parameter that can be used as an additional data in the evaluation of symptoms in relation to the NYHA functional class and in the prediction of the progression of LV systolic dysfunction in a group of patients with severe AS. Severe AS is associated with increased morbidity and mortality. Therefore, proper timing of aortic valve replacement (AVR) is critical (9). Despite the low risk associated with modern approaches to AVR, current recommendations indicate it only in the presence of symptoms associated with severe AS or in the development of LV systolic dysfunction. Early detection of symptoms or systolic dysfunction in a group of asymptomatic patients with severe AS is very important. The next step, based on the recommendations for asymptomatic patients indicate, in addition to the level of type B natriuretic peptide (BNP), the implementation of a stress test. AVR is also indicated in the case of MG ≥ 60 mmHg or v max > 5 m/s, severe valve calcification and rapid progression of stenosis (defined as an increase in v max > 0.3 m/s per year) (1). The latest studies show that mortality in the group of asymptomatic patients may be higher than previously assumed (10 – 12). Expanding the AS diagnostic algorithm would be helpful in early detection of symptoms or progression of LV systolic dysfunction. In clinical practice, the deformation parameters determined by the method of speckle tracking echocardiography (STE) are already starting to be used as a standard practice. In AS, it is mainly global longitudinal deformation (GLS) that has prognostic value in asymptomatic patients with severe AS and preserved LV systolic function (13 – 16). The progression of the degree of severity of AS leads to an increase in afterload, hypertrophy, and fibrosis of the LV and subsequently to its systolic and/or diastolic dysfunction. It is known that chronically increased LV afterload in AS causes structural and functional changes in the LA. The LA enlarges and the pressure overload leads to disruption of its three functional phases (reservoir, conduit and contraction). Compared with other echocardiographic variables, LA volume and functional parameters better reflect heart remodeling associated with AS (17). LASct < 12%, LASr < 20% and LAScd < 6% were associated with the primary outcome, that was a composite of all-cause mortality, heart failure hospitalization, acute coronary syndrome or syncope. (18) Although LA strain outperformed AS hemodynamic indices and LV GLS in predicting outcomes, it showed no or weak correlations with LV EF and no correlation with peak velocity and mean pressure gradient (18). According to the results of our study, LACI was significantly correlated with reduction of LV EF. Therefore, this parameter can expand diagnostic potential of LA functional parameters in severe AS. Moreover, to the best of our knowledge, no article has been published including the role of LACI along with LA strain in patients with severe symptomatic AS. According to the results of our study, LACI was significantly correlated with the degree of NYHA functional class and the reduction of LV EF. Therefore, its increasing values may indicate the progression of structural and clinical changes in patients with severe AS. The clinical use of LA strain and LACI together with the standard parameters evaluated in AS and in the subsequent corresponding timing of AVR is prospective. After evaluating all indicated investigations, LACI can be a useful parameter in deciding on the correct timing or intensification of therapy in patients with severe AS.

Limitations

In our study, we did not focus on the relation of LA deformational parameters and LACI to the mortality and hospitalizations of patients with severe AS. At the same time, due to the retrospective study, we did not have NT-proBNP values available for all patients, so they were not used in the study. However, only symptomatic patients were included. LACI can only be evaluated in sinus rhythm. To establish a clinically applicable LACI cut-off value in relation to severe AS, an expansion of the patient population will be necessary in the future.

Conclusion

Based on the results of our study, LACI presents a prospective echocardiographic parameter that can be included in the diagnostic algorithm in the future and early warning of the progression of clinical changes in patients with severe AS.*

*__Declaration of conflict of interest.__ The authors declare that they have no conflict of interest and all authors have read and approve the text. Informed consent was obtained from all trial participants.This article was not supported by any grant.

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