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Evaluation of strain echocardiography and atrial electromechanical delay in patients with idiopathic carpal tunnel syndrome

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ABSTRACT

Aim: Carpal tunnel syndrome (CTS) could be an early marker for amyloidosis before developing of overt symptoms of cardiac amyloidosis (CA). CA characterized with left ventricular (LV) diastolic dysfunction and impairment of LV deformation-based parameters. There is limited data about echocardiographic parameters such as strain value of LV, diastolic parameters and atrial EMD in patients with idiopathic CTS. In this study, we investigated LV strain values, diastolic parameters of LV and atrial EMD in patients with idiopathic CTS. Then, we compared these parameters in CTS patients to control group.

Material and Method: Thirty-four patients with idiopathic CTS and twenty-four aged and sex matched volunteers were enrolled to study. Patients with known amyloidosis, heart failure, diabetes mellitus and secondary etiologic states for CTS such as trauma or rheumatologic disease were excluded from the study. ECG and echocardiographic examination of each patient were performed and recorded by cardiology specialist. Conventional and strain imaging echocardiography were performed. Atrial electromechanical delays (EMD) were measured.

Results: Baseline characteristics features were not different in groups. Mitral inflow velocities (mitral E and A wave), mitral E wave deceleration time, tissue Doppler velocities (lateral annular E' and A wave), E/A and E/E' ratios were similar in two groups. Septal basal strain values increased in CTS group (-21.3±4.83% vs -25.7±2.96%, p<0.001). Septal apical to base ratio (SAB) and relative apical sparing (RELAPS) were increased in CTS group compared to control group (0.94±0.43 vs 0.66±0.12, 0.90±0.31 vs 0.73±0.08, p=0.004, p=0.013, respectively). PA lateral, PA septal, inter-atrial EMD and intra-atrial EMD were significantly higher in CTS group compared to control group (78.2±12.3 ms vs 70.6±9.9 ms, 64.1±8.42 ms vs 58.3±10.1 ms, 25.8±9.09 ms vs 20.7±5.31 ms, 11.68±5.11 ms vs 8.46±3.02 ms, p=0.015, p=0.023, p=0.009 and p=.008, respectively).

Conclusion: In CTS group, mean basal strain decreased compared to control group. SAB and RELAPS which associate with CA, decreased in CTS group. Atrial EMD prolonged in CTS group. These changes may associate with increased risk of CA and AF in patients with CTS.

Keywords: Carpal tunnel syndrome, strain echocardiography, atrial electromechanical delay

INTRODUCTION

Carpal tunnel syndrome (CTS) is a peripheral nerve entrapment syndrome which is sometimes associated with amyloidosis. Amyloids accumulate over the flexor tenosynovium and transverse carpal ligament of the hand and make symptoms of CTS (1). Recent studies showed that CTS could be an early marker for amyloidosis before developing of overt symptoms of cardiac amyloidosis (CA) (1,2).

Heart failure with preserved ejection fraction (HFPEF) negatively affect quality of life and life expectation (3). Frequency of HFPEF increase in the population from years to years(4). CA is often missed cause of HFPEF (5). CA characterized with left ventricular (LV) diastolic dysfunction and impairment of LV deformation-based parameters (6, 7). Diastolic dysfunction associate with higher LV filling pressure and consequence of left atrial (LA) enlargement which makes electrical instability (8). Atrial electromechanical delay (EMD) is non-invasive method that is used marker for developing atrial fibrillation (AF) (9). There is limited data about echocardiographic parameters such as strain value of LV, diastolic parameters and atrial EMD in patients with idiopathic CTS.

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In this study, we investigated LV strain values, diastolic parameters of LV and atrial EMD in patients with idiopathic CTS. Then, we compared these parameters in CTS patients to control group.

MATERIAL AND METHOD

The study was carried out with the permission of Kayseri City Education and Research Hospital, Noninvasive Clinical Ethics Committee (Date: 04.03.2021, Decision No: 318). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Thirty-four patients who examined in electroneuromyography (EMG) and diagnosed CTS enrolled to CTS group. Twenty-four aged and sex matched volunteers were enrolled to study as a control group. Detailed neurological and EMG examinations were performed by neurology specialist. Patients with idiopathic CTS which defines as Katz diagnostic definition were included to study (10). Patients with known amyloidosis, heart failure, diabetes mellitus and secondary etiologic states for CTS such as trauma or rheumatologic disease were excluded from the study. ECG and echocardiographic examination of each patient were performed and recorded by cardiology specialist. Informed consent was signed by the participants.

Electroneuromyography

EMG studies were achieved at room temperature, using the EMG device (Dantec Keypoint system, by Natus Neurology) and the skin temperature was 32°C.

Both upper extremity median and ulnar nerves were used for conduction properties. Neurology specialist agreed with general standards of EMG. Motor conduction properties were calculated using superficial disc electrodes and orthodromic method, sensory conduction studies were performed using ring electrodes and antidromic method. Conduction velocity and amplitudes were recorded as well as motor and sensory latencies of the median and ulnar nerves.

Echocardiography

Echocardiographic examinations of all participants were performed by a cardiology specialist. Left lateral position and apical 2 and 4 cavity images were obtained from the parasternal short and long axes. M-mode was used to measure the left ventricular (LV) end-systolic and end-diastolic diameters from the parasternal long axis (at the mitral chordal level perpendicular to the long axis of the ventricle). Eccentricity index calculated as the ratio of interventricular septum thickness at end diastole over the posterior wall thickness at end diastole. Relative wall thickness's (RWT) formula is calculated as; 2x(posterior wall thickness at end diastole) /LV end-diastolic diameter. Longitudinal strain analyses of the LV were performed offline (QLab 7.0, Philips Medical Systems, USA) using zoom mode images of the LV in four and two chamber views. Point and select method was used to manually trace the endocardial edge of the LV. The region of interest was fitted to the thickness of the ventricular myocardium. In each view, the LV was automatically divided into six segments giving longitudinal strain curves from a sum of 12 segments. Septal apical to base ratio (SAB) and relative apical sparing (RELAPS) were calculated and defined as below. SAB is ratio of septal apical strain to septal basal strain. RELAPS is ratio of average apical strain values of LV to average basal and mid strain values of LV.

Atrial EMD was defined as the time interval from the onset of atrial electrical activity (P wave on surface ECG) to the beginning of mechanical atrial contraction (late diastolic A wave). All values were averaged over 3 consecutive beats. Atrial EMD was measured from the lateral mitral annulus and called 'PA lateral', from the septal mitral annulus, called 'PA septal', and from the right ventricle tricuspid annulus, called 'PA tricuspid' (9).

Statistical Analyses

The Statistical Package for Social Sciences software program (SPSS, version 25,0 for Windows) was used for statistical analysis. Continuous variables were given as means±SD; categorical variables were defined as percentages. The Shapiro-Wilk or Kolmogorov-Smirnov tests were used to test the normality of the distribution of continuous variables. Continuous variables were compared between groups using the Student's t test or Mann-Whitney U test as appropriate. The $\chi 2$ test was used for univariate analysis of the categorical variables. A probability value of $p < 0.05$ was considered significant, and 2-tailed p values were used for all statistics.

RESULTS

Baseline characteristics features were shown in **Table 1**. Age and female sex ratios were not different in two groups, statistically (52.8±11.6 years vs 53.6±11.0 years, %44 vs %41, respectively). Echocardiographic parameters were shown in **Table 2**. LA diameter and area were higher in CTS group, but the changes did not reach to statistical significancy (3.46±0.35 cm vs 3.32±0.29 cm, 13.45±2.91 cm^2 vs 12.37±2.00 cm^2 , p=0.109, p=0.120, respectively). LV diameters were similar in two groups. Mitral inflow velocities (mitral E and A wave), mitral E wave deceleration time, tissue Doppler velocities (lateral annular E' and A wave), E/A and E/E' ratios were similar in two groups. Strain values were shown in **Table 3**. Septal basal strain values increased in CTS group (-21.3±4.83 % vs -25.7±2.96 %,

p<0.001) (**Figure 1**). SAB and RELAPS were increased in CTS group compared to control group (0.94±0.43 vs 0.66±0.12, 0.90±0.31 vs 0.73±0.08, p=0.004, p=0.013, respectively) (**Figure 2**).

Table 1. Baseline demographic and clinical features of groups

	CTS group n=34	Control group n=24	P
Age, years	52.8±11.6	53.6±11.0	0.793
Female sex	15 (44%)	10 (41%)	0.424
Hypertension	16 (47%)	16 (66%)	0.183
Smoking	13 (38%)	8 (33%)	0.786
BMI, kg/m²	25.9±3.2	26.3±3.3	0.649
Systolic blood pressure, mmHg	124.7±14.7	124.6±15.0	0.801
Diastolic blood pressure,mmHg	77.7±8.4	79.2±9.9	0.549

BMI= Body mass index

Table 2. Echocardiographic parameters of groups

	CTS group n=34	Control group n=24	P
LA Diameter, cm	3.46±0.35	3.32±0.29	0.109
LA Area, cm²	13.45±2.91	12.37 2.00	0.120
LVSd, cm	3.26±0.30	3.33±0.30	0.382
LVDd, cm	4.89±0.38	5.05±0.45	0.132
IVSd, cm	1.10±0.13	1.07±0.15	0.514
PWd, cm	1.06±0.11	1.02±0.10	0.222
LVEF, %	62.60±3.72	62.8±3.10	0.808
Eccentricity index	1.03±0.053	1.05±0.077	0.493
RWT	0.435±0.048	0.405±0.036	0.014
Mitral E wave velocity, cm/s	0.78±0.16	0.80±0.12	0.645
Mitral A wave velocity, cm/s	0.67±0.08	0.63 0.9	0.149
DT, ms	176.1±23.5	170±24.4	0.398
Lateral E', cm/s	10.2±2.65	10.9 2.49	0.299
Lateral A', cm/s	8.15 1.94	7.92±1.71	0.643
E/A	1.18±0.27	1.29±0.30	0.154
E/E'	0.79±0.017	0.75±0.14	0.372
Global longitudinal strain,%	-20.2±2.4	-21.0±1.37	0.118
Mean basal strain, %	-21.3±4.83	-25.7±2.96	<0.001
Mean mid strain,%	-20.77±3.95	-20.45±2.71	0.737
Mean apical strain,%	-18.46±5.22	-16.95±1.98	0.183
SAB	0.94±0.43	0.66±0.12	0.004
RELAPS	0.90±0.31	0.73±0.08	0.013

LA=Left atrium; LVDD=Left ventricle end-diastolic dimension; LVSD=Left ventricle end-systolic dimension; IVS=interventricular septum thickness; PW=posterior wall thickness; LVEF=Left ventricle ejection fraction; DT=deceleration time; IVRT=isovolumic relaxation time; RWT= Relative wall thickness; SAB= septal apical to base longitudinal strain; RELAPS= relative apical sparing (ratio of apical longitudinal /sum of base and mid longitudinal strain)

Table 3. Atrial electromechanical delay values of groups

	CTS group n=34	Control group n=24	P
PA lateral, ms	78.2±12.3	70.6±9.9	0.015
PA septal, ms	64.1±8.42	58.3±10.1	0.023
PA tricuspid, ms	52.4±6.44	49.9±10.2	0.255
Inter-atrial EMD, ms	25.8±9.09	20.7±5.31	0.009
Intra-atrial EMD, ms	11.68±5.11	8.46±3.02	0.008
Left-atrial EMD, ms	14.15±5.47	12.25±4.79	0.177

EMD= Electromechanical delay

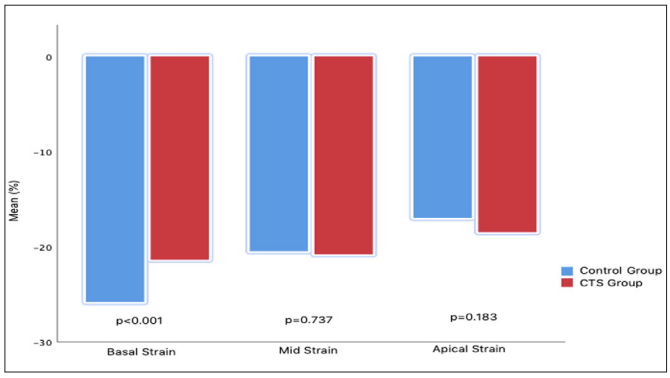

Figure 1. Longitudinal strain values of left ventricular segments of groups

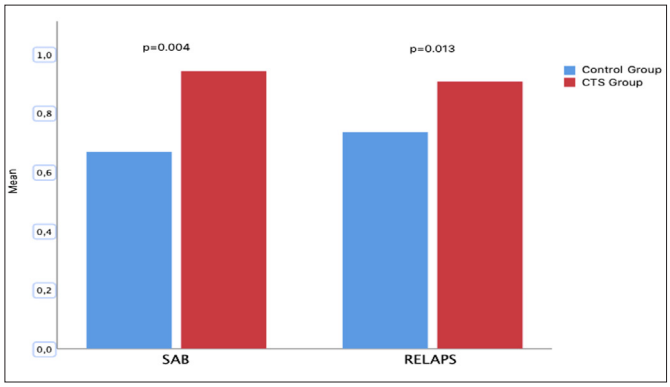

Figure 2. Septal apical to base ratio (SAB) and relative apical sparing (RELAPS) values of groups

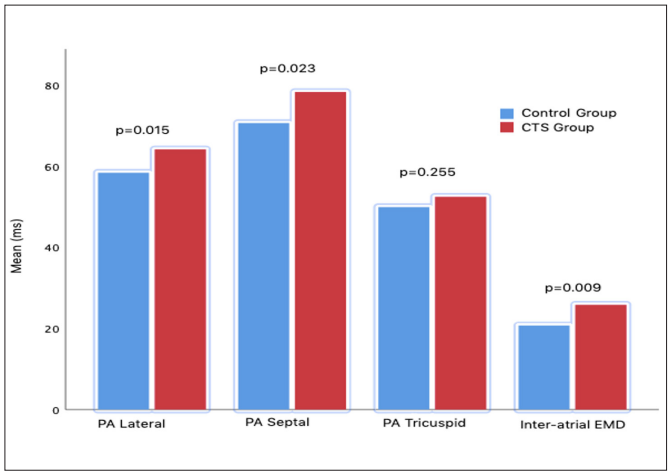

Figure 3. Atrial electromechanical delay values of groups

Table 3 showed atrial EMD values of the groups. PA lateral, PA septal, inter-atrial EMD and intra-atrial EMD were significantly higher in CTS group compared to control group (78.2±12.3 ms vs 70.6±9.9 ms, 64.1±8.42 ms vs 58.3±10.1ms, 25.8±9.09 ms vs 20.7±5.31 ms, 11.68±5.11 ms vs 8.46±3.02 ms, p=0.015, p=0.023, p=0.009 and p=.008, respectively). PA tricuspid and left-atrial EMD were also higher in CTS group but not statistically significant (52.4±6.44 ms vs 49.9±10.2 ms, 14.15±5.47 ms vs 12.25±4.79 ms, p=0.255 and p=0.177, respectively). Figure 3 showed the atrial EMD parameters of the groups.

DISCUSSION

In our knowledge, this is the first study which evaluate echo parameters in patients with idiopathic CTS. Three important findings were revealed in this study. First, there is no differences in conventional echocardiography parameters in two groups. Second, LV basal segments strain were decreased in CTS group. Another finding is that atrial EMD delayed in CTS group.

Systemic wild-type ATTR (ATTRwt) amyloidosis whose prevalence increase with age, is a disease occurred by the extracellular deposition of amyloid fibrils composed of wild-type transthyretin (TTR)(11). Systemic ATTRwt amyloidosis is rarely diagnosed in general population. Nakagawa et al. (12) found that CTS is the most common first symptom of systemic (ATTRwt) amyloidosis. CA can be diagnosed years after CTS symptoms (13). So, patients with CTS may prone to CA.

Previous studies showed basal strain values significantly decrease patients with CA. Phelan et al. (7) found global longitudinal strain significantly decreased in patients with CA. Especially basal segments were more affected from the decreasing. They found the mean value of %-8.9 for global longitudinal strain and %-3.3 for basal segments longitudinal strain. In our study, although global longitudinal strain did not decrease, basal strain values decreased in patients with CTS compared to control. We found %-21.3 value for mean basal segment longitudinal strain for CTS group. However, mean basal segments strain decreased in CTS group compared to control group, these changes did not reach to CA's values. These results may be related to initial changes.

Another important finding is that atrial EMD time prolonged in CTS group. Atrial EMD is an excellent non-invasive method which is used for predicting atrial arrhythmias such as AF (14). Previously, atrial EMD prolonged in various situations such as diastolic dysfunction, hypertension, psoriasis and Behcet disease (9, 15–17). LV hypertrophy is hypothesized mechanism for prolongation atrial EMD in hypertension, diastolic dysfunction, and other disease(15). LV hypertrophy associated with low oxygen demand to myocardium (18). This ischemia is thought link to prolongation of atrial EMD. In our study, we found that LV wall thickness increased in CTS group but not statistically significant. These changes may contribute to prolong of atrial EMD in CTS group.

CA associated with diastolic and systolic dysfunction of LV therefore it is a cause of heart failure. Recently, Sood et al. (19) reported systemic amyloidosis can be diagnosed after carpal tunnel release procedure and heart failure increased 4,68-fold the risk of systemic amyloidosis diagnosis after carpal tunnel release. Heart failure is a risk factor for atrial enlargement and AF(20). Also, heart failure associated with prolonged atrial EMD(20). In our study, the prolongation of atrial EMD in CTS group may link to tendency to heart failure in patients with CTS.

Many inflammatory statements connect to prolongation atrial EMD (9, 17). Inflammatory cells have been observed in the atria of patients with AF. Inflammatory indicators in plasma (e.g., plasma C-reactive protein, interleukin-6 and tumor necrosis factor-α) seem to associate with the achievement of electrical cardioversion and recurrence of AF following cardioversion (21). Karimi et al. (22) found that IL-1, IL-6, IL-10 and tumor necrosis factor-α increase in patients with idiopathic CTS. Increased inflammatory markers in idiopathic CTS may associate with prolonged atrial EMD and higher AF incidence. Our findings support this hypothesis

Future studies which will evaluate inflammatory markers such as IL-1, IL-6, IL-10, tumor necrosis factor- α, atrial EMD and strain echocardiography in patients with idiopathic CTS, may clearly reveal the association between inflammation and echocardiographic changes. Another study that will investigate echocardiographic parameters and carpal tunnel biopsy exhibit amyloidosis, amyloidosis severity and type, will be valuable for understanding association between idiopathic CTS and CA.

In this study, there are several limitations. First, amyloidosis can detect invasively with carpal tunnel release biopsy. If we did carpal tunnel release biopsy, echocardiographic changes could have attributed to CA. Another limitation is relatively small sample size. Data from larger sample size can give more reliable results.

CONCLUSION

In CTS group, mean basal strain decreased compared to control group. SAB and RELAPS which associate with CA, decreased in CTS group. Atrial EMD prolonged in CTS group. These changes may associate with increased risk of CA and AF in patients with CTS

ETHICAL DECLARATIONS

Ethics committee approval: The study was carried out with the permission of Kayseri City Education and Research Hospital, Noninvasive Clinical Ethics Committee (Date: 04.03.2021, Decision No: 318).

Informed consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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