International Educational Applied Research Journal
Volume: 1 | Issue: 1 | October 2017

THE SIGNIFICANCE OF THE LEFT ATRIAL VOLUME INDEX IN PREDICTION OF ATRIAL FIBRILLATION RECURRENCE AFTER ELECTRICAL CARDIOVERSION.

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Abstract - ***Aim:*** *The purpose of this study is to evaluate of the significance of the left atrial volume index (LAVI) measurement performed before ECV in predicting the recurrence of the AF.*

Methods and materials: *Fifty-one patients with AF, selected for ECV were studied in the cardiology department of Tabriz University of medical sciences. The clinical and demographic data of all the patients were recorded. Echocardiography was performed before and also three months after ECV. Patients were divided into two groups: those who maintained SR and those with recurrent AF based on their clinical manifestations and ECG taken after three months.*

Results: *SR was maintained in 76.5 percent of the patients following the three months after ECV. The age, sex and the BMI were not significantly different between SR and AF groups. Two groups showed no significant differences considering pre-ECV medical history including medications and systemic diseases. The initial LAVI was significantly different between two groups. The cut-off point of LAVI value in predicting the maintenance of SR was 55 ml/m2. The LAVI of SR group decreased significantly after three months.*

Conclusion: The present study demonstrates that LAVI is a powerful predictor of the recurrence of AF after ECV. The LAVI measurement could be a useful method in the selection of the patients with AF for ECV.

Keywords : Atrial fibrillation, cardioversion, left atrial volume.

Introduction

The prevalence of atrial fibrillation (AF) is approximately 1.5-2 percent of the general population and is the most common sustained cardiac arrhythmia encountered in clinical practice and its prevalence increases with age. The general treatment strategy of persistent AF is to restore and maintain the sinus rhythm (SR).(Camm et al., 2012, Frick et al., 2001, Lip et al., 2012, Miyasaka et al., 2006) Electrical cardioversion (ECV) is a simple and safe technique used for the restoration of the (SR) in patients with AF. Previous studies reported the initial success of ECV as 50-90%. However, recurrence of AF occurred in almost 60% within three to six months, especially in the first two months.(Kuppahally et al., 2009) Many factors could affect and predict recurrence of AF after ECV and better treatment strategies may be planned by understanding them. Previous studies have reported various potential predictors including the age, underlying heart disease, duration of AF, cardiovascular risk factors, inflammatory markers and the size of the left atrium.(Frick et al., 2001, Masson et al., 2010, Aribas et al., 2013, European Heart Rhythm et al., 2010)

The relationship between the size of the left atrium and the recurrence of the AF has been investigated in many studies. Many of them reported this link using the left atrial diameter (mostly the anteroposterior dimension).(Brodsky et al., 1989, Kosior et al., 2005, Mitchell et al., 2003) However, this measurement may not reflect the complex changes in the size of left atrium. In a limited number of studies, the left atrial volume index (LAVI) has been shown to be stronger than the anteroposterior left atrial dimension in predicting the recurrence of the AF.(Wang et al., 2005, Akdemir et al., 2013) The aim of our study is to evaluate of the efficiency of the LAVI measurement performed before ECV in predicting the recurrence of the AF.

Methods and Materials

Study design

This study was designed as a prospective cohort of patients with AF.

Study population

A total of 70 patients over the age of 18, who were admitted to the Cardiology Center of Tabriz University of Medical Sciences and diagnosed with non-valvular persistent AF, were enrolled in the study (2013-2015). Written informed consent was obtained from all the patients. The study was approved by the ethics committee of Tabriz University of Medical Sciences. Diagnoses were based on the patient history, physical examination and electrocardiography (ECG) findings; and then the patients were found to be eligible for ECV procedure. Exclusion criteria were history of other atrial arrhythmias (including paroxysmal AF), acute coronary syndrome, congenital heart disease, severe valvular heart disease, mechanical or bio-prosthetic heart valves, permanent pacemaker, patients in which a thrombus was detected in the left atrium, thyroid dysfunction and finally history of cardiac surgery.

Clinical examinations

The clinical and demographic data of all the patients were recorded before the echocardiographic evaluation. Clinical data including age, sex, body mass index (BMI), hypertension, diabetes mellitus, coronary artery disease, medications and duration of the AF were recorded for each patient.

Echocardiographic measurements

Two-dimensional transthoracic (TTE) and transesophageal (TEE) echocardiographic examinations were carried out in all patients before and three months after ECV with the GE-Vingmed Vivid 7 system (GE-Vingmed Ultrasound AS, Horten, Norway) ultrasound device and a 3S-RS (3.5 MHz) probe. Two-dimensional (2D) imaging (using apical four-chamber and apical two-chamber views), M-Mode and Doppler echocardiographic techniques were performed by an experienced cardiologist (blinded to the patients' medical history). Examinations were performed according to the guidelines of American Society of Echocardiography. The left ventricle wall thickness, systolic and diastolic ventricular dimension, ejection fraction, left atrial dimension were measured. The LAVI was determined using the biplane area length method after measuring the area in the apical four-chamber view (A1) (not taking the initiation of pulmonary veins and left atrial appendage into account), two-chamber view (A2) (after detection of teapot sign for accuracy) (Toufan et al., 2015) and the long axis length of the left atrium at ventricular end-systole. LAVI was then calculated according to the following formula: (0.85A1*A2)/L. LAVI was defined after the correction for BSA.

Electrical cardioversion

In our study, the ECV procedure was performed by an experienced cardiologist blinded to the patients' history. Sedative medications (Midazolam 1.5mg IV) were administered to all the patients before the cardioversion while the patients were constantly monitored. Shocks were administered using a bi-phasic defibrillator (Lifepak 20e defibrillator/monitor, Physio-Control, Inc., Redmond, USA). Paddles were placed on the second right intercostal space and the left side of the mid-axillary line. External bi-phasic DC shocks were started with 100 Joules (J) and followed by 200J and 300J in the case of failure in generating the SR. Those patients in which SR was achieved and maintained for 24 hours without recurrence of AF were included in the next follow-up.

Clinical follow-up

Patients with maintained SR were prescribed Warfarin (5mg, orally) for 6 weeks in order to achieve an INR of 2 to 3 and the antiarrhythmic therapy (Tab Amiodarone 200 mg BD in 15, Tab Propafenone 150 mg BD in 21, and Tab Felecainide 100 mg BD in 15 paitients) to prevent the recurrence of AF. Other medications were left at the physician's discretion who followed the patients. Patients were divided into two groups: those who maintained SR and those with recurrent AF based on their clinical manifestations and ECG taken after three months (SR and AF groups). Clinical and echocardiographic examinations were performed again at this point.

Statistical analysis

Descriptive statistics including frequency distribution, mean value and standard deviation were used to define the sample. Normality was tested by Kolmogorov-Smirnov and group comparisons were performed using Chi-square and Mann-Whitney U-test. Receiver operating characteristic (ROC) analysis were produced to evaluate LAVI as a predictor of maintenance of SR after ECV and to determine an appropriate cutoff point for LAVI for the prediction of AF recurrence, according to sensitivity and specificity. All tests are two-sided, and P-value less than 0.05 was considered to be significant. Statistical analysis was conducted using SPSS 18 (SPSS Inc., Chicago, USA).

Results

Nine patients were dropped out of study because of the detection of exclusion criteria during the study. Four patient were not included in the post-ECV follow-up for failure in maintaining SR and six people were dropped out of study for personal reasons. Among the remaining fifty-one patients who were included in the evaluation, the mean age was 58±12 (21 to 80) and 52.9 percent (n=27) were male. SR was maintained in 76.5 percent (n=39) of the patients following the three months after ECV, whereas the AF reoccurred in 23.5 percent (n=12). The age (p=0.657), sex (p=0.276) and the BMI (p=0.261) were not significantly different between SR and AF groups.

Two groups showed no significant differences considering pre-ECV medical history including medications and systemic diseases (Table I). Echocardiographic findings of two groups are shown in Table II (before ECV). The initial LAVI was significantly different between two groups. ROC curve are illustrated in Figure I to evaluate LAVI as a predictor of maintenance of SR after ECV. The cut-off point of LAVI value in predicting the maintenance of SR was 55 ml/m2 (sensitivity:

75.0%, specificity: 89.7%). The LAVI of SR group decreased significantly (5.69±0.74 ml/m2) after three months. (p=0.000)

Discussion:

In our study, 76.5 percent of patients could maintain SR three months after ECV which is in total agreement with previous studies.(Frick et al., 2001, Van Gelder et al., 1991, Brodsky et al., 1989, Carlsson et al., 1996, Kuppahally et al., 2009) Several studies have been focusing on the predictors of AF recurrence after conversion.(Frick et al., 2001, Carlsson et al., 1996, Brodsky et al., 1989, Marchese et al., 2011, Osmanagic et al., 2016, Kuppahally et al., 2009) According to the demographic data of present study including age and sex, patients didn't show any significant difference. The BMI didn't also affect AF recurrence significantly. This result is similar to the findings of Frick (Frick et al., 2001), Akdemir (Akdemir et al., 2013), and Osmanagic (Osmanagic et al., 2016) but it's opposed to Blich's.(Blich and Edoute, 2006) None of the co-morbid conditions and systemic diseases influenced significantly the recurrence rate of AF in our study. Previous studies have also not reported significant relationship in most conditions,(Kuppahally et al., 2009, Osmanagic et al., 2016, Akdemir et al., 2013, Frick et al., 2001) However some of them mentioned hypertension(Frick et al., 2001, Marchese et al., 2011), diabetes mellitus(Marchese et al., 2011) and history of Previous AF cardioversion (Marchese et al., 2011) as influencing factors. In present study, according to many earlier investigations (Akdemir et al., 2013, Osmanagic et al., 2016), no significant difference was found in the recurrence of AF regarding pre-ECV medications, although some medications such as beta-blockers have been reported with possible effect on the recurrence.(Frick et al., 2001, Marchese et al., 2011)

An increase in left atrial size is known to be associated with cardiovascular diseases. The effect of left atrial size on the recurrence of AF has been reported previously and many parameters (readily by anteroposterior diameter) have been suggested in earlier studies to evaluate it.(Van Gelder et al., 1991, Brodsky et al., 1989, Wang et al., 2005, Shin et al., 2008, Sievers et al., 2004) Measurement of anteroposterior linear left atrium dimension by M-mode echocardiography is easy, but not reliable, since the left atrium is not uniformly spherical and anteriorly constrained by the sternum and aortic root and posteriorly by the relatively rigid tracheal bifurcation and spine. Therefore enlargement often takes place in the superior-inferior or mediolateral axis. Thus this unidimensional measurement cannot reflects the exact complexity of changes.(Akdemir et al., 2013, Lester et al., 1999)

The size of left atrium could be measured more accurately by the left atrial volume by two-dimensional echocardiography when compared with reference standards such as magnetic resonance imaging and three-dimensional echocardiography.(Pritchett et al., 2003, Maddukuri et al., 2006, Rodevan et al., 1999) The measurement of left atrial volume has been described by two-dimensional echocardiography previously.(Schabelman et al., 1981, Wang et al., 1984) The LAVI has been applied to investigate cardiovascular conditions by recent studies increasingly.(Lim et al., 2006, Sousa, 2006, Kim et al., 2007, Ristow et al., 2008)

A limited number of studies have evaluated the relationship between the LAVI and the recurrence of AF. Wang stated that the LAVI is higher in the patients with atrial fibrillation recurrence after conversion.(Wang et al., 2005) Kim (Kim et al., 2007) and then Kataoka (Kataoka et al., 2010) declared that the LAVI, as opposed to the conventional left atrial dimension, was supposed to be an important predictor of successful sinus rhythm restoration after the maze operation. Similar statement was suggested by Lee for occurrence of atrial fibrillation after ablation of typical atrial flutter.(Lee et al., 2010) Marchese (Marchese et al., 2011) and Akdemir (Akdemir et al., 2013) concluded that larger LAVI before ECV, as a more accurate measure than left atrium diameter, was strongly associated with higher risks of AF recurrence.

Among our echocardiographic data, LAVI is the only measurement which predicts the recurrence of AF. Ejection fraction (EF), left ventricular diastolic diameter (LVDD), and left ventricular systolic diameter (LVSD) were not significantly different between SR and AF groups. These are in total agreement with the results of Akdemir (Akdemir et al., 2013) and Marchese (Marchese et al., 2011). The LAVI values of SR group in Marchese (31.4+4.6 ml/m2) and Akdemir (35.3±11.5 ml/m2) studies were close to our results (43.4±1.9 ml/m2) and also the values of normal patients (34 ml/m2)(Lang et al., 2015). However, the patients with the recurrence of AF had larger LAVI in our study. (96.1±15.0 ml/m2 in our study comparing to 39.7+8.4 ml/m2 in Marchese and 53.1±10.1 ml/m2 in Akdemir studies)

The cutoff point of LAVI value in predicting the maintenance of SR was 55 ml/m2 (sensitivity: 75.0%, specificity: 89.7%) in our study which was higher than 40 ml/m2 (sensitivity: 38%, specificity: 96%) in Marchese and 36 ml/m2 (sensitivity: 100%, specificity: 82.5%) in Akdemir studies. The higher LAVI values of AF group in our study may be associated with the longer duration of AF before the ECV, the difference in the measurement method of LAVI, the characteristics of the patient population and/or the duration of follow-up after ECV.

Another founding of present study was a decrease in LAVI after a three month maintenance of SR. This result besides the aforementioned role of LAVI in prediction of AF recurrence could lead us to the concept of left atrial remodeling. Left atrial remodeling refers to a time-dependent adaptive regulation of cardiac myocytes in order to maintain homeostasis against external stressors. The type and extent of remodeling depends on the strength and the duration of exposure to the stressors. The most common stressors of atrial myocytes include tachycardia with high rates of cell depolarization and volume/pressure overload such as in AF. Increased volume/pressure overload gives rise to dilatation and stretch of the atrium. Atrial remodeling finally could results in many structural, functional, electrical, metabolic, and neurohormonal consequences which are mostly reversible (in cellular level, the apoptosis and fibrosis are usually irreversible).(Casaclang-Verzosa et al., 2008, Marchese et al., 2011)

The atrial size and specifically LAVI could reflect the macroscopic aspect of this remodeling. Determining of an irreversible threshold for atrial remodeling in AF may be difficult but achievable. This study presents cutoff point of LAVI enlargement which could be a used as a clinical value for distinguishing AF recurrence based on the undermining microscopic irreversible changes.

Study limitations

The main limitation of this study is the relatively small study population which may not devaluate the results of this investigation due to a statistically well-controlled sampling and analysis. Another limitation would be that the continuous event recorder didn't used during follow-up and missing of transient asymptomatic episodes of AF were possible.

Conclusion

The present study demonstrates that LAVI is a powerful predictor of the recurrence of AF after ECV. The LAVI measurement could be a useful method in the selection of the patients with AF for ECV. Despite the evidence from our study and also previously mentioned investigations, the latest guidelines(European Heart Rhythm et al., 2010) for AF management have not included the LAVI in echocardiographic examination yet.

Acknowledgement

We would like to thank Dr. SohrabPourkhamneh for his valuable assistance. Cardiovascular Research Center of Tabriz University of Medical Sciences supported the grant of present research.

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Table I. The clinical data of two groups (SR and AF).

	SR	AF	P-value
HT	25 (49.0%)	8 (15.7%)	0.871
CAD	4 (7.8%)	2 (3.9%)	0.547
CHF	3 (5.9%)	1 (2.0%)	0.942
DM	8 (15.7%)	0 (0%)	0.088
Smoking	7	0	0.114
AFH	6 (11.8%)	3 (5.9%)	0.445
β-Blocker	30 (58.8%)	10 (19.6%)	0.637
CCB	4 (7.8%)	2 (3.9%)	0.547
ACE/ARB	22 (43.1%)	6 (11.8%)	0.583

Data are presented as number (percentage).

Chi-square tests were performed. P-value less than 0.05 is significant (*).

ACE/ARB: angiotensin converting enzyme inhibitor/angiotensin II receptor blocker, AFH: atrial fibrillation history, CAD: coronary artery disease, CCB: calcium channel blocker, CHF: congestive heart failure, DM: diabetes mellitus, HT: hypertension.

Table II. Echocardiographic findings of two groups (SR and AF) before ECV.

	SR	AF	P-value
EF (%)	48.9±1.67	49.00±2.46	0.696
LVDD (cm)	4.70±0.14	4.90±0.26	0.284
LVSD (cm)	3.31±0.12	3.84±0.44	0.211
LAVI (ml/m^2)	43.4±1.9	96.1±15.0	0.000*

Data are presented as mean±standard deviation.

Mann-Whitney U-test tests were performed. P-value less than 0.05 is significant (*).

EF: ejection fraction, LAVI: left atrial volume index, LVDD: left ventricular diastolic diameter, LVSD - left ventricular systolic diameter.

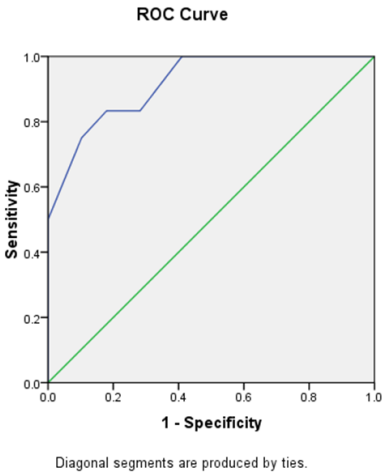

Figure I. ROC of LAVI as a predictor of maintenance of SR after ECV.