ORIGINAL PAPER

Decreased left atrial strain parameters are associated with prolonged total atrial conduction time in lichen planus

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Abstract: *Background:* Lichen planus (LP) carries the increased risk of cardiovascular events as it is a chronic inflammatory disease. This study aimed at determining the relationship between total atrial conduction time (TACT), P-wave dispersion, and the left atrium (LA) global strain in the patients with LP. *Methods:* Forty people as a control group and 40 patients with LP were included in this study. Patient assessed global longitudinal LA strain by two-dimensional speckle-tracking strain echocardiography. *Results:* The global peak systolic LA myocardium strain during the left ventricular systole (LAGLSRs) and the global peak negative LA myocardial strain rate during the early ventricular diastole (LAGLSRe) values were significantly lower in the patients with LP in proportion to the control group according to the strain measurements (1.7 ± 0.07 vs. $1.9 \pm 0.1\%$, $p = 0.001$; 1.23 ± 0.04 vs. 1.2 ± 0.08 s^{-1}, $p = 0.001$), respectively. TACT value was found to be significantly longer (102.6 ± 6.3 ms) in the patients with LP than the control group (96.3 ± 5.3 ms, $p = 0.001$), considering the terms of the artial conduction features. *Conclusion:* This study demonstrated that the subclinical cardiac involvement in LP can determine the prolonged TACT and the impaired left atrial myocardial deformation values.

Keywords: left atrium, lichen planus, strain, echocardiography, electromechanical delay, atrial conduction

Introduction

Lichen planus (LP) is a subacute and chronic disease affecting skin, mucous membranes, hair follicles, and nails [1]. This relatively common disease in the society affects 0.1%–4.0% of the general population and this frequency is equal to psoriasis, a better known one [2]. The basic of the pathogenesis of LP is the direct or indirect attack of primarily T lymphocytes and the mononuclear inflammatory cells to the basal layer cells of the squamous epithelium. LP is related to dyslipidemia, diabetes mellitus, and the increased oxidative stress [3]. LP has the risk of increased cardiovascular events as it is a chronic inflammatory disease similar to psoriasis. Arrhythmias are the main risk factors especially in terms of cardiovascular events. P-wave dispersion (PWD) in LP was investigated in a small number of study performed recently. In the study of Sahin et al. [4], an increase in PWD in the newly diagnosed LP was detected. PWD increase is closely related to the atrial arrhythmias, because it demonstrates the heterogeneity of the sinus impulses and they are blocked. However, the left atrium (LA) global longitudinal systolic strain (LAGLSs) and total atrial conduction time (TACT) are the markers

researched in different diseases besides PWD to indicate the subclinical electrophysiological dysfunction. Despite this, there is no study in the literature to research about the relationship between PWD, LAGLSs, and TACT in LP. Therefore, we aimed to carry out such a study assuming that this relationship would contribute to predict the atrial arrhythmias.

Materials and Methods

Patient population

This study was performed in accordance with Helsinki Declaration after the consent of the local ethics committee. All the patients were informed before the study and received approval. The present observational study was performed at the Recep Tayyip Erdoğan University Education and Research Hospital. We selected 40 patients with LP disease duration of 3 years and who were previously diagnosed and admitted to the Dermatology Department (LP patients). Also, 40 age- and sex-matched healthy individuals were included in this study as the control group. The exclusion criteria of this study were as follows: hypertension (HT), diabetes mellitus, coronary artery disease history, lung diseases and/or pulmonary HT, significant valvular heart diseases, chronic liver or kidney diseases, collagen vascular diseases, rhythms other than sinus, any cardiovascular drug use, obese subjects [body mass index (BMI) $\geq$ 30 kg/m^2], abnormal thyroid function, or serum electrolyte. The age, gender, the age of onset, the duration of the disease, and the drug history of each patient were recorded. The height, weight, BMI, and the waist circumference were assessed in all patients. Serum triglycerides, lipid, glucose levels, and highly sensitive C-reactive protein (hsCRP) levels were determined in the samples collected between 8 and 9 am after a 12-h fasting period. Also, Holter electrocardiography (ECG) was recorded.

Echocardiographical assessment

Transthoracic echocardiographic researches were carried out using S5-1 probe (5–1 MHz) transducer with Philips iE33 Medical ultrasound Systems device. All measurements were repeated during three consecutive heartbeats and averaged. American Society of Echocardiography's standards were used as a base for all the measurements [5].

Left ventricular ejection fraction (LVEF) and the LA diameter were calculated using parasternal long axis. In PW Doppler examination apical four-chamber view of LV filling, the Doppler sample volume in parallel with LV long axis and at mitral annulus was measured and averaged. For the assessment, the early diastolic flow velocity (E), the late diastolic flow velocity (A), E/Em, the deceleration time (DT), and the isovolumetric relaxation time (IVRT) were recorded. In apical four-chamber view, 5-mm width pulsed wave (PW) Doppler sample volume was placed on the point of intersection of the posterior wall and the mitral annulus and performed. By ensuring the sample volume to be parallel with the wall axis, the peak early (Em) diastolic flow velocity was in turn recorded. LA volumes were measured using the area–length method from apical four- and two-chamber views. LA maximum volume (LAVmax) was measured when the mitral valve was completely opened, LA minimum volume (LAVmin) was measured when the mitral valve was completely closed and the following parameters were calculated using these measurements: LAV reservoir (ml): LAVmax–LAVmin.

For 2D speckle tracking analysis, we obtained the gray scale views that were digitally stored. Echocardiograms were digitally stored and later analyzed offline using acoustic-tracking software (QLAB, Philips, Germany). The global strain and the strain rate were calculated by averaging the values measured in 15 atrial segments. The frame rate was 50–80 frames/s. The global peak systolic LA myocardium strain during the left ventricular systole (LAGLSs) (Fig. 1), the global peak systolic positive LA myocardial strain rate during the left ventricular systole (LAGLSRs), the global peak negative LA myocardial strain rate during the early ventricular diastole (LAGLSRe), and the global peak negative LA myocardial strain rate during the late ventricular diastole (LAGLSRa) were obtained. Atrial tissue Doppler imaging TACT – the time from initiation of the electrocardiographic P-wave (lead II) to the local lateral left atrial activation time was determined by transthoracic echocardiography [6]. This was measured by placing the sample volume in the left atrial basal portion and then measuring the time between the initiation of the electrocardiographic P-wave and the peak velocity, using tissue velocity imaging. ECG analysis of the onset of P-wave was defined as the first elevation and depression from the isoelectric line on positive and negative waves, respectively. The point of return to the isoelectric line was defined as the end of the P-wave. Pmax and Pmin durations were measured for all patients. The difference between Pmax and Pmin durations on the ECG was considered as the PWD [7].

The statistical analysis and the evaluation

Continuous data were presented as mean + standard deviation and dichotomous data in percentage. The statistical analysis of the clinical data between two groups consisted of unpaired t-tests for normally distributed data and Mann–Whitney U test analysis for non-normally
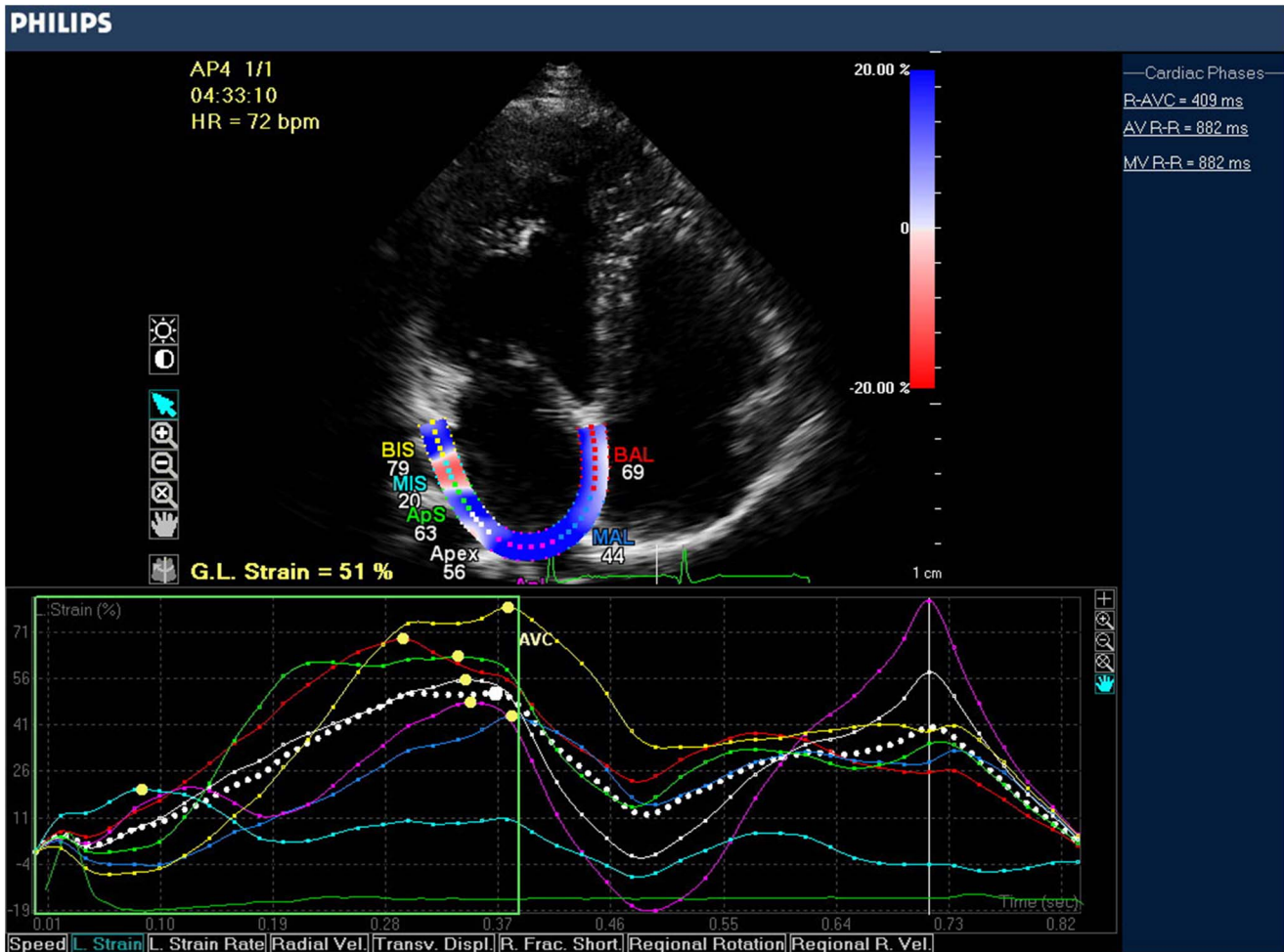
Fig. 1. Measurement of left atrium myocardial strain

distributed data. The Kolmogorov–Smirnov test was used to verify the normality of the distribution of the continuous variables. The correlations were assessed with the Pearson's and Spearman's correlation coefficient and the χ^2 test was used for categorical variables. The analyses were performed using PASW 18 (SPSS/IBM, Chicago, IL, USA) software and two-tailed P value less than 0.05 was considered statistically significant.

Findings

Forty LP patients [23 females (57.5%) and 17 males (42.5%)] were included in the study. The cutaneous lesions were present in all 40 cases. The mucosal lesions were present in 22 patients (55%) in the form of white, reticular streaks on the buccal mucosa. None of the patients had erosive oral LP. The nail involvement was also present in 18 patients (45%) in the form of ridging, grooving, and longitudinal striations. Twenty-three patients (57.5%) presented with classic LP, 10 patients

(25%) had the actinic type, and 7 patients (17.5%) had the hypertrophic type.

The comparison of demographical and clinical characteristics of the groups

The average duration of LP was 7 years. hsCRP was higher in the patient group with LP than the control group [in turn LP patients; 1.4 (1.1–1.7); control group; 0.39 (0.2–0.6); $p < 0.05$]. The atrial arrhythmia was not detected in Holter ECG. The comparison of demographical and clinical characteristics of the groups is shown in *Table I*. While the average age in LP patients was 36.5 (29–48), it was 33.5 (31–52) in control group. There was no difference between the groups in terms of age ($p = 0.12$). Also, there was no statistical difference between the groups in terms of gender, BMI, smoking, waist circumference, systolic and diastolic blood pressure, fasting glucose, and heart rate. Low-density lipoprotein–cholesterol and triglyceride levels

Table I ▌ The comparison of the demographical and the clinical characteristics of the groups

Parameters	Lichen planus ($n = 40$)	Control group ($n = 40$)	P value
Age (years)	36.5 (29–48)	33.5 (31–52)	0.12
Sex (female/male)	23/17	24/16	0.47
Body mass index (kg/m^2)	24.6 (23–26)	23.9 (22–24)	0.13
Smoking (n)	10	9	0.72
Hypercholesterolemia (%)	36	30	0.63
SBP (mmHg)	128.3 ± 7.2	126.3 ± 7.8	0.23
DBP (mmHg)	74.3 ± 5.0	72.5 ± 4.4	0.06
Heart rate (beat/dk)	86.3 ± 7.4	85.2 ± 6.7	0.50
Fasting glucose (mg/dl)	81.7 ± 8.3	83.3 ± 6.9	0.39
hsCRP (mg/dl)	1.4 (1.1–1.7)	0.39 (0.2–0.6)	0.001

SBP: systolic blood pressure; DBP: diastolic blood pressure; hsCRP: high-sensitivity C-reactive protein.

$p < 0.05$ is indicated as significant

were significantly higher in LP patients than in the control group ($p = 0.001$).

The comparison of echocardiographical and electrocardiographical characteristics of the groups

The comparison of echocardiographical and electrocardiographical characteristics of the groups is shown in *Table II*. There was no statistically significant difference between the groups in terms of LVEF, E-wave, A-wave, E/Em, DT, IVRT, LA diameter, LAVmax, LAVmin, LAVreservoir, and LAGLSRa ($p > 0.05$). The average peak values of left atrial strain during the left ventricular systole (LAGLS) value were significantly lower in LP patients than in control group (in turn LP patients, 27.2 ± 3.9; control group, 38.2 ± 6.6, $p < 0.001$). Also, LAGLSRs value was significantly lower in LP patients than in control group ($p < 0.001$). LAGLSRe value was significantly lower in LP patients than in control group ($p < 0.001$). With regard to the atrial conduction characteristics, TACT was significantly longer in LP patients than in control group (in turn LP patients, 102.6 ± 6.3; control group, 96.3 ± 5.3, $p < 0.001$). Also, PWD was more in LP patients than in control group [in turn LP patients, 63 (43–65); control group, 60 (53–64), $p = 0.001$].

There was a significant and negative significant correlation between LAGLS and TACT ($r = -0.37$, $p = 0.01$). There was a significant negative strong correlation between LAGLS and the disease duration ($r = -0.67$, $p < 0.001$) (*Fig. 2*). There was a significant positive moderate correlation between TACT and the disease duration ($r = 0.56$, $p < 0.001$). Also, there was a significant negative strong correlation between hsCRP and LAGLSs ($r = -0.68$, $p < 0.05$). There was a significant positive moderate correlation between hsCRP and TACT ($r = 0.46$, $p = 0.01$).

Discussion

In this study, we found that left atrial strain parameters decreased, left atrial electromechanical conduction time parameters prolonged in the patients with LP. A negative strong relation between LAGLS and TACT was found. Also, while there was a strong negative correlation between LAGLS and the disease duration, there was positive significant correlation between TACT and the disease duration. These findings suggest that it is possible to observe subclinical atrial electromechanical functions in LP patients.

LP is a chronic autoimmune mucocutaneous disease that affects the oral mucosa, skin, genital mucosa, scalp, and nails [8]. The disease occurs in 0.4%–1.9% of the population, mostly the middle-aged patients and particularly in women [9]. The exact pathogenesis of the disease remains unclear, but both the antibodies and T-cell mediation have been implicated. The activated T-cells release cytokines, leading to the attraction of inflammatory cells and the destruction of keratinocytes through cell-mediated cytotoxicity [10]. It has also been suggested that the increased reactive oxygen species and lipid peroxides may affect the pathogenesis of LP [11]. The studies have shown that LP is associated with the extreme cardiovascular risks, including dyslipidemia, [12] diabetes mellitus [13], and the increased oxidative stress [14]. The most cardiovascular disorders (including atherosclerosis, HT, insulin resistance, dyslipidemia, and arrhythmias) share the similar pathogenetic mechanisms, such as chronic inflammation, endothelial dysfunction, and the increased oxidative stress [15].

The cytokines involved in LP pathogenesis (such as TNF-a, IL-6, IL-10, and IL-4) could explain the association with dyslipidemia [2]. Some studies have hypothesized that the inflammatory markers, such as hsCRP, may provide an adjunctive method to globally assess the

Table II | The comparison of the echocardiographical and the electrocardiographical characteristics of the groups

Parameters	Lichen planus ($n = 40$)	Control group ($n = 40$)	P value
LVEF (%)	63.5 (61–66)	64 (53–66)	0.38
E-wave (m/s)	0.81 ± 0.06	0.79 ± 0.08	0.36
A-wave (m/s)	0.76 ± 0.06	0.73 ± 0.12	0.22
E/Em	7.8 (7.5–9.6)	7.7 (5.3–8.3)	0.06
DT (ms)	183.0 ± 16.0	182.0 ± 13.0	0.73
IVRT (ms)	82.0 ± 10	83.0 ± 7.0	0.71
LA diameter (mm)	37.6 ± 1.5	35.9 ± 0.8	0.20
LAVmax (ml)	41.2 ± 3.3	40.8 ± 1.8	0.43
LAVmin (ml)	13.8 ± 2.5	14.1 ± 1.8	0.45
LAV reservoir (ml)	27.5 ± 2.8	26.6 ± 3.1	0.26
LAGLSs (%)	27.2 ± 3.9	38.2 ± 6.6	0.001
LAGLSRs (s^{-1})	1.7 ± 0.07	1.9 ± 0.1	0.001
LAGLSRe (s^{-1})	1.23 ± 0.04	1.2 ± 0.08	0.001
LAGLSRa (s^{-1})	1.52 (1.41–1.99)	1.48 (1.39–1.99)	0.39
TACT (ms)	102.6 ± 6.3	96.3 ± 5.3	0.001
PWD (ms)	63 (43–65)	60 (53–64)	0.001

LVEF: left ventricular ejection fraction; DT: deceleration time; IVRT: isovolumetric relaxation time; LA: left atrium; LAVmax: LA maximum volume; LAVmin: LA minimum volume; LAV reservoir: LAVmax–LAVmin; LAGLSs: global peak systolic LA myocardium strain during the left ventricular systole; LAGLSRs: global peak systolic positive LA myocardial strain rate during the left ventricular systole; LAGLSRe: global peak negative LA myocardial strain rate during the early ventricular diastole; LAGLSRa: global peak negative LA myocardial strain rate; TACT: total atrial conduction time; PWD: P-wave duration difference.
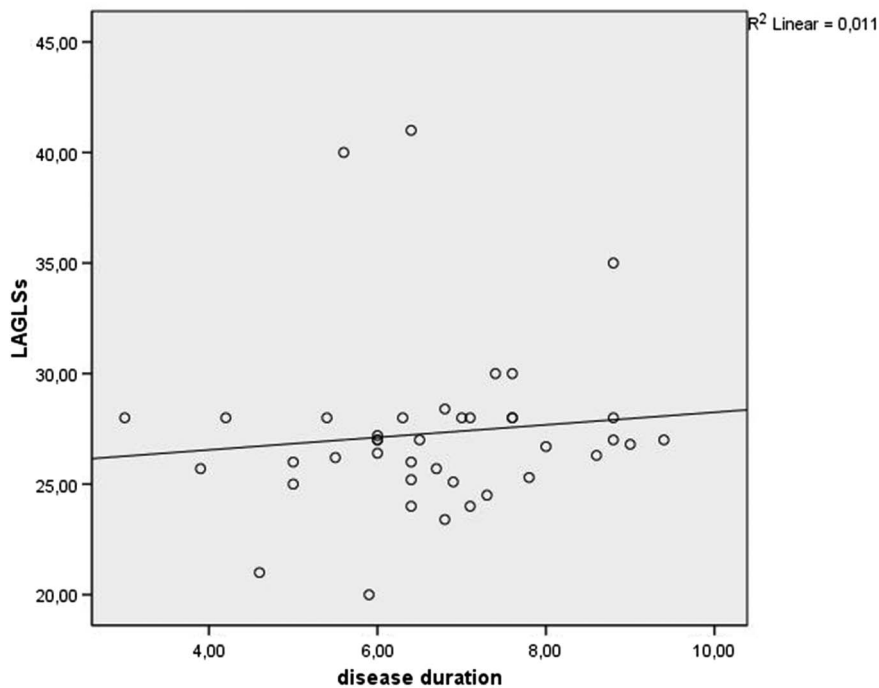$p < 0.05$ is indicated as significant

Fig. 2. | Left atrium global longitudinal systolic strain correlation graph. LAGLSs: left atrium global longitudinal systolic strain

cardiovascular risk [16, 17]. The ongoing inflammation might affect the myocardium, and the increased inflammatory activity is almost always associated with poor cardiac prognosis. The increased hsCRP levels demonstrate the activity of this chronic disease and are independent risk factors for arrhythmias [18]. The recent studies

have found a close association between atrial fibrillation (AF) and inflammation; the AF was found to be more common in the cases with high hsCRP levels following the coronary bypass and the cute pericarditis [19, 20]. In this study too, a correlation was detected between hsCRP and PWD, LAGLSs and TACT demonstrated to have a relation to the risk of arrhythmia. In this regard, we think the increased PWD, the prolonged TACT, and the decreased LAGLSs in the patients with LP will contribute to predict the increased risk of arrhythmia. In their review, Cameli et al. [21] told that LA strain has high sensitivity in identifying raised atrial stiffness and wall fibrosis and interstitial atrial remodeling and LA mechanical dysfunction. In this study, a significant decrease in left atrial strain parameters was observed in LP patients and according to this, correlation between disease duration and these parameters was determined. We have no information about the atrial inflammation in the patients with LP. Moreover, there are no long-term follow-up studies related to the atrial arrhythmias in the patients with LP. However, in the different inflammatory diseases, a correlation was found between the increased PWD, the prolonged TACT, and the decreased LAGLSs and AF. Sahin et al. [4] showed an increase in PWD, which may be indicative of subclinical cardiac involvement and can cause a tendency toward AF in LP patients. Tasal et al. [22] also found a positive correlation between hsCRP and atrial conduction parameters in psoriasis, an inflammatory disease, such as LP. The findings of this study may contribute to demonstrate the subclinical electrophysiological dysfunction and to predict the atrial arrhythmias. Besides, there is a need for the additional studies to indicate the risk of atrial arrhythmia by the long-term follow-up studies in the patients with LP.

The limitations of the study

The main limitation of this study is the insufficient number of patients and no long-term follow-up of the patients in terms of atrial arrhythmia.

Conclusions

The study results are useful in terms of determining the LP patients with the increased cardiovascular risk and enabling to give information by the doctors. We found in this study that LAGLS decreased, TACT prolonged, and PWD increased in the patients with LP. Also, we detected a significant association between hsCRP and PWD, TACT, and LAGLSs. These results show that LAGLS, TACT, and PWD are important markers detecting the subclinical electrophysiological changes in the patients with LP. Also, ECG, the speckle tracking echocardiography and the atrial tissue Doppler imaging in determining the cardiovascular risk in the patients undergoing a systemic treatment could be used as a screening test.

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Authors' contribution: HD, HD, and ND prepared the manuscript. YÇ gathered data. HD and DT searched the literature. HD and AU analyzed data. All authors read and approved the final manuscript.

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