

Correlations between left ventricular and left atrial function assessed by speckle tracking echocardiography in patients with treated well-controlled arterial hypertension

Beata Uziebło-Życzkowska (✉ buzieblo-zyczkowska@wim.mil.pl)

Military Institute of Medicine <https://orcid.org/0000-0001-8997-6568>

Paweł Krześciński

Military Institute of Medicine, Department of Cardiology and Internal Diseases

Research

Keywords: arterial hypertension, left atrial strain, left ventricular strain, speckle tracking echocardiography

DOI: <https://doi.org/10.21203/rs.3.rs-35662/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

Background

Even in patients with well-controlled arterial hypertension (AH) and without significant comorbidities left ventricular (LV) and left atrial (LA) strain abnormalities may sometimes be found in speckle-tracking echocardiography. Therefore, the aim of this study was to investigate the correlation between LA strain and LV diastolic and systolic function in a group of patients with treated, well-controlled AH.

Methods

LA contractile, conduit, and reservoir function, together with echocardiographic signs of LV diastolic function and LV global longitudinal strain (LV GLS), were assessed in 101 patients with treated, well-controlled AH who met the standard criteria of normal LV ejection fraction (LVEF) and normal LV diastolic function.

Result

A relevant percentage of study participants presented lower than reference LV and LA strain values. Moreover, there were statistically significant differences in LA longitudinal strain (LAS) values (LAS during reservoir phase—LASr ($p < 0.001$) and LAS during conduit phase—LAScd ($p = 0.008$)) between patients with high and lower LV GLS, confirmed by significant correlations between LASr, LAScd, and GLS. In the correlations analysis between LAS values and LV diastolic function parameters, statistical significance was obtained for the following: LASct (contraction) vs. e'_{avg} , LASct vs. E/A, LASct vs. A, LAScd vs. e'_{avg} , LAScd vs. E/A, and LAScd vs. A.

Conclusions

LV and LA strain abnormalities occurred within a significant percentage of patients with treated, well-controlled AH. Impaired LA strain is associated with lower LV strain and reduced LV diastolic function parameters, reflecting both the passive and active properties of the LA.

Background

Arterial hypertension (AH) is one of the most prevalent cardiovascular diseases. European guidelines present strong evidence for the use of antihypertensive treatment in moderate and severe AH, but the usage of pharmacotherapy in patients with mild AH is still debated [1]. Especially in young people, marginally elevated blood pressure (BP) is thought to have no significant clinical consequences. However, the results of the Systolic Blood Pressure Intervention *Trial* (SPRINT) [2], which forced the American cardiology societies to decrease BP thresholds for diagnosing AH [3], sparked a discussion on cardiovascular risk in mild AH.

Even in patients with well-controlled AH, without significant comorbidities and with normal echocardiographic indices of left ventricular (LV) systolic and diastolic dysfunction, LV and left atrial (LA) strain abnormalities may sometimes be found in speckle-tracking echocardiography (STE) [4,5,6]. In our

earlier study, we revealed that in hypertensive patients with normal LV ejection fraction (EF), left ventricular global longitudinal strain (LV GLS) is reduced compared to healthy people, and its value improves after effective antihypertensive treatment [4]. Also, for left atrial (LA) function, recent studies using STE showed that in hypertensives, LA strain parameters might be impaired, despite normal LA size [7,8].

Based on these reports, we hypothesized that even in the early stage of AH, there might be some interrelated subclinical LV and LA abnormalities, detectable by STE. Therefore, we decided to investigate the relation between LA strain and LV diastolic and systolic function in a group of patients with treated, well-controlled AH.

Material And Methods

Study group

We retrospectively analyzed the data collected in the Non-invasive Haemodynamic Assessment in Hypertension (FINE-PATH) study (ClinicalTrials.gov Identifier NCT01996085), which was conducted in the Department of Cardiology and Internal Medicine within the Military Institute of Medicine during the period 2011–2014 [9]. In brief, this trial had a prospective, randomized, controlled design (144 patients enrolled) to assess a novel approach to the treatment of AH; the study involved patients with at least a three-month history of AH defined according to the European Society of Cardiology guidelines [1]. The exclusion criteria included secondary AH, chronic kidney disease, systolic heart failure, cardiomyopathy, significant arrhythmias, significant valvular heart disease, chronic obstructive pulmonary disease, previously diagnosed diabetes mellitus, polyneuropathy, and peripheral vascular disease. The following drug classes were used: beta-blockers, angiotensin- converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, and diuretics, either alone or in combination. The study protocol was approved by the Institutional Review Board at the Military Institute of Medicine (no. 21/WIM/2011), and each patient provided written consent.

In this secondary analysis from among the whole group who attended a controlled visit after 12 months of treatment (n=121), 108 patients with acceptable ultrasound image quality were selected. In the final analysis, 101 patients with normal LV diastolic function evaluated based on current guidelines [10] were included. Collected data included demographic characteristics, the results of a complete clinical examination, 24-h ambulatory blood pressure (ABP) monitoring (ABPM), antihypertensive treatment, and transthoracic echocardiography.

Ambulatory blood pressure monitoring

Ambulatory blood pressure monitoring (Spacelabs 90207, Spacelabs, Medical Inc, Redmond, USA) was performed within 2 weeks before echocardiography. The time from 6 a.m. to 10 p.m. was considered daily activity period (daytime) with automatic blood pressure measurement in 10-minute intervals. During night rest (night-time: 10 p.m. – 6 a.m.) the measurement was performed every 30 minutes. As a good blood pressure control (well-treated hypertension) was considered a mean 24-hour systolic BP<130 mmHg and

diastolic BP<80 mmHg, a daytime systolic BP<135 mmHg and diastolic BP<85 mmHg, and a night-time systolic BP<120 mmHg and diastolic BP<70 mmHg

Standard transthoracic echocardiography

Transthoracic echocardiography was performed using a high-quality echocardiograph (Vivid 7 or E95, General Electric, United States). The examinations were analyzed off-line by an experienced echocardiographer accredited by the Section of Echocardiography of the Polish Cardiac Society, echocardiography laboratory. All LV and LA measurements were made according to the current guidelines of the European Society of Cardiology [11]. To estimate the size and function of the LA, the following standard parameters were measured: LA end-diastolic diameter, LA area, LA volume (LAV), and LA indexed volume (LAVI). LAV and LAVI were measured using a biplane algorithm from the apical four-chamber (A4C) and two-chamber (A2C) views. LA enlargement was defined as LAVI >34ml/m². To assess LV function, LVEF was calculated using the biplane Simpson formula. LV mass (LVM) was calculated using the linear method according to the recommendations for cardiac chamber quantification by echocardiography in adults [11]. Using the parasternal longitudinal axis view), the thicknesses of the interventricular septal, the inferolateral walls, and the LV end-diastolic and end-systolic diameters were obtained. To diagnose LV hypertrophy, LVM was indexed to the body surface area (BSA) and calculated using the DuBois formula (indexed LVM–LVMI). Left ventricular hypertrophy (LVH) was diagnosed as recommended (cutoff values for women are LVMI >95 g/m² and for men, LVMI >115 g/m²).

Diagnosis of LV diastolic dysfunction was based on the current guidelines [10], where the parameters for its identification and their cutoffs are as follows: LAVI >34 ml/m², septal annular e' velocity < 7 cm/s, lateral annular e' velocity <10 cm/s, average E/e' ratio >14, and peak tricuspid regurgitation velocity >2.8 m/s. Waves E and A of the mitral inflow velocity by pulsed wave Doppler from the apical four-chamber view, the E/A ratio, and the velocity waves (e' and a') of the mitral annulus septal and lateral regions were recorded using tissue Doppler imaging. An average value of septal and lateral mitral annulus velocities was used to estimate E/e' ratio.

Speckle-tracking echocardiography (STE)

Regional and global longitudinal 2D LA and LV strain was analyzed by STE using GE EchoPAC BT 12 software. LV GLS was assessed using automated imaging software. Detection of the tracked area was performed semi-automatically with two points selected at the level of the mitral annulus and the third point at the apex with the possibility of manual adjustments. The LV GLS values were averaged for all 17 LV segments: seven in the apical four-chamber view, six in the apical two-chamber view, and six in the apical three-chamber view.

Analysis of LA strain was performed off-line, obtained from a non-foreshortened apical, both A4C- and A2C-view images, using conventional 2D gray-scale echocardiography. High frame rates (60–80 frames per second) were used for analysis as recommended in the Expert Consensus Statement [12]. The analysis was performed by an experienced echocardiographer using acoustic-tracking software (EchoPAC, General Electric, USA), allowing off-line semi-automated analysis of speckle-based strain. The LA endocardial border

was manually traced in both the A4C and A2C views. An epicardial border was automatically generated by the software, creating a region of interest. The LA was contoured, extrapolating across the pulmonary veins and LA appendage orifice. Then, after eventual manual adjustment of the ROI shape, the software divided the region of interest into six segments and generated a longitudinal strain curve. To assess all LA strain values, the QRS wave onset was set as a reference point as recommended in the consensus document [13]. The obtained LA longitudinal strain (LAS) parameters were as follows [13]: positive peak strain during the reservoir phase (LASr), corresponding to the atrial reservoir function (positive value); next strain value during early diastole, corresponding to the atrial conduit function and identified as the LA-strain-during-conduit phase (LAScd—negative value), and the LA strain during late diastole, corresponding to active atrial contraction and identified as the LA-strain-during-contraction phase (LASct—negative value). LASr, LAScd, and LASct were calculated by averaging the values observed in all the LA segments (global LASr, LAScd, and LASct). When some segments were excluded due to the inability to achieve adequate tracking, LAS was calculated by averaging the values measured in the remaining segments. All measurements were obtained during sinus rhythm. As reference LA strain values, we adopted those given in a large meta-analysis carried out by Pathan et al., which included 2,542 healthy subjects [14]. Detailed measurements of LASr, LAScd, and LASct are presented in Figure 1.

To assess the intraobserver variability of LASr A4C, LASr A2C, LASct A4C, and LASct A2C, 20 patients were randomly selected. Intraobserver variability coefficients were calculated using images independently recorded at two different times by the same observer. The intraclass correlation coefficient together with the mean difference (95% CI) of two measurements in Bland-Altman analysis, divided by the mean of those two measurements and given as percentages, were calculated for intraobserver variability. The repeatability of the LAS measurements was high. The intraclass correlation coefficients for the intraobserver variability of LASs was 0.99 for LASr A4C, 0.98 for LASr A2C, 0.99 for LASct A4C, and 0.98 for LASct A2C. The mean difference divided by the mean of two measurements for intraobserver variability was 0.4 % (-1.1%–2.0%) for LASr A4C, 0.6% (-1.6%–28%) for LASr A2C, 0.2% (-3.7%–6.6%) for LASct A4C, and 0.5% (-3.1%–4.1%) for LASct A2C.

Statistical analysis

Statistical analyses were conducted with Statistica 12.0 (StatSoft Inc., Tulsa, OK, USA). The distribution and normality of data were assessed visually and with the Shapiro-Wilk test. Continuous variables were presented as the mean \pm standard deviation (SD), whereas categorical variables were presented as absolute and relative values (percentages). A comparison analysis was conducted for two subgroups: patients with high GLS (>the absolute value of -20%; "High GLS"; n=30) and lower GLS (\leq the absolute value of -20%; "Lower GLS"; n=71). The cut-off value was in accordance with the current recommendations [11]. The student's t-test was used for normally distributed data, whereas the Mann–Whitney U-test was used for data with non-normal distribution. A p-value of <0.05 was considered statistically significant.

Results

A total of 101 patients (64 men with a mean age of 45.2 years) with well-controlled blood pressure and heart rate control were selected to participate in the study. The mean values of SBP and DBP obtained from ABPM for all patients were 119.7 ± 9.2 mm Hg and 76.7 ± 7.5 mm Hg, respectively. Details of their demographic, clinical, and treatment data are presented in Table 1. **Echocardiographic assessment** The mean value of LAVI was $29.1 (6.8)$ ml/m², and only 17 (16.8%) patients fulfilled the criteria of LA enlargement. Myocardial hypertrophy was diagnosed in 14 (13.9%) subjects, and the mean LVMI for the whole group was $89.5 (\pm 17.5)$ g/m². The study population was characterized by normal LVEF ($65.2 \pm 3.3\%$). However, the mean LV GLS ($-18.7 \pm 2.6\%$) was lower than the value (-20%) which is called as a high in a healthy person according to ESC guidelines [1]. Also, analysis of LAS revealed lower values than those previously reported as normal (39% for LASr, -17% for LASct, and -23% for LAScd) [14]. In our group, these LAS parameters were 32.9%, -15.9%, and -13.9%, respectively. Detailed echocardiographic data is summarized in Table 2. **Comparison of subgroups with respect to LV GLS** There were no differences between the subgroups "High GLS" and "Lower GLS" for age, sex distribution, or antihypertensive treatment. LA strain measurements were significantly lower in patients with lower GLS as compared to those with high GLS. Patients in the "Lower GLS" subgroup presented significantly reduced LASr ($p = 0.0007$) and LAScd ($p = 0.008$) as well as an increased E/e' ratio ($p = 0.037$). These results were supported by correlations with LV GLS for LASr, LAScd, E/e' ratio, and E' value. GLS also proved to be correlated with LVEF. Detailed comparative data are presented in Table 3 and graphic presentation for significant correlations in Figure 2.

Correlation of atrial strain with LV diastolic function parameters

In the correlation analysis of LAS values and LV diastolic function parameters, significant results were obtained for LASct vs. e'avg ($p = 0.002$), LASct vs. E/A ($p < 0.001$), LASct vs. A ($p = 0.004$), LAScd vs. e'avg ($p = 0.004$), LAScd vs. E/A ($p = 0.001$), and LAScd vs. A ($p = 0.001$) (see Table 4).

Discussion

Our results revealed that even in patients with treated well-controlled AH, who have good BP control and no LV dysfunction in standard echocardiographic evaluation, the values of LV and LA strain measured by STE might be impaired. We also noted that LV GLS is the best correlated with LA strain. Surprisingly, its correlations with LASr and LAScd were even stronger than with LVEF. The interplay between LV diastolic pressures and LA function was also identified and confirmed in correlations of some LAS with E/A and e'.

We intended to investigate a group of young, well-treated hypertensives, mostly free from heart function impairment in standard echocardiography (LVH confirmed in only 14%). The exclusion of subjects with reduced and mid-range LVEF from the FINEPATH study along with the additional criteria for this particular analysis (LV diastolic dysfunction) provided a set of data fulfilling these assumptions. Even the prevalence of myocardial hypertrophy was very low (13.9%).

However, the use of novel echocardiographic parameters revealed a high frequency of subtle abnormalities occurring in this group. More than two-thirds of patients showed LV GLS values below -20% , and LAS values were also lower than reference values. Previous studies also reported that in hypertensive patients,

LV GLS is decreased despite the lack of other comorbidities [5,6]. In our earlier group of 125 patients with mild hypertension [5], we revealed impaired LV GLS values (mean -18.1%) despite normal LVEF (mean 65.3%). Moreover, we observed an association between LV GLS values and the occurrence of LV diastolic dysfunction. The incidence of LV diastolic dysfunction grew higher as the GLS value was more impaired (from 48.4% in the group of subjects with LV GLS $<$ the absolute value of -16.3% to none in the group of patients with GLS $<$ the absolute value of -19.9%) [5]. Similar findings were reported in a study by Galderisi et al. [6], in which reduced LV GLS was noticed in young patients with AH, and its strong dependence on LV diastolic dysfunction and the degree of LV hypertrophy were found.

Dividing our study group depending on the LV GLS showed that patients with lower LV GLS are characterized by decreased values in parameters reflecting reservoir and conduit LA function. Only contractile LA function was comparable between the two groups of patients. Our results agree with previous reports on LAS in AH. Jarasunas et al. noticed impaired values of all LA function, including reservoir, conduit, and pump, in 63 patients with AH. Both LA conduit and reservoir function decreased with an increasing number of parameters showing LV dysfunction, while contractile function did not change [15]. It is worth mentioning that the study by Jarasunas et al. included patients with concomitant paroxysmal atrial fibrillation. This atrial arrhythmia may itself lead to impaired LAS [16,17,18]. It was also suggested that the LASr value proved to be a strong parameter of LA fibrosis in patients with AF [19].

The correlations of LA reservoir (LASr) and conduit (LAScd) strain with LV GLS values and chosen indices of LV diastolic function imply a complex interplay between LA and LV hemodynamics. It seems logical that an interplay was revealed between LA function represented by both reservoir and conduit LA strain and LV systolic function. LA reservoir strain reflects LA relaxation that lasts throughout the period of LV systole. We can treat LASr as an indicator of LA compliance. LA conduit strain spans early LV filling, so it is closely related to LV relaxation. LA contractile strain depends on LA myocardial shortening and LV filling pressures, and it is usually impaired in more advanced LA dysfunction [20]. Our results confirmed that LV longitudinal contraction is related to reservoir and conduit LA strain. We did not find any published papers reporting such observations.

Our investigation of relations between LAS and LV diastolic function indices revealed correlations between both conduit (LAScd) and contractile (LASct) strain and e'_{avg} , A, and E/A. The pathophysiological mechanisms of LA function can explain these correlations. Conduit LA strain reflects early LV filling; meanwhile, contractile LA strain reflects LV filling during late diastole. Therefore, it seems natural to associate LAScd and LASct with the parameters of both mitral inflow and LV myocardial velocities (especially LAScd with E and E' velocity, LASct with A and A' velocity, and both LAScd and LASct with E/A ratio) [21]. Olsen et al.'s study of patients with cryptogenic stroke revealed that those with impaired LASr $<$ 28.2% have more reduced e' value and increased E/ e' ratio compared to subjects with LASr $\geq 28.2\%$ [22]. No previous studies have confirmed the relations we found among patients with mild hypertension and without any other comorbidities.

Other researchers have reported correlations between LAS and E/ e' ratio, which is quite a good parameter for non-invasive estimation of LV filling pressure. In a study of hypertensive patients with confirmed LV diastolic

dysfunction, Morris et al. [23] demonstrated that LA function assessed by STE strain was inversely related to the degree of LV diastolic dysfunction and to LV filling pressure (measured by mitral E/e' ratio). Other authors have demonstrated that global LASr provides an even better estimation of LV filling pressure [24]. However, both of these studies concerned patients with more advanced LV dysfunction and higher cardiovascular risk compared to ours.

Strengths and limitations

We realize that the methodology and role of STE in the assessment of LA deformation dynamics is still not well established. We assessed strain parameters referring to actual state-of-the-art. Moreover, the measurements were performed by an experienced echocardiographer, and their reproducibility was checked earlier on 20 randomly selected patients. Additionally, the definition of lower LV GLS and LAS values are still unclear. The expert recommendations speak that a peak GLS in the range of -20% can be expected in a healthy person and we decided to that's why we decided to use this LV GLS cut-off point. Similarly, we tried to compare our LAS values with these obtained in a large meta-analysis. The strength of our results lays in the homogenous nature of our group—we recruited only hypertensive patients with no concomitant diseases.

Conclusions

Lower LV and LA strain values occur with a significant percentage of patients with treated, well-controlled, mild-stage AH. In particular, reduced values apply to LA reservoir (LASr) and conduit (LAScd) strain parameters. Impaired LA strain is associated with lower LV strain and reduced LV diastolic function parameters, reflecting both the passive and active

Abbreviations

ABP: 24-h ambulatory blood pressure

ABPM: 24-h ambulatory blood pressure monitoring

AH: Arterial hypertension

A2C: Apical two chamber

A4C: Apical four chamber

ACE-I: Angiotensin-converting-enzyme inhibitors

AF: Atrial fibrillation

ARB: Angiotensin receptor blockers

BP: Blood pressure

LA: Left atrium

LAa: Left atrium area

LAScd: Left atrial strain during conduit phase

LAS: Left atrial strain

LASct: Left atrial strain during contraction phase

LAd: Left atrial end-diastolic diameter

LASr: Left atrial strain during reservoir phase

LAV: Left atrial volume

LAVI: Left atrial volume index

LV: Left ventricle

LVEF: Left ventricular ejection fraction

LV GLS: Left ventricular global longitudinal strain

LVH: Left ventricular hypertrophy

LVM: Left ventricular mass

LVMI: Left ventricular mass index

ROI: Region of interest

STE: Speckle tracking echocardiography

TEE: Transesophageal echocardiography

TTE: Transthoracic echocardiography

2D: Two dimensional

Declarations

Ethics approval and consent to participate

The studies were conducted according to Good Clinical Practice guidelines and the Declaration of Helsinki. The patients were participants of the clinical study (ClinicalTrials.gov NCT01996085). The study protocol was approved by the local ethics committee. Written informed consents were obtained from all the patients.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding statement

The FINEPATH study was supported by the Ministry of Science and Higher Education/Military Institute of Medicine, Warsaw, Poland (grants no 148/WIM and 335/WIM).

Authors' contributions

BUŻ conceived the concept of the study. BUŻ and PK contributed to the study design. BUŻ and PK conducted data analysis and interpretation as well as wrote the manuscript. All authors were involved in data collection, editing and approving the final version of the manuscript.

Acknowledgements

Not applicable

Authors' information

Not applicable

References

1. Mancia G, Fagard R, Narkiewicz K, Redón J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC Guide-lines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the Euro-pean Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens.* 2013; 31: 1281–1357.
2. Wright JT Jr, Williamson JD, Whelton PK, Snyder JK, Sink KM, Rocco MV, et al. SPRINT Research Group, A Randomized Trial of Intensive versus Standard Blood-Pressure Control. *N Engl J Med.* 2015; 373(22): 2103-16.
3. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Himmelfarb CD, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report

- of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *J Am Coll Cardiol*. 2018; 71: 2199–2269.
4. Uziębło-Życzkowska B, Krześciński P, Gielerak G, Skrobowski A. Speckle tracking echocardiography and tissue Doppler imaging reveal beneficial effect of pharmacotherapy in hypertensives with asymptomatic left ventricular dysfunction. *Journal of the American Society of Hypertension*. 2017; 11: 334-342.
 5. Krześciński P, Uziębło-Życzkowska B, Gielerak G, Stańczyk A, Kurpaska M, Piotrowicz K. Global longitudinal two-dimensional systolic strain is associated with hemodynamic alterations in arterial hypertension. *J Am Soc Hypertens*. 2015; 9(9): 680-689.
 6. Galderisi M, Lomoriello VS, Santoro A, Esposito R, Olibet M, Raia R, et al. Differences of myocardial systolic deformation and correlates of diastolic function in competitive rowers and young hypertensives: a speckle-tracking echocardiography study. *J Am Soc Echocardiogr*. 2011; 23(11): 1190-1198.
 7. Mondillo S, Cameli M, Caputo ML, Lisi M, Palmerini E, Padeletti M, et al. Early detection of left atrial strain abnormalities by speckle-tracking in hypertensive and diabetic patients with normal left atrial size. *J Am Soc Echocardiogr*. 2011; 24(8): 898-908.
 8. Sahebjam M, Mazareei A, Lotfi-Tokaldany M, Ghaffari N, Zoroufian A, Sheikhatollahi M. Comparison of left atrial function between hypertensive patients with normal atrial size and normotensive subjects using strain rate imaging technique. *Arch Cardiovasc Imaging*. 2014; 2: e16081.
 9. Krześciński P, Gielerak G, Stańczyk A, Piotrowicz K, Uziębło-Życzkowska B, Banak M, et al. The effect of hemodynamically-guided hypotensive therapy in one-year observation: Randomized, prospective and controlled trial (FINEPATH study). *Cardiol J*. 2016; 23(2): 132-140.
 10. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2016; 29: 277–314.
 11. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2015; 28(1): 1-39.
 12. Mor-Avi V, Lang RM, Badano LP, Belohlavek M, Cardim NM, Derumeaux G et al. Current and evolving echocardiographic techniques for the quantitative evaluation of cardiac mechanics: ASE/EAE consensus statement on methodology and indications endorsed by the Japanese Society of Echocardiography. *J Am Soc Echocardiogr*. 2011; 24(3): 277-313.
 13. Badano LP, Koliass TJ, Muraru D, Abraham TP, Aurigemma G, Edvardsen T, et al. Standardization of left atrial, right ventricular, and right atrial deformation imaging using two-dimensional speckle tracking echocardiography: a consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *European Heart Journal - Cardiovascular Imaging*. 2018; 19 (6): 591–600.

14. Pathan F, D'Elia N, Nolan MT, Marwick TH, Negishi K. Normal Ranges of Left Atrial Strain by Speckle-Tracking Echocardiography: A Systematic Review and Meta-Analysis. *J Am Soc Echocardiogr.* 2017; 30(1): 59-70. e8.
15. Jarasunas J, Aidietis A, Aidietiene S. Left atrial strain - an early marker of left ventricular diastolic dysfunction in patients with hypertension and paroxysmal atrial fibrillation. *Cardiovascular Ultrasound.* 2018; 16: 29.
16. Yuda S, Muranaka A, Miura T. Clinical implications of left atrial function assessed by speckle tracking echocardiography. *J Echocardiogr.* 2016; 14(3): 104-112.
17. Yoon YE, Oh IY, Kim SA, Park KH, Kim SH, Park JH, et al. Echocardiographic Predictors of Progression to Persistent or Permanent Atrial Fibrillation in Patients with Paroxysmal Atrial Fibrillation (E6P Study). *J Am Soc Echocardiogr.* 2015; 28(6): 709-717.
18. Kojima T, Kawasaki M, Tanaka R, Ono K, Hirose T, Iwama M, et al. Left atrial global and regional function in patients with paroxysmal atrial fibrillation has already been impaired before enlargement of left atrium: velocity vector imaging echocardiography study. *Eur Heart J Cardiovasc Imaging.* 2012; 13(3): 227-234.
19. Leung M, Abou R, van Rosendaal PJ, van der Bijl P, van Wijngaarden SE, Regeer MV, et al. Relation of Echocardiographic Markers of Left Atrial Fibrosis to Atrial Fibrillation Burden. *Am J Cardiol.* 2018; 122(4): 584-591.
20. Donal E, Behagel A, Feneon D. Value of left atrial strain: a highly promising field of investigation. *European Heart Journal - Cardiovascular Imaging.* 2015; 16(4): 356–357.
21. Hoit BD. Left atrial size and function. *Journal of Am Coll Cardiol.* 2014; 63(6): 493-505.
22. Olsen FJ, Christensen LM, Krieger DW, Højberg S, Høst N, Karlsen FM, et al. Relationship between left atrial strain, diastolic dysfunction and subclinical atrial fibrillation in patients with cryptogenic stroke: the SURPRISE echo substudy. *Int J Cardiovasc Imaging.* 2020; 36(1): 79-89.
23. Morris DA, Takeuchi M, Krisper M, Köhncke C, Bekfani T, Carstensen T, et al. Normal values and clinical relevance of left atrial myocardial function analysed by speckle-tracking echocardiography: multicentre study. *Eur Heart J Cardiovasc Imaging.* 2015; 16(4): 364-372.
24. Cameli M, Sparla S, Losito M, Righini FM, Menci D, Lisi M, et al. Correlation of Left Atrial Strain and Doppler Measurements with Invasive Measurement of Left Ventricular End-Diastolic Pressure in Patients Stratified for Different Values of Ejection Fraction. *Echocardiography.* 2016; 33(3): 398-405.

Tables

Table 1. Demographic, clinical, and treatment data for the study population

Variable	Study population, n=101
Demographic data	
age [years], mean (SD)	45.2 (10.2)
male, n (%)	64 (63.4)
Clinical data, mean (SD)	
heart rhythm [bpm], mean (SD)	66.9 (8.5)
24-h average systolic blood pressure, mean (SD)	119.9 (9.8)
24-h average diastolic blood pressure, mean (SD)	76.9 (7.5)
Antihypertensive treatment	
ACEI, n (%)	69 (68.3)
ARB, n (%)	12 (11.9)
diuretics, n (%)	31 (30.7)
beta-blocker, n (%)	23 (22.8)
calcium channel blocker, n (%)	13 (12.9)
Therapy	
monotherapy, n (%)	48 (47.5)
dual therapy, n (%)	39 (38.6)
triple therapy, n (%)	8 (7.9)
only non-pharmacological recommendations, n (%)	6 (5.9)
Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.	

Table 2. Echocardiography data for the study population

Variable	Study population, n=101
Standard echocardiography findings	
LAVI, ml/m ² , mean (SD)	29.1 (6.8)
enlargement LA*, n (%)	17 (16.9%)
E/A<0,8, n (%)	17 (16.8)
e'avg (cm/s), mean (SD)	10.9 (2.3)
E/e' avg, mean (SD)	6.7 (1.6)
E (cm/s), mean (SD)	71.3 (15.8)
A (cm/s), mean (SD)	62.3 (13.2)
LVEF (%), mean (SD)	65.2 (3.3)
E/A, mean (SD)	1.19 (0.35)
LVMI (g/m ²), mean (SD)	89.5 (17.5)
LVH **, n (%)	14 (13.9)
Speckle tracking echocardiography findings	
LASr (%), mean (SD)	32.9 (6.4)
LASct (%), mean (SD)	15.9 (3.9)
LAScd (%), mean (SD)	13.9 (4.7)
LV GLS (%), mean (SD)	18.7 (2.6)
GLS<20%, n (%)	71 (67.3)
Abbreviations: LA, left atrial; LAScd, left atrial strain conduit; LASct, left atrial strain contraction; LASr, left atrial strain reservoir; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; LV GLS, left ventricular global longitudinal strain; LVH, left ventricular hypertrophy; LVMI, left ventricular mass index.	
* enlargement LA defined as LAVI>20ml/m ²	
**LVH defined as LVMI>95g/m ² for Female and LVMI >115g/m ² for men	

Table 3. The comparison between "High GLS" and the "Lower GLS" subgroups and correlation analysis between the LV GLS and other variables

	LV Lower GLS subgroup, mean (SD)	LV High GLS subgroup, mean (SD)	p (for comparison)	correlations LV GLS vs. variable (R)	p (for correlations)
Age, years, mean(SD)	44.86 (10.02)	46.13 (10.70)	0.57	0.13	0.18
Men/women, n (%)	48 (67.6)	16 (53.3)	0.17	-	-
Echocardiography parameters, mean (SD)					
e'm (cm/s)	9.38 (1.94)	9.53 (2.10)	0.75	-0.02	0.86
e'l (cm/s)	12.56 (3.55)	12.23 (2.14)	0.62	-0.06	0.57
e'avg (cm/s)	10.97 (2.43)	10.88 (1.89)	0.86	-0.02	0.60
E/e' avg	6.48 (1.60)	7.10 (1.51)	0.04	0.23	0.02
E (cm/s)	69.42 (16.30)	75.77 (13.89)	0.06	0.25	0.012
A (cm/s)	61.82 (13.32)	63.60 (13.00)	0.54	0.19	0.06
a'm (cm/s)	9.82 (1.55)	9.53 (1.31)	0.39	0.04	0.70
a'l (cm/s)	10.86 (2.21)	10.17 (2.51)	0.14	0.03	0.79
LVEF (%)	64.68 (3.22)	66.47 (3.08)	0.01	0.27	0.007
E/A	1.17 (0.36)	1.23 (0.31)	0.37	0.01	0.99
LVMII (g/m ²)	90.1 (17.4)	87.8 (18.2)	0.57	-0.11	0.30
LAVI (ml/m ²)	28.51 (6.61)	30.50 (6.99)	0.05	0.17	0.09
Speckle tracking echocardiography parameters, mean (SD)					
LASr (%)	31.43 (5.5)	36.33 (7.20)	0.0007	0.37	<0.001
LASct (%)	-15.80 (3.96)	-16.16 (3.88)	0.67	0.18	0.08
LAScd (%)	-13.09 (4.11)	-15.79 (5.42)	0.008	0.29	0.003
LV GLS (%)	-17.40 (1.73)	-21.79 (1.18)	<0.0001	-	-

Abbreviations: as in Table 2.

Table 4. Correlation of LAS values with LV diastolic function parameters

	e'avg (cm/s)	E/e' avg	E/A	E (cm/s)	A (cm/s)
	R (p)				
LASr (%)	0.07 (ns)	0.14 (ns)	-0.01 (ns)	0.17 (ns)	0.16 (ns)
LASct (%)	-0.30 (0.002)	0.11 (ns)	-0.37 (<0.001)	-0.18 (ns)	0.28 (0.004)
LAScd (%)	-0.28 (0.004)	0.17 (ns)	-0.31 (0.001)	-0.07 (ns)	-0.32 (0.001)

Abbreviations: as in Table 2.

Figures

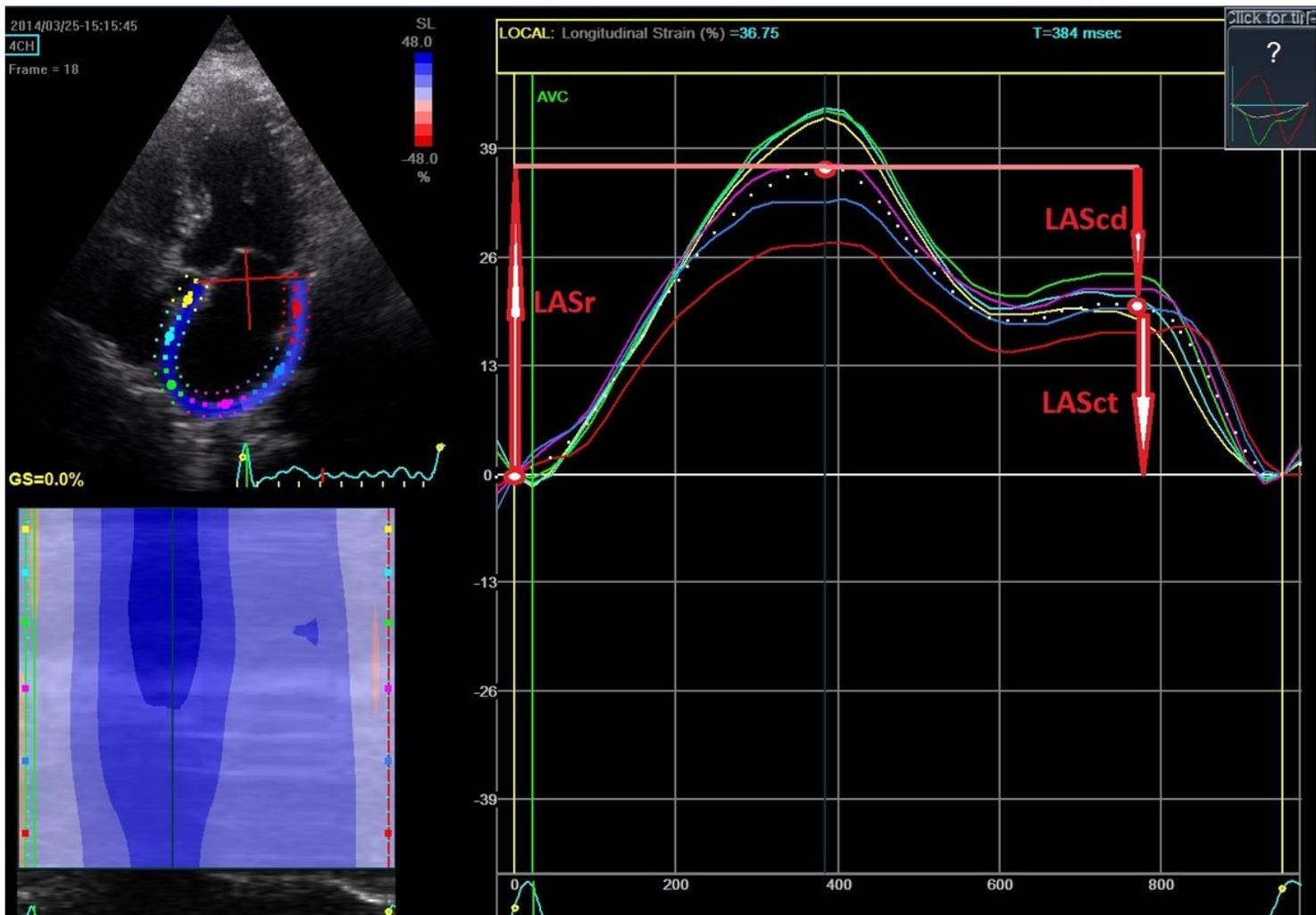


Figure 1

Measurements of left atrial strain parameters with the zero strain reference at the end-diastole (LASr, left atrial strain during reservoir phase; LAScd, left atrial strain during conduit phase; LASct, left atrial strain during contraction phase)

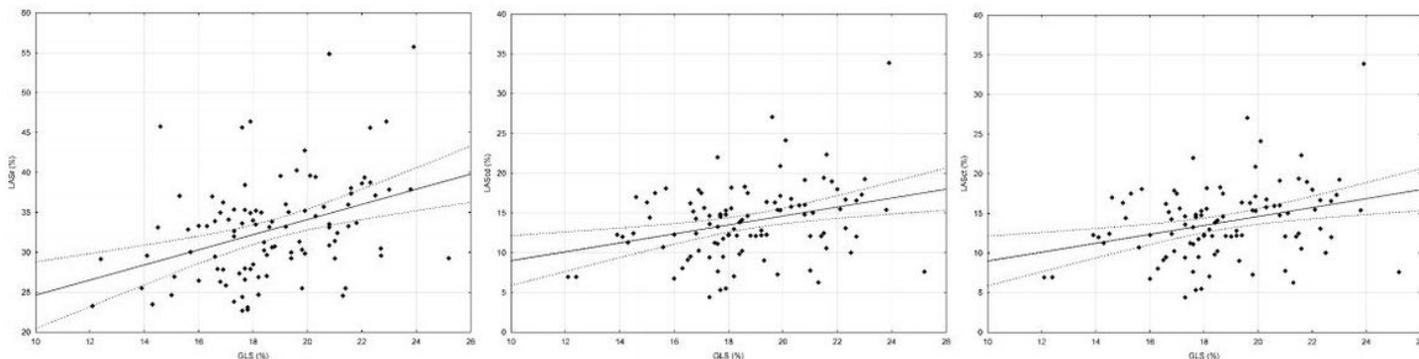


Figure 2

Correlations plots for: GLS vs LASr ($R = 0.37$; $p < 0.001$, left chart), GLS vs LAScd ($R = 0.29$, $p < 0.01$; middle chart) and GLS vs LASct ($R = 0.18$, ns; right chart) (LASr, left atrial strain during reservoir phase; LAScd, left

atrial strain during conduit phase; LASct, left atrial strain during contraction phase; GLS, left ventricular global longitudinal strain)