The significance of the left atrial volume index in cardioversion success and its relationship with recurrence in patients with non-valvular atrial fibrillation subjected to electrical cardioversion: a study on diagnostic accuracy

Elektriksel kardiyoversiyon planlanan valvüler olmayan atriyal fibrilasyonlu hastalarda sol atriyum volüm indeksinin kardiyoversiyon başarısı ve erken dönem atriyal fibrilasyon tekrarı ile ilişkisi; Bir tanısal doğruluk çalışması

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Abstract

Objective: The aim of this study was to assess the predictive value of the left atrial volume index (LAVI) in electrical cardioversion (ECV) and observe the recurrence rate of atrial fibrillation (AF) after a successful ECV in patients with non-valvular atrial fibrillation.

Method: This study was designed as a diagnostic accuracy and prospective cohort study. Eighty patients (mean age 62±12 years; 52.5% female) were enrolled in study. LAVI was measured using the area-length method and the indexed body surface area. Patients in whom the sinus rhythm (SR) was established following the ECV were assessed according to the clinical and electrocardiography (ECG) findings at the first month and grouped as those with continued SR or recurrent AF. The Student's t, Mann-Whitney U, Fisher's exact, Chi-square tests, ROC and logistic regression analyses were used for statistical analysis.

Results: Subsequent to the ECV, SR was achieved in 62.5% (n=50) of the patients. In those where SR was established, the AP-Lad (4.32±0.62 vs. 4.77±0.4 cm/p=0.002) and LAVI (35.3±11.5 vs. 53.1±10.1 mL/m^2/p<0.001) values were observed to be lower. ECV success was found to be associated only with the LAVI (OR:1.122, 95%CI: 1.058-1.191, p<0.001). The AUC was found as 0.892±0.041 for the LAVI (95% CI:0.075-0.285, p<0.001). During the controls at the end of the 1st month, SR was maintained in 72% (n=36) of the successful ECV group. Among the patients with maintained SR, the antero-posterior left atrial dimension (4.17±0.62 vs. 4.72±0.5 cm/p=0.004) and LAVI (30.8±6.2 vs. 46.8±13.9 mL/m^2/p<0.001) values were also observed to be lower. Only the LAVI was found to be associated with the recurrence of the AF (OR:1.355, 95% CI: 1.154-1.591, p<0.001). The AUC was found as 0.950±0.029 for the LAVI (95% CI:0.063-0.313, p=0.003)

Conclusion: Lower LAVI values before the ECV are strong and independent predictors of the success of the ECV and the maintenance of SR after a successful ECV. *(Anadolu Kardiyol Derg 2013; 13: 18-25)*

Key words: Atrial fibrillation, cardioversion, left atrial volume index, regression analysis, diagnostic accuracy, sensitivity, specificity

Özet

Amaç: Çalışmamızın amacı, valvüler olmayan atriyal fibrilasyonlu (AF) hastalarda, sol atriyum volüm indeksi (SAVİ) ile elektif elektriksel kardiyoversiyon (EKV) başarısı ve başarılı EKV sonrası erken dönem AF tekrarı arasındaki ilişkiyi araştırmaktır.

Yöntem: Bu araştırma tanısal ve ileriye dönük kohort bir çalışma olarak tasarlandı. Çalışmamıza toplam 80 hasta (ortalama yaş 62±12 yıl, %52.5 kadın) alındı. Sol atriyal volüm alan-uzunluk yöntemi ile belirlendi, vücut-yüzey alanına bölünerek SAVİ hesaplandı. Hastalar öncelikle EKV'nin sonucuna göre sinüs ritmi (SR)-AF olarak ve EKV sonrası SR sağlananlar kendi içerisinde 1. ay klinik ve elektrokardiyografi (EKG) bulgularına göre SR devam edenler ve AF gelişenler olarak ayrıldı. Student's t, Mann-Whitney U, Fisher's exact, Chi-square testleri, ROC ve lojistik regresyon analizleri istatistiksel değerlendirme için kullanıldı.

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Bulgular: EKV sonrası hastaların %62.5'inde (n=50) SR sağlandı. SR sağlananlarda ÖA-SAÇ (4.32±0.62-4.77±0.4 cm/p=0.002) ve SAVİ (35.3±11.5-53.1±10.1 mL/m^2/p<0.001) değerleri daha düşük bulundu. Regresyon analizinde EKV başarısı sadece SAVİ ile ilişkili bulundu (OR:1.122, %95 CI:1.058-1.191, p<0.001). SAVİ için eğri altında kalan alan 0.892±0.041 bulundu (%95 CI:0.075-0.285, p<0.001). Birinci ay kontrollerinde başarılı EKV grubunun %72'inde (n=36) SR devam etmekteydi. SR devam edenlerde ön-arka-sol atriyal çap (4.17±0.62-4.72±0.5 cm/p=0.004) ve SAVİ (30.8±6.2-46.8±13.9 mL/m^2/p<0.001) değerleri düşük bulundu. Regresyon analizinde AF rekürrensi ile sadece SAVİ ilişkili bulundu (OR: 1.355, %95 CI:1.154-1.591, p<0.001). SAVI için eğri altında kalan alan 0.950±0.029 bulundu (%95 CI:0.063-0.313, p=0.003).
Sonuç: Bu çalışmanın sonuçları, EKV planlanan valvüler olmayan AF'li hastalarda düşük SAVİ değerlerinin EKV başarısını ve AF rekürrensini tahmin etmede güçlü ve bağımsız bir belirleyici olabileceğini göstermektedir. *(Anadolu Kardiyol Derg 2013; 13: 18-25)*
Anahtar kelimeler: Atriyal fibrilasyon, kardiyoversiyon, sol atriyum volüm indeksi, regresyon analizi, tanısal doğruluk, özgüllük, duyarlılık

Introduction

External transthoracic synchronized electrical cardioversion (ECV) is a simple, safe and highly successful technique used for the restoration of the sinus rhythm in patients with AF. The initial success of ECV has been reported as 50-90% in previous studies. However, 60% of the patients are reported to experience a recurrence of AF within three to six months, with the highest number of recurrences observed in the first two months (1). Understanding the factors relevant to the recurrence of AF after ECV may lead to better management strategies and a better selection of the patients for ECV. Many investigators have tried to find out the factors influencing the recurrence of AF after ECV, and various potential predictors have been reported including the age, underlying heart disease, duration of AF, cardiovascular risk factors and the size of the left atrium (LA) (2).

The relationship among the size of the LA, success of the CV and the recurrence of the AF has been investigated in various studies using the antero-posterior left atrial dimension (AP-LAd) measurement method (3, 4). In a limited number of studies where patients in which a sinus rhythm (SR) was established following a successful electrical or medical cardioversion were evaluated together, the link between the recurrence of the AF and LAVI has been shown to be stronger than the relationship between AF and AP-LAd. However, the relationship of these values with the established SR and the subsequent recurrence of AF in patients who have solely undergone ECV have not been studied in detail (5).

The aim of our study is to evaluate of the efficiency of the LAVI measurement performed before the cardioversion in predicting the success of the ECV and the recurrence of the AF subsequent to the procedure in patients with nonvalvular atrial fibrillation for longer than a week, in which an electrical cardioversion is planned.

Methods

Study design

This study was designed as a study on diagnostic accuracy performed on prospective cohort of patients with AF.

Study population

A total of 110 consecutive patients over the age of 18 who presented to the cardiology clinic of Akdeniz University Faculty of Medicine between August 2010 and May 2011 and were diagnosed with nonvalvular persistent AF based on the patient history, physical examination and electrocardiography (ECG) findings; and were found to be eligible for an elective ECV procedure have been enrolled in the study.

Patients with a history of other atrial arrhythmias, congenital heart disease, moderate to severe valvular heart disease (valvular regurgitation was assessed semiquantitatively by the color Doppler method and valvular stenosis was assessed by Doppler analysis) (6), mechanical or bioprosthetic heart valves, ejection fraction <45%, decompensated heart failure, permanent pacemaker, history of electrical or medical cardioversion, history of cerebrovascular events, thyroid dysfunction, individuals with systemic or metabolic diseases that could adversely affect the cardiac structure and functions, and those who were diagnosed with and treated for acute coronary syndrome within the last 3 months were excluded from the study. In addition, patients who had undergone surgical procedures due to cardiac reasons within last 6 months and non-cardiac reasons within the last 3 months were also excluded from the study. Finally, patients in which a thrombus or grade 4 spontaneous echo-contrast (SEC) was detected in the LA or LA appendage during the transesophageal echocardiography performed before the electrical cardioversion were excluded from the study.

The enrolled patients were grouped according to the duration of the AF as those who had AF for less than 3 months and those who had AF for a longer period.

Clinical examinations

The clinical and demographic data of all the patients were recorded before the echocardiographic evaluation. Clinical data including age, sex, height, weight, hypertension (in the physical examination, patients with a systolic blood pressure value of >140 and diastolic blood pressure value of >90 mmHg after averaging three separate blood pressure measurements taken at 10 minute intervals, as well as patients receiving antihypertensive treatment, were accepted as hypertensive), diabetes mellitus (patients who were already diagnosed with diabetes mellitus and under treatment, or those with a fasting blood sugar level >126 mg/dL or HbA1c ≥6.5%), coronary artery disease (those under suspicion of CAD according to the patient history, physical examination, ECG, echocardiography findings and those with angiographically proven coronary artery disease), medications and duration of the AF were recorded for each patient. Duration

of the AF was defined as the time from the onset of the AF documented by an ECG until the time of enrollment in the study. The body mass index (BMI) and body surface area (BSA) values were calculated based on the anthropometric measures.

Echocardiographic measurements

Two-dimensional transthoracic (TTE) and transesophageal (TOE) echocardiographic examinations were carried out in all patients before the ECV. Echocardiography was performed in the left lateral decubitus position with the GE-Vingmed Vivid 7 system (GE-Vingmed Ultrasound AS, Horten, Norway) ultrasound device and a 3S-RS (3.5 MHz) probe. The TOE was performed with the same ultrasound device using a 5 MHz multiphase probe. The examinations were performed by an experienced cardiologist blinded to the patients' clinical and demographic characteristics. The echocardiographic data evaluated in the study were determined by calculating the arithmetic mean of 5 consecutive cycles.

Images were obtained from the parasternal long axis and apical position using the 2D, M-Mode and Doppler echocardiographic techniques. The 2D and M-mode echocardiographic examinations were performed according to the guidelines of American Society of Echocardiography for the evaluation of the left ventricle wall thickness, systolic and diastolic dimension, left atrial dimension, and the calculation of the values based on the related functions. The left ventricular ejection fraction was calculated according to the Teicholtz formula based on the diastolic and systolic diameters of the left ventricle. LV mass was determined by the Devereux Formula and indexed body surface area (7). The LA volume was determined using the biplane area-length method after measuring the area and the long axis length of the LA at ventricular end-systole in the apical 4-chamber (A1) and 2-chamber (A2) views. The LA volume was then calculated according to the following formula: (0.85XA1XA2)/L. The LA volume index was defined after the correction for BSA (8).

Electrical cardioversion

Before the ECV was performed, the procedure and its risks were explained to all the patients. After this information, verbal and written consent was obtained from all the patients expressing their acceptance of the procedure. The study was approved by the local ethics committee of Akdeniz University.

In our study, the ECV procedure was performed by a cardiologist blinded to the demographic, clinical, and echocardiographic data of the patients. Intravenous unfractionated heparin was administered to all the patients before the cardioversion under monitoring of a target activated partial thromboplastin time (aPTT) of 1.5-2 times the normal rate for 24 hours. The elective ECV cardioversion procedure was performed routinely. Briefly, an experienced anesthesiologist applied general anesthesia with intravenous midazolam (0.05 mg/kg) for the DC cardioversion while the patients were constantly monitored. Shocks were administered using a monophasic defibrillator (Hewlett Packard Codemaster). Paddles were placed in the second right intercostal space and laterally on the left side along the midaxillary line. External monophasic DC shocks were applied by an experienced cardiologist, starting with 200 Joules (J) and followed by 300J and 360J. The procedure was discontinued upon failure to achieve a sinus rhythm (SR) despite two shocks on the highest energy level (360J). Those patients in which SR was achieved and maintained for 24 hours following the procedure without recurrence of AF were accepted as successful cases of ECV. Patients in which no SR was achieved, or those in which AF returned within the first 24 hours after the ECV in spite of the initial SR were accepted as unsuccessful cases of cardioversion.

Clinical follow-up

Patients with maintained SR subsequent to a successful ECV were prescribed coumadin for 6 weeks in order to achieve an INR of 2 to 3. Following the successful electrical cardioversion, the selection of the antiarrhythmic therapy to prevent the recurrence of AF, and the upstream therapy [angiotensin converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB), statins, spironolactone, omega-3 polyunsaturated fatty acids (PUFA)] were left at the physician's discretion that performed the ECV. Patients with SR following the ECV were divided into two groups as those with continued SR and those with recurrent AF based on their ECG taken during their control at the 1st month. The evaluation of the patients at the end of the 1st month was carried out by the same cardiologist who was blinded to the clinical and echocardiographic data of the patients before the ECV.

Study endpoints

The primary endpoint of our study was the investigation of the relationship between the LAVI and the success of the ECV and the recurrence of the AF following the ECV. The secondary endpoint was the comparison of the efficiency of LAVI and AP-LAd in terms of the clinical results.

Statistical analysis

Data were analysed using the SPSS 18.0 (SPSS Inc., Chicago, USA) and MedCalc version 12.2.10 (Mariakerke, Belgium) software. Descriptive statistics like frequency distribution, mean value and standard deviation were used to define the sample. We used Student's t-test for the continuous variables with normal distribution, while the Mann-Whitney U-test was employed for the continuous variables outside the normal distribution between the ECV success and the recurrence risk of the atrial fibrillation groups. Fisher's exact test or the Chi-square test was applied to compare the influence of the categorical variables on the success of the ECV and the recurrence risk of the AF. As a result of the univariate analyses, the variables related to the ECV success and AF recurrence have been specified. Multiple logistic regression analyses were employed to find out the factors affecting the ECV success and the recurrence risk of the AF.

AP-LAd and LAVI parameters used to assess the ECV success and predict the recurrence risk of AF were compared in terms of the area under the receiver operating characteristic (ROC) curve. We conducted the ROC curve analysis to determine the cut -off point, and the sensitivities and specificities for LAVI and AP-LAd. We used the method by DeLong et al. (9) for the comparison of the ROC curves. All tests were two sided and a result of $p<0.05$ was considered as significant.

Results

Among the patients enrolled in this study on ECV, 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 95 patients were applied the ECV and 15 among them were left out of the evaluation since they carried exclusion criteria like thyroid dysfunction (n=4), moderate to severe valvular heart disease (n=6), EF<45% (n=3), or a previous cardioversion (n=2). Among the 80 patients who were included in the evaluation, the mean age was 62±12 (25 to 82) and 52.5% (n=52) were female.

Electrical cardioversion outcomes

SR was achieved in 62.5% (n=50) of the patients following the ECV, whereas the AF continued in 37.5% (n=30). When the demographic, clinical and echocardiographic data of the groups were evaluated, the age (p=0.015), LAVI (p<0.001) and AP-LAd (p=0.002) values were observed to be lower in the patients where SR was achieved. On the other hand, the number of the individuals with a duration of the AF below 3 months was higher in the same group (p=0.041). The demographic, clinical and echocardiographic data of the groups are presented in Table 1. The mean energy level for a successful ECV was 261.14±26.64J (minimum: 200, maximum: 305, median: 250). A moderate correlation was observed between the LAVI and the energy level required for a successful ECV (r: 0.597 p<0.001).

In the multiple logistic regression analysis carried out with the model based on the parameters related to ECV success, only the relationship with LAVI was observed to be prevalent. Each 1 ml/m^2 increase in the LAVI was found to be related with a 13% decrease in the success of the ECV independently from the other parameters (p<0.001). The results of the regression analysis where the related factors of cardioversion success are evaluated are presented in Table 2.

When the AP-LAd and LAVI, which are parameters used to predict the success of cardioversion, were compared in the ROC analysis, the area under the curve was found as 0.892±0.041 for the LAVI (p<0.001) and 0.712±0.058 for the AP-LAd (p=0.002). The distinguishing LAVI value in predicting cardioversion success was found as 40.5 ml/m^2 (sensitivity: 97%, specificity: 88%), while the AP-LAd value was 46.5mm (sensitivity: 73%, specificity: 63%). The sensitivity and specificity of the LAVI in predicting the success of ECV was found to be higher than the AP-LAd (p<0.001). The comparison of the AP-LAd diameter and the LAVI through the ROC analysis in terms of predicting the success of the ECV is presented in Figure 1A.

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

Demographic and clinical variables	Sinus rhythm (n=50)	Atrial fibrillation (n=30)	p
Age, years	59.54±12.9 61 (25-82)	66.5±8.3 69 (50-78)	0.015[b]
Women, n (%)	24 (48)	18 (60)	0.298[c]
BMI, kg/m^2	28.2±5.06 27.38 (18.52-43.7)	28.1±3.66 28.63 (20.02-35.76)	0.619[b]
HT, n (%)	33 (66)	22 (73.3)	0.493[c]
DM, n (%)	13 (26)	9 (30)	0.698[c]
CAD, n (%)	9 (18)	1 (3.3)	0.081[d]
AF duration<3 months	34 (73.9)	12 (40)	0.014[c]
ACE/ARB, n (%)	26 (59.1)	24 (66.7)	0.486[c]
Beta-blocker, n (%)	24 (48)	15 (50)	0.862[c]
Statin, n (%)	3 (6)	4 (13)	0.261[d]
Echocardiographic variables			
LVDD, cm	4.73±0.54	4.82±0.61	0.505[a]
LVSD, cm	3.15±0.45	3.27±0.58	0.316[a]
EF, %	60.4± 7.4 62 (45-72)	59.1±8.4 60 (45-76)	0.427[b]
LVMI, gr/m^2	119.3± 33.3 140 (62-215)	121.5±36.6 170 (66-238)	0.968[b]
AP-LAd, cm	4.32±0.62 3.5 (3-5.4)	4.77±0.4 4.9 (3.6-5.8)	0.002[b]
LAVI, mL/m^2	35.3±11.5 38 (21-78)	53.1±10.1 51 (28-72)	<0.001[b]

Data are presented as number (percentage), mean±standard deviation and median (minimum-maximum) values
a- independent samples t-test, b- Mann-Whitney U test, c- Pearson Chi-Square test, d- Fischer Exact test
ACE/ARB - angiotensin converting enzyme inhibitor/angiotensin II receptor blocker, 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

Table 2. Predictors of the electrical cardioversion success: multiple logistic regression analysis

Parameters	β	OR	95% CI	p
Age	0.029	1.030	0.968-1.096	0.353
AP-LAd	0.021	1.021	0.900-1.158	0.746
LAVI	0.116	1.122	1.058-1.191	<0.001

AP-LAd-anterior - posterior left atrial diameter, CI - confidence interval, LAVI - left atrial volume index, OR - odds ratio

Table 3. Demographic, clinical and echocardiographic variables of patients with successful electrical cardioversion according to their electrocardiography result 1 month after cardioversion

Demographic and clinical variables	Sinus rhythm (n=36)	Atrial fibrillation (n=14)	p
Age, years	57.2±13.7	65.6±8.6	0.037[a]
Women, n (%)	14 (39)	10(71)	0.039[c]
BMI, kg/m^2	27.1±4.1 24.5 (18.52-39.79)	31.1±6.2 28.6 (26.04-43.7)	0.047[b]
HT, n (%)	23 (63)	10 (71)	0.746[d]
DM, n (%)	9 (25)	4 (29)	0.999[d]
CAD, n (%)	7 (19)	2 (14)	0.999[d]
AF duration<3 months	25 (69)	9 (64)	0.746[d]
Energy level, J	256.22±27.91 245 (200-305)	273.78±18.39 265 (250-287)	0.034[b]
ACE/ARB, n (%)	21 (58)	5 (36)	0.151[c]
Beta -blocker, n (%)	19 (52)	5 (36)	0.278[c]
Statin, n (%)	3 (8)	0 (0)	0.265[d]
Echocardiographic variables			
LVDD, cm	4.65±0.54	4.94±0.52	0.088[a]
LVDD, cm	3.1±0.44	3.27±0.49	0.250[a]
EF, %	61.4±6.6 60 (45-72)	58±8.9 59 (45-69)	0.184[b]
LVMI, gr/m^2	111.5±28.8	139.5±36.6	0.006[a]
AP-LAd, cm	4.17±0.62	4.72±0.5	0.004[a]
LAVI, mL/m^2	30.8±6.2 34 (21-54)	46.8±13.9 49 (35-78)	<0.001[b]

Data are presented as number(percentage), mean±standard deviation and median (minimum-maximum) values
a- independent samples t-test, b- Mann-Whitney U test, c- Pearson Chi-Square test, d- Fischer Exact test
ACE/ARB - angiotensin converting enzyme inhibitor/angiotensin II receptor blocker, 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

Table 4. Predictors of AF recurrence: The multiple logistic regression analysis results

Parameter	β	OR	95%CI	p
Age	0.066	1.069	0.971-1.176	0.175
Sex	0.638	0.528	0.099-2.814	0.455
BMI	0.165	1.180	0.936-1.487	0.162
LVMI	0.010	0.010	0.963-1.018	0.485
AP-LAd	0.044	1.045	0.852-1.281	0.673
LAVI	0.304	1.355	1.154-1.591	<0.001

AF - atrial fibrillation, AP-LAd-anterior - posterior left atrial diameter, BMI - body mass index, CI - confidence interval, LAVI - left atrial volume index, LVMI - left ventricular mass index, OR - odds ratio

The outcomes at the first month

According to the control ECGs performed at the end of the first month, among the patients in which SR was achieved, AF was observed to recur in 28% (n=14), while the SR continued in 62% (n=36). When the demographic, clinical and echocardiographic data of the groups are evaluated, the age (p=0.037), female sex (p=0.039), and the BMI (p=0.047), LVMI (p=0.006), AP-LAd (p=0.004), and LAVI (p<0.001) values were observed to be higher in the group where AF was observed to recur. For the antiarrhythmic therapy, 28% (n=14) of the patients with SR were prescribed amiodarone and 72% (n=36) were given propafenone. No difference was observed between amiodarone and propafenone in relation to the recurrence of AF (p>0.05). At the end of the first month, no difference was observed in terms of the ACE/ARB use between the patients in which SR was maintained, and in which the AF recurred (p=0.151). In the group where AF was observed to recur, the energy level required to achieve SR during the CV was higher than those where SR was maintained (p=0.034). The demographic, clinical and echocardiographic data of the groups are presented in Table 3.

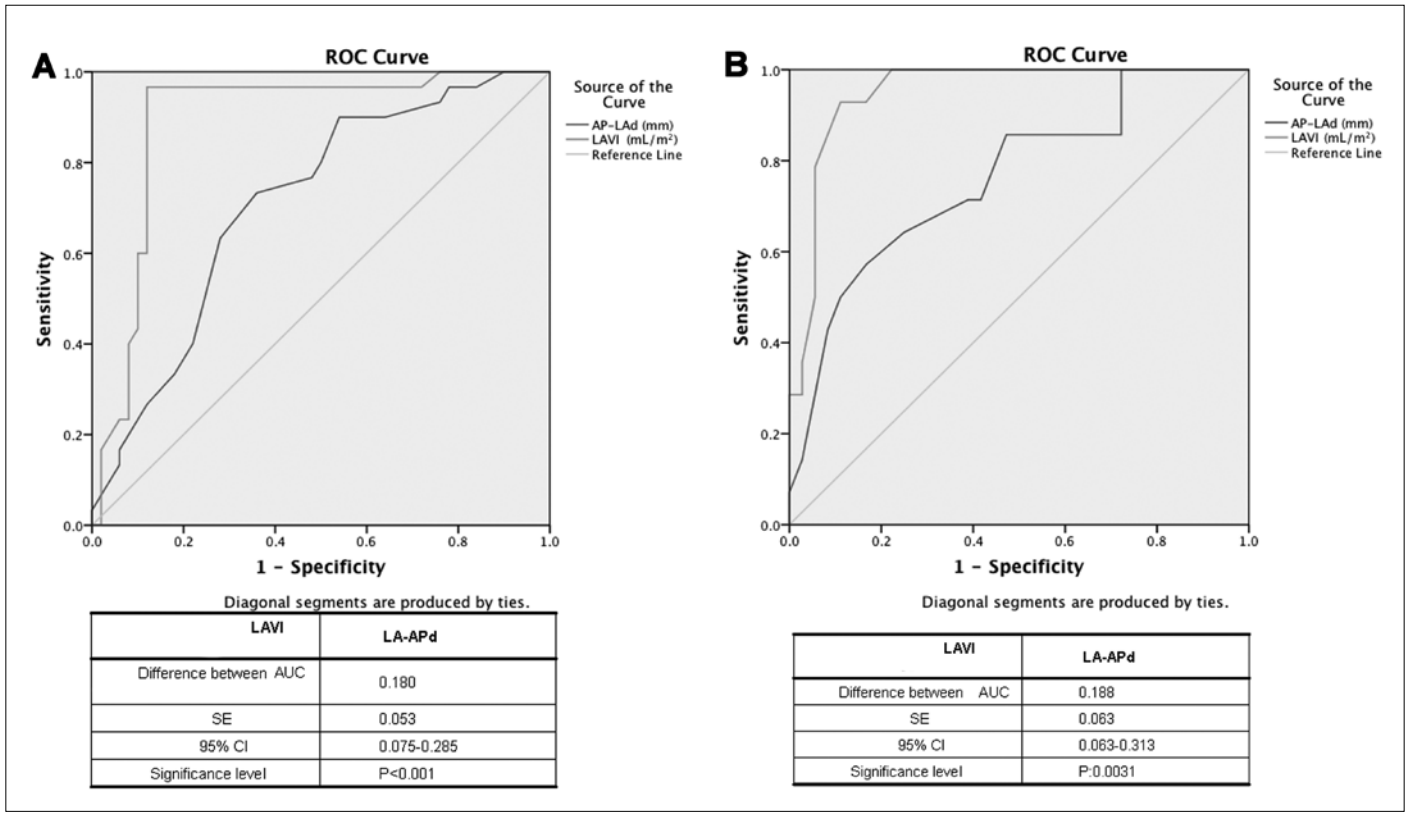
In the multiple logistic regression analysis carried out after the formation of the model based on the parameters related to AF recurrence, only the relationship with LAVI was observed to be prevalent. Each 1 ml/m^2 increase in the LAVI was found to be related with a 35% increase in the risk for the recurrence of the AF independently from the other parameters (p<0.001). The results of the regression analysis where the related factors of AF recurrence are evaluated are presented in Table 4.

When the AP-LAd and LAVI - the parameters used to predict the risk for the recurrence of the AF - were compared in the ROC analysis, the area under the curve was found as 0.950±0.029 for the LAVI (p<0.001) and 0.762±0.076 for the AP-LAd (p=0.004). The distinguishing LAVI value in predicting the risk for the recurrence of the AF was found as 36 ml/m^2 (sensitivity: 100%, specificity: 82.5%), while the AP-LAd value was 41mm (sensitivity: 90%, specificity: 50%). The sensitivity and specificity of the LAVI in predicting the risk for the recurrence of the AF was found to be higher than the AP-LAd (p<0.003). The comparison of the AP-LAd diameter and the LAVI through the ROC analysis in terms of predicting the risk for the recurrence of the AF is presented in Figure 1B.

Discussion

In our study, ECV success was observed to diminish at LAVI values over 40 mL/m^2, and an increase of 1mL/m^2 in LAVI specifically lowered the success of the ECV by 12%. The rate of recurrence of the AF following a successful ECV especially increases in LAVI values over 36mL/m^2, and every 1mL/m^2 increase in the LAVI was found to increase the recurrence risk of the AF by 35%. When the LAVI and AP-LAd were evaluated together with the other parameters related to AF in our study, only LAVI was observed to be associated with ECV success and AF recurrence.

External cardioversion is a safe and effective treatment modality in AF. In the present study, the overall success of ECV in restoring AF to SR in our centre was 62.5%, although AF



LAVI	LA-APd
Difference between AUC	0.180
SE	0.053
95% CI	0.075-0.285
Significance level	P<0.001

LAVI	LA-APd
Difference between AUC	0.188
SE	0.063
95% CI	0.063-0.313
Significance level	P:0.0031

Figure 1. A-ROC curves generated to compare AP-LAd and LAVI as predictors of a successful electrical cardioversion B- ROC curves generated to compare AP-LAd and LAVI as predictors of atrial fibrillation recurrence after the successful electrical cardioversion

AUC - area under the curve, CI - confidence interval, LA-APd - left atrial anterior - posterior diameter, LAVI - left atrial volume index, ROC - receiver operating characteristic curves, SE - standard error

recurred in 28% of the patients in which SR was initially achieved after the ECV. There are various clinical investigations focusing on the predictors of ECV success and AF recurrence. Several clinical parameters have been reported to be relevant to the ECV success and the recurrence of AF (2, 3, 10, 11). In our study, when the parameters of age, female sex, BMI and LVMI were individually evaluated, they were observed to be associated with the ECV success and/or the recurrence of AF after a successful ECV. Various clinical and echocardiographic studies have suggested that any diastolic dysfunction accompanying these parameters may affect the LA structure and function in a way to lead to atrial fibrillation and the recurrence of AF after the cardioversion (12-14).

The echocardiographically determined LA size is known to be closely associated with the development of AF, and the LA size has been reported to be an independent predictor of the sinus rhythm restoration after the cardioversion (15, 16). The moderate correlation observed between the LAVI and the energy level required for a successful ECV in our study, as well as the higher risk for the recurrence of the AF during the follow-up of the patients in which higher energy levels were needed in order to achieve the sinus rhythm, point to a relationship between the LAVI and the electrical instability.

The M-mode antero-posterior LA diameter, which is a unidimensional measure of the LA size, was shown to be related to the clinical risk factors predicting the ECV success and AF recurrence. However, since the LA is anteriorly constrained by the aortic root (and to some extent, the right ventricular outflow tract) and posteriorly by the relatively rigid tracheal bifurcation, LA enlargement often occurs in the superior-inferior or medial-lateral axis (17). Consequently, smaller increments of the M-mode LA dimension are associated with greater changes in the LA volume, especially for larger atria. Therefore, the changes in AP diameter may not be proportionate to - and often underestimate - the changes in other LA dimensions (18). The most recent recommendations for echocardiographic chamber quantification indicate that LA and LAVI provide an accurate measurement of the asymmetrical remodeling of the LA chamber. These parameters are increased in patients with AF and are also important predictors of the cardiovascular outcome, including the occurrence of AF. This supports the concept that LAVI is a hallmark of atrial remodeling (19).

LA remodeling refers to a time-dependent adaptive regulation of the cardiac myocytes in order to maintain homeostasis against external 'stressors'. The type, extent and reversibility of atrial remodeling depend on the strength and duration of the exposure to the stressors (20). The most common stressor of atrial myocytes includes the duration of the AF. A long duration of AF causes atrial dilatation, enabling formation of more re-entry wavelets. Fibrosis and inflammation of the atrial myocardium slow down the interatrial conduction velocity, and this result in persistent and recurrent AF. The duration of the AF has

most consistently been found to correlate with a lower success rate and the recurrence of the AF (21). When the results of our study are evaluated in terms of the duration of the AF, the ECV success and the recurrence of the AF following a successful ECV; higher rates of success following an ECV were observed together with lower recurrence rates of AF in the patients who had AF for less than 3 months. These results support similar studies suggesting that a shorter duration of AF is a determinant of the ECV success and the subsequent maintenance of the SR (1, 22, 23).

While there are no studies focusing solely on the association between the LAVI and CV in the literature, a limited number of studies have evaluated the relationship between the LAVI and the recurrence of AF after a successful CV (in patients who underwent both medical and electrical cardioversion) (24). In two separate studies by Marchese et al., (19, 25) patients who had undergone successful CV procedures were followed up for one year. Although the LAVI values of those with maintained SR were similar to our results, the LAVI in the patients in which AF recurred was observed to be lower in our study. Also, the risk of developing AF accompanying each 1mL/m^2 increase in the LAVI was found to be higher in our study.

The duration of AF prior to the CV reported in the study by Marchese et al. (25) is shorter than the duration in our study population. Since approximately 50-60% of our patients had AF for 3 months or longer, the higher LAVI values observed especially in the group where AF recurred may be associated with the longer duration of AF before the CV. Also, the different method we used to measure the LAVI in comparison to the other 2 studies and the characteristics of the patient population may have led to the difference in the LAVI values. The observation that LAVI came to the forefront as the most important parameter in predicting the clinical results in all three studies in spite of the different LAVI results points out that LAVI is a significant parameter predicting the success of the CV and the maintenance of the SR to be used in the selection of the patients independently from the CV method to be applied.

LAVI gave superior results to the clinical risk factors in predicting the ECV success and the recurrence of AF, probably because LA remodeling represents the final and macroscopic result of the sum of each single clinical predictor. Although later guidelines for the management of AF mention the LA size assessment just in terms of M-mode AP dimension, the results obtained from our study point out that LAVI measured prior to the ECV is a more sensitive parameter than AP-LAd in predicting the ECV success and the early recurrence of AF after the ECV.

Study limitations

The relatively small total study population is the main limitation of this study. However, we think that the clear difference between the groups renders our results sufficiently valid. Secondly, because of the short duration of the follow-up period, we cannot conclude that our results can be projected to longer follow-up periods. Patients did not have continuous ECG monitoring for the recurrence of AF after the cardioversion. Instead, the ECG's were performed at the times of clinic follow-up and as clinically indicated. It is possible that transient asymptomatic episodes of AF were missed. We would expect such episodes to be uncommon, given that we excluded patients with paroxysmal AF and all patients required ECV to establish the sinus rhythm at study entry. Since the main target of our study was to evaluate the relationship of the LA dimensions with the clinical results, the relationship among the CHADS score, the success of the ECV and recurrence of the AF has not been taken into consideration. The association among the administered medication, the success of the ECV and the recurrence of AF has not been assessed in our study since the small number of the patients could present a statistical limitation.

Conclusion

The present study demonstrates that LAVI is a significant and independent predictor of the success of ECV, as well as the recurrence of the AF after a successful ECV. LAVI is superior to AP-LAd, because it allows a more accurate assessment of the asymmetric remodeling of the LA. These findings may make the LAVI measurement a useful, non-invasive and simple method in the selection of the patients who should undergo elective ECV for nonvalvular AF. Larger prospective studies are needed to establish the utility of LAVI in the management of AF with ECV.

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