The Role of Atrial Myocardial Deformation Parameters in Determining Cardioversion Success in Atrial Fibrillation Patients

Atrial Fibrillation Hastalarında Kardiyoversiyon Başarısını Belirlemede Atriyal Miyokard Deformasyon Parametrelerinin Rolü

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ABSTRACT

Aim: To investigate the role of left atrial myocardial deformation parameters measured by speckle tracking method in predicting cardioversion success in addition to conventional echocardiographic measurements in cardioversion (CV) planned patients with persistent atrial fibrillation (AF).

Material and Methods: 60 patients scheduled for cardioversion were evaluated and 40 patients with atrial fibrillation were included in the study. Patients with sinus rhythm continuing after 24 hour monitoring were classified as group 1, and patients with AF were classified as group 2. Group 1 patients are divided into 2 groups according to 1st month ECG, as sinus rhythm maintained group and AF detected group.

Results: The global left atrial strain S (LA S-S) and the global left atrial strain rate S (LA SR-S) measured before and after cardioversion were found to be significantly lower in the group with failed cardioversion (group 2) than those with successful group (group 1). The predictive value of LAVI value in cardioversion success was found to be 39 mL/m². At first month; LA SR-S measured before and after cardioversion in the maintained sinus rhythm group was significantly higher than the atrial fibrillation recurrence group. Also; the LA S-S, measured after cardioversion, was found to be significantly higher in the maintained sinus rhythm group.

Conclusion: We showed that atrial myocardial deformation parameters could play role in determining CV success in patients with persistent atrial fibrillation. In addition; we determined that the LA S-S value was as sensitive and specific parameter as LAVI in predicting cardioversion success.

Key Words: Atrial fibrillation, electrical cardioversion, left atrial volume index, left atrial strain

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ÖZET

Amaç: Kardiyoversiyon (KV) planlanan persistan atrial fibrilasyon (AF) hastalarında konvansiyonel ekokardiografik ölçümlere ek olarak benek izleme yöntemi ile ölçülen sol atrial miyokard deformasyon parametrelerinin kardiyoversiyon başarısını öngördürmedeki rolünü araştırmak.

Materiyl ve Method: Kardiyoversiyon planlanan 60 hasta değerlendirildi ve çalışmaya alınma kriterlerine uyayan 40 persistan AF hastası çalışmaya alınmıştı. 24 saat monitörizasyon sonrasında sinus ritmi devam eden hastalar grup 1, AF tespit edilen hastalar grup 2 olarak kabul edildi. Grup 1 hastaların 1. ay EKG'lerinde sinus ritimi devam eden ve AF tespit edilenlerin 2 gruba ayrıldı.

Bulgular: Kardiyoversiyonun başarısız olduğu grupta (grup 2) kardiyoversiyon öncesi ve sonrası ölçülen globel sol atrial strain S (SA S-S) ve global sol atrial strain rate S (SA SR-S), başarılı olan grubu (grup 1) göre anlamlı şekilde düşük saptandı. Kardiyoversiyon başarısını öngörme en ayırt edici sol atrial volüm indeksi (SAVI) değeri 39 mL/m² olarak bulundu. 1. ayda kardiyoversiyon öncesi ve sonrası ölçülen SA S-S, sinüs ritimi devam eden grupta, atrial fibrilasyon tekrarlayan gruba göre istatistiksel olarak anlamlı şekilde yüksek saptandı. Ayrıca; kardiyoversiyon sonrası ölçülen SA S-S, sinüs ritimi devam eden gruba anlamlı şekilde yüksek saptandı.

Sonuç: Atriyal miyokard deformasyon parametrelerinin; persistan atrial fibrilasyon hastalarındaki kardiyoversiyon başarısını belirlemekte rol oynamayabileceğini gösterdik. Ek olarak SA SR-S değerini; kardiyoversiyon başarısını öngördüğe en az SAVI kadar duyarlı ve özgül bir parametre olarak tespit ettik.

Anahtar Sözcükler: Atriyal fibrilasyon, elektriksel kardiyoversiyon, sol atrial volüm indeksi, sol atriyal strain

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INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice and is more frequent with advancing age (1-3). Structural and functional changes in the atrial myocardium (with advancing age and presence of comorbidities) lead to AF initiation and maintenance. This atrial structural remodeling is characterized by atrial fibrosis and myofiber disarray (4,5).

Traditionally the left atrium function was assessed by measuring the left atrium size or volume using two dimensional (2D) echocardiography. While these methods assess the myocardial functions of the left atrium indirectly, two dimensional speckle tracking echocardiography (2D-STE) can directly assess the myocardial left atrial (LA) functions. Speckle tracking echocardiography allows a direct and angle independent analysis of the myocardial deformation, thus providing sensitive and reproducible indices of myocardial fiber dysfunction (6). This analysis may allow a more direct assessment of the left atrial endocardial contractility and passive deformation.

The aim of our study is to evaluate the role of left atrial deformation parameters in determining cardioversion (CV) success in patients with persistent atrial fibrillation.

MATERIAL and METHODS

Study design

This study was performed on prospective cohort of patients with atrial fibrillation.

Study population

A total of 60 consecutive patients who were diagnosed with nonvalvular persistent AF (AF duration < 1 year) and were found to be eligible for an elective cardioversion (ECV) have been included in the study. Patients with a history of other arrhythmias, congenital heart disease, moderate to severe valvular heart disease, prosthetic heart valves, acute-chronic heart failure, patients with systemic or metabolic diseases that could affect the study results, patients with malignancy, acute-chronic infectious disease, post operative AF patients, chronic kidney disease (serum cr >2.0 mg/dl or GFR < 60 ml/dk), patients in which a thrombus or grade 4 spontaneous echo contrast (SEC) was detected in the left atrium or left atrial appendage were excluded from the study. Also patients with poor image quality which would lead to inadequate speckle tracking analysis were excluded from the study.

Clinical examinations

The clinical and demographic data of all the patients were recorded on admission. Clinical data including age, gender, body mass index, hypertension (patients with a systolic blood pressure value of >140 and diastolic blood pressure value of >90 mmHg as well as patients using antihypertensive drugs), were accepted as hypertensive), diabetes mellitus (patients who were under treatment with oral antidiabetic drugs, or those with a fasting blood glucose level >126 mg/dl or HbA1c ≥6.5%), coronary artery disease were recorded for study population. The body mass index (BMI) and body surface area (BSA) values were calculated according to anthropometric measures.

Echocardiographic measurements

Two-dimensional transthoracic echocardiography (TTE) was performed prior to elective cardioversion and was repeated 24 hour later post cardioversion in sinus rythm. All patients were evaluated with transesophageal echocardiographic examination (TOE) before the cardioversion. The GE-Vingmed Vivid 7 system (GE-Vingmed Ultrasound AS, Horten, Norway) ultrasound device and a 3S-RS (3.5 MHz) probe was used for echocardiographic examination. The TOE was performed with the same device using a 5 MHz multiphase probe. The examinations were performed by a cardiologist who was blinded to the patients’ clinical and demographic status. The echocardiographic examination was performed according to the guidelines of American Society of Echocardiography. The Teicholz formula was used to calculate the left ventricular ejection fraction. The Devereux formula was used to determine LV mass (LVM) and indexed by body surface area (LVMI). The left atrial long axis length and area at ventricular end-systole in the apical 4-chamber (A4C) and 2-chamber (A2C) views were used to determine left atrium volume. The left atrium volume was then calculated by the following formula: (0.85X4A1X2)/L. The correction for BSA was done in order to define the left atrium volume index (LAVI). For LA 2D-STE analysis, images of apical four and two chamber views were provided using conventional, two dimensional gray scale echocardiography with an electrocardiography recording. All images were provided at a frame rate of 70-90 frames/sec.

Study endpoints

The primary end point of our study was the investigation of the relationship between the left atrial deformation parameters and the success of the ECV and the recurrence of the AF following the ECV. The secondary end point was the comparison of the efficiency of LAVI and LA deformation parameters in terms of the clinical results.

Statistical analysis

SPSS 18.0 (SPSS Inc., Chicago, USA) and MedCalc version 12.2.10 (Mariakerke, Belgium) software were used for statistical analysis. The data were presented as mean ± standard deviation. Student’s t-test or Mann-Whitney U-test were used for the continuous variables. Fisher’s exact test or the Chi-square test was used to compare the categorical variables between the study groups. Spearman test was used for correlation analysis between left atrial deformation parameters and LAVI. Left atrial strain and strain rate parameters, LAVI were compared by the area under the receiver operating characteristic (ROC) curve in order to state cardioversion success and determine the cut off points, and the sensitivities - specificities for LAVI and left atrial deformation parameters. The p value less than 0.05 was considered as significant.

Inter and Intra-observer variability

After the first measurement by an observer in randomly selected AF patients, intra-observer variability was determined, repeating the measurement of LA global strain and strain rate two weeks later by a different observer. Inter-observer variability was determined by measuring these variables in the same database by a second observer. Blant Altman analysis method was used to assess the differences between measurements.
RESULTS

Among the study population, 15 did not undergo the ECV because of the detection of a thrombus and/or grade 4 SEC in the left atrial appendage during the transesophageal echocardiography performed in preparation for the procedure. The remaining 45 patients were applied the ECV and 5 among them were left out of the evaluation since they carried exclusion criteria. Among the 40 patients who were included in the evaluation, the mean age was 63±12.9 (31 to 86) and 57.5% (n=23) were male.

Electrical cardioversion outcomes

Sinus rhythm was achieved in %62.5 (n=25, group 1) of the patients following the ECV, whereas the AF continued in 37.5% (n=15, group 2). When the demographic, clinical and echocardiographic data of the groups were evaluated, LAVI (p<0.001) value was observed to be lower and global pre-CV LA S-S (p<0.001) , pre-CV LA SR-S (p=0.001) values were observed to be higher in the patients where sinus rhythm was achieved. The demographic, clinical and echocardiographic data of the groups are presented in Table 1.

Table 1. Clinical, demographic, and echocardiographic variables of patients according to elective cardioversion results

| Demographic and clinical variables | Sinus rhythm (Group 1) | Atrial fibrillation (Group 2) | p |
|------------------------------------|------------------------|-------------------------------|---|
| Age, years                         | 62.2±13                | 64.6±12.9                     | 0.583 |
| men, n                             | 16                     | 7                             | 0.283 |
| BMI, kg/m²                         | 28.7(24.2-43.6)        | 29.3(23.4-40.3)               | 0.812 |
| HT, n (%)                          | 14(56)                 | 8(53.3)                       | 0.870 |
| DM, n (%)                          | 9(36)                  | 5(33.3)                       | 0.864 |
| CAD, n (%)                         | 4(16)                  | 1(6.7)                        | 0.633 |

Echocardiographic variables

| LVDD, cm                           | 4.9±0.34               | 4.68±0.40                     | 0.157 |
| LVSD, cm                           | 3.3±0.44               | 3.1±0.31                      | 0.137 |
| EF, %                              | 57±7.54                | 58.8±6.10                     | 0.664 |
| LVMI, gr/m²                        | 94.9±18.2              | 91.5±19.9                     | 0.585 |
| AP-LAd, cm                         | 4.44±0.41              | 4.58±0.36                     | 0.280 |
| LAVI, mL/m²                        | 35 (22-64)             | 49 (44-72)                    | <0.001 |
| Pre-CV LA S-S,%                    | 8.8±1.6                | 7.52±0.9                      | 0.011 |
| Pre-CV LA SR-S                     | 0.8±0.21               | 0.51±0.10                     | <0.001 |
| Pre-CV LA SR-E                     | -0.96±0.15             | -0.939±0.11                   | 0.512 |

Data are presented as number (percentage), mean±standard deviation and median (minimum-maximum) values

AF - atrial fibrillation, AP-LAd - anterior - posterior left atrial diameter, BMI - body mass index, CAD - coronary artery disease, DM - diabetes mellitus, EF - ejection fraction, HT - hypertension, LAVI - left atrial volume index, LVDD - left ventricular diastolic diameter, LVMI - left ventricular mass index, LVSD - left ventricular systolic diameter, pre-CV- before cardioversion, LA S-S – left atrial systolic strain, LA SR-S – left atrial systolic strain rate, LA SR-E – left atrial early diastolic strain rate

A significant correlation was observed between the LAVI and global pre-CV LA S-S, pre-CV LA SR-S values (r: -0.365 p=0.0223 , r: -0.684 p= 0.001). When the LAVI, pre-CV LA S-S, pre-CV LA SR-S which are parameters used to predict the success of cardioversion, were compared in the ROC analysis, the area under the curve was found as 0.851±0.065 for the LAVI (p<0.001); 0.744±0.082 for the pre-CV LA S-S (p=0.0032) and 0.889±0.053 for the pre-CV LA SR-S (p<0.001). The distinguishing LAVI value in predicting cardioversion success was found as 39 ml/m² (sensitivity: 80%, specificity: 97%), while the pre-CV LA S-S value was % 7.465 (sensitivity: 92%, specificity: 60%) and the pre-CV LA SR-S value was 0.7 (sensitivity: 72%,specificity: 93%) (shown in Figure 1,2,3).

Figure 1. ROC curve analysis generated to evaluate pre-CV LA S-S as a predictor of a successful electrical cardioversion
The outcomes at the first month

According to the control ECGs performed at the end of the first month, among the patients with successful cardioversion, AF recurrence was observed in 7 patients while the sinus rhythm was maintained in 18 patients. When the demographic, clinical and echocardiographic data of the groups are evaluated, LVMI (p: 0.018), LVM (p: 0.049), AP-LAd (p=0.005) and LAVI (p<0.001) values were observed to be lower in the maintained sinus rhythm group (MSR group). There was no significant difference in terms of pre-CV LA S-S (p:0.333) values between two groups. The pre-CV LA S-S (p<0.001), post-CV LA S-S (p:0.004) and post-CV LA SR-S (p<0.001) values were observed to be higher in the MSR group compared to the AF recurrence (AFR) group. The demographic, clinical and echocardiographic data of the groups are presented in Table 2.

Table 2. Clinical, demographic, and echocardiographic variables of patients with successful electrical cardioversion according to their 1st month ECG results

| Demographic and clinical variables | Sinus rhythm n:18 | Atrial fibrillation n:7 | p |
|-----------------------------------|-------------------|-------------------------|---|
| Age, years                        | 61.5(31-80)       | 66(49-80)               | 0.193 |
| men, n                            | 12                | 4                       | 0.673 |
| BMI, kg/m²                        | 28.8(24.2-33.2)   | 28.2(26.2-43.6)         | 0.904 |
| HT, n (%)                         | 9(50)             | 5(71.4)                 | 0.407 |
| DM, n (%)                         | 6(33.3)           | 3(42.9)                 | 0.673 |
| CAD, n (%)                        | 2(11.1)           | 2(28.6)                 | 0.548 |

| Echocardiographic variables       |                   |                         |   |
|-----------------------------------|-------------------|-------------------------|---|
| LVDD, cm                          | 4.75(4.3-5.5)     | 5.0(4.4-5.4)            | 0.260 |
| LVSD, cm                          | 3.1(2.4-4.3)      | 3.4(3.0-4.0)            | 0.314 |
| EF, %                             | 60.5(35-65)       | 55(50-65)               | 0.394 |
| LVMi, gr/m²                       | 93.45(67.7-112.4) | 109.1(68.1-140.4)       | 0.018 |
| AP-LAd, cm                        | 4.3(3.8-4.8)      | 5.0(4.0-5.4)            | 0.005 |
| LAVI, mL/m²                       | 33(22-39)         | 63(38-64)               | <0.001 |
| Pre-CV LA S-S,%                   | 8.44(6.40-13.8)   | 8.40(7.60-9.20)         | 0.333 |
| Pre-CV LA SR-S                    | 0.87(0.53-1.28)   | 0.56(0.42-0.71)         | <0.001 |
| Pre-CV LA SR-E                    | -0.99(-1.20--0.71)| -0.91(-1.01--0.84)      | 0.204 |
| Post-CV LA S-S,%                  | 10.48(8.18-15.97) | 9.15(8.15-10.62)        | 0.004 |
| Post-CV LA SR-S                   | 0.92(0.61-1.33)   | 0.61(0.46-0.73)         | <0.001 |
| Post-CV LA SR-E                   | -0.99(-1.24--0.72)| -0.91(-1.01--0.71)      | 0.115 |

Data are presented as number (percentage) and median (minimum-maximum) values

AF - atrial fibrillation, AP-LAd - anterior - posterior left atrial diameter, BMI - body mass index, CAD - coronary artery disease, DM - diabetes mellitus, EF - ejection fraction, HT - hypertension, LAVI - left atrial volume index, LVDD - left ventricular diastolic diameter, LVMI - left ventricular mass index, LVSD - left ventricular systolic diameter, pre-CV- before cardioversion, post-CV – after cardioversion, LA S-S – left atrial systolic strain, LA SR-S – left atrial systolic strain rate, LA SR-E – left atrial early diastolic strain rate
Twenty patients were randomly selected for the assessment of intra- and inter-observer variabilities in measurements of LA strain and strain rate parameters. Bland-Altman analysis results of intra- and inter-observer variabilities were shown in Table 3.

### Table 3. Bland-Altman analysis results of intra- and inter-observer variabilities for left atrium strain and strain rate parameters.

| Interobserver | Change difference | 95% CI | Intraobserver | Change difference | 95% CI |
|---------------|------------------|-------|--------------|------------------|-------|
| Pre-CV Strain (%) | 0.02 | -0.325 to 0.358 | 0.07 | 0.02 to 0.121 |
| Pre-CV Strain Rate (1/s) | -0.01 | -0.131 to 0.103 | 0.01 | -0.01 to 0.029 |
| Post-CV Strain (%) | 0.13 | -0.223 to 0.492 | 0.02 | -0.628 to 0.678 |
| Post-CV Strain Rate (1/s) | -0.07 | -0.156 to 0.025 | -0.06 | -0.145 to 0.026 |

CI: Confidence interval, E: Early diastole, related to left atrium conduit function, S: Systol, related to left atrium reservoir function

### DISCUSSION

Atrial fibrillation is the leading type of arrhythmia that causes increased cardiac morbidity and mortality. Diminished left atrial compliance besides an increase in the left atrium pressure plays a crucial role in the onset and continuation of AF. Restoring and maintaining the sinus rhythm in patients with AF may prevent left atrial dilatation and the development of atrial cardiomyopathy (7).

There is only limited data about the role of the LA deformation parameters in the success of the CV and the maintenance of the sinus rhythm in patients with AF. Previous studies have shown that the patients with AF have diminished LA deformation values compared to the healthy individuals (8-11).

In a study conducted on patients with lone AF, who had undergone CV within 3 months, it was observed that the left atrial myocardial deformation characteristics were diminished in all the walls of left atrium and found that the peak systolic strain and strain rate values measured before the CV were significantly reduced in the recurrence group. The authors have not observed any significant difference in the early diastolic atrial myocardial velocity, strain and strain rate values (8). In a study by Wang et al., the early diastolic SR value was observed to be lower in the group in which AF recurrence was observed after successful CV due to AF. This value was determined to be the predictor of CV success (10). In our study, no significant difference was observed between the successful and unsuccessful CV groups, or between the groups with or without AF recurrence in terms of the LA SR-E (early diastolic SR) values measured before the CV and on the 1st day after the CV. During early diastole, the left atrial functions are greatly affected by the left ventricular compliance. This finding has been revealed through the strong correlation between the strain and strain rate values in early diastole and the left ventricular global diastolic function parameters. Di Salvo et al., have associated the deformation that occurs in the left atrium in early diastole with left ventricular diastolic functions (8). For this reason, it is only expectable that there is no difference between the groups in terms of the atrial deformation parameters in early diastole.

In the previous studies, the LA strain and SR values have been assessed using the tissue Doppler technique (8,10). In these studies based on tissue Doppler, the analyses were limited to the specific segments of the left atrium. The 2D speckle tracking echocardiography gives the opportunity to visualise all the segments of the LA wall. The left atrial endocardial contractility and passive deformation parameters can be evaluated more directly by 2D-STE (12).

In a study conducted on patients with mitral insufficiency and a history of paroxysmal atrial fibrillation (PAF), it has been shown that the LA global strain values are significantly lower in the patients with a history of PAF compared to the other group.

A history of PAF in patients with mitral insufficiency is associated with the severity of the impairment in the left atrial myocardial reservoir functions and the 2D-STE gives the chance to evaluate the left atrial dysfunction noninvasively in these patients (13). In another study, in 70 patients who had undergone CABG surgery, decreased LA strain and SR values measured by the 2D-STE were observed to be independent predictors of postoperative AF development in addition to advanced age, atrial fibrillation, and mitral valve regurgitation (14).

Hwang et al., evaluated the atrial myocardial deformation parameters by the speckle tracking method in a radiofrequency ablation (RFA) study and the global left atrial systolic strain and strain rate values were observed to be lower in the patients with AF in comparison to the healthy volunteers. The recurrence rates during the 9 months follow up period were found to be associated with sex, LAVI and global strain in RFA group (15). Mirza et al., have suggested that the decreased LA strain rate values are independent predictors of AF recurrence observed after RFA (16). In our study, the LA S-S and the LA SR-S values measured before the CV were observed to be lower in the unsuccessful CV group. Also, the LA SR-S values measured by the speckle tracking method in patients with AF-R group were found to be significantly lower compared to the patients in MSR group. In various studies, the atrial remodelling associated with AF has been demonstrated to be caused by varying degrees of fibrosis, atrial myocyte hypertrophy, disrupted myofibillary organization and apoptosis (17,18). The increased left atrial fibrosis observed in AF leads to an impairment in the left atrial reservoir function. As indicators of the reservoir function; the LA S-S and LA SR-S values measured by the 2D-STE indicate the success of the CV and serve as predictors of maintenance of sinus rhythm after one month in our study. However, the duration of persistent AF may affect the predictive value of the left atrial deformation parameters in cardioversion success.

In a prospective cardioversion study, it has been demonstrated that the change in LA peak systolic longitudinal strain after CV may be a useful predictor of recurrent AF (19). Also, LA strain rate values in AF patients were observed to be lower than the healthy controls in previous studies (20,21). In our study, when the patients with successful cardioversion after one month were compared to those with AF recurrence, no significant difference was observed between groups in terms of the LA S-S value measured before the CV. However, the LA S-S value measured on the 1st day after the CV was found to be significantly higher in the patients with sinus rhythm. In the patients with successful cardioversion, the improvement in the left atrial functions is accepted as functional positive atrial remodelling (22). Thomas et al., have evaluated the left atrial deformation functions by the speckle tracking method in the successful CV patients with chronic AF by using strain rate imaging in pre and post CV period. They observed that after the sinus rhythm was established, the late atrial SR gradually increased on the 1st day, 1st month and 6th month following the CV (23). In the light of these findings, the improvement in the left atrial SR observed in the early phase after the CV may be associated with a structural positive remodelling as well as the restoration of the atrial contraction. The improvement in the atrial functions is observed within a maximum of 4 weeks subsequent to the successful CV (23).
In a study by Marchese et al., the LAVI has been found to be a strong and an independent parameter to predict the success of CV and maintenance of sinus rhythm [24]. In another study, the LAVI and the LVMi were observed to be significantly increased in hypertensive patients accompanied by paroxysmal atrial fibrillation compared to the non-hypertensive patients [25]. Hypertension increases the LV wall stress and leads to myocardial wall thickening, myocyte hypertrophy and myocardial fibrosis. Decreased myocardial relaxation and increased LV diastolic thickness lead to LV diastolic filling pressure. These findings culminate in left atrial expansion, which is accepted as an indicator of LV diastolic dysfunction [26-28].

In our study, the LAVI was observed to correlate with the LA S'-S and LA SR- S values measured before the CV and the LAVI value was observed to be lower in the group with successful cardioversion compared to the group with unsuccessful cardioversion. Similarly, the LAVI and LVMi values were observed to be significantly lower in the MS group.

In addition to the existing parameters, our study has showed that the atrial myocardial deformation parameters may play a role in determining the success of CV in patients with persistent atrial fibrillation. In the light of these findings, the 2D-STE may give more detailed information about left atrial functions.

CONCLUSION

In addition to the existing parameters, our study has showed that the atrial myocardial deformation parameters may play a role in determining the success of CV in patients with persistent atrial fibrillation. In the light of these findings, the 2D-STE may give more detailed information about left atrial functions.

Conflict of interest

No conflict of interest was declared by the authors.

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