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Original Article

Atrial Fibrillation

NUMERIC VALUE OF LEFT ATRIAL APPENDAGE MEAN DIASTOLIC EMPTYING VELOCITY IN PATIENTS WITH PERSISTENT ATRIAL FIBRILLATION, ASSESSED BY TRANS-ESOPHAGEAL ECHOCARDIOGRAPHY FOR PREDICTION OF RESTORATION OF SINUS RHYTHM UNDERGOING DIRECT CURRENT CARDIOVERSION AND EVEN OF CLOT FORMATION IN IT

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ABSTRACT

Objective: To determine the value of left atrial appendage mean diastolic emptying velocity at which there is restoration of normal sinus rhythm from atrial fibrillation either by electrical cardioversion or pharmacological cardioversion, development of clot in left atrial appendage or left atrium and long-term (at one month) sinus rhythm maintenance and to measure the value of left atrial appendage late diastolic emptying velocity after restoration of sinus rhythm at one month duration.
Study Design: Cross-sectional prospective study.
Place and Duration of Study: Department of Cardiac Electrophysiology, AFIC/NIHD Rawalpindi, from Oct 2020 to Apr 2021.
Methodology: Transthoracic echocardiography was used to gather standard echocardiographic data from individuals with atrial fibrillation, and trans-esophageal echocardiography was used to determine mean diastolic emptying velocities in the left atrial appendage. All patients fulfilling inclusion criteria underwent direct current cardioversion and the late diastolic emptying velocity of left atrial appendage was measured after restoring sinus rhythm at one month of follow up by again performing trans-esophageal echocardiography. The diastolic emptying velocities of successful cardioverted patients and those still in atrial fibrillation (unsuccessful direct current cardioversion were compared and analyzed.
Results: Out of 61 patients, normal sinus rhythm was restored by successful cardioversion in 56 (91.8%) patients and all same (91.8%) patients had maintained normal sinus rhythm at 1 month interval checked on follow up. Patients who had their normal sinus rhythm restored by cardioversion had greater left atrial appendage mean diastolic emptying velocities, with a mean of 24.043.06 cm/s, than patients who had failed cardioversions, with a mean of 19.601. Out of 51cm/s (p=0.002). Patients who were remained in normal sinus rhythm at 1 month had lower left atrial volumes indexed to body surface area with a mean value of 27.023. Of 33 ml/m^2 (p=0.001) and greater left atrial appendage late diastolic emptying velocities with a mean value of 45.394. Out of 70cm/s (p=0.001) compared to the patients who were still in atrial fibrillation.
Conclusion: As a marker of mechanical remodeling, left atrial appendage diastolic emptying velocity can anticipate successful cardioversion, short-term and long-term sinus rhythm maintenance after electrical cardioversion in AF patients and even presence of clot in left atrial appendage when having lower values.

Keywords: Atrial fibrillation, Left atrial appendage, Normal sinus rhythm, Trans-esophageal echocardiography.

INTRODUCTION

Atrial fibrillation (AF) is one of the well-known rhythm disorders of the heart and it is related with a pro-thrombotic condition and substantial morbidity with development of stroke and heart failure. As a result of restoring and keeping normal sinus rhythm (NSR), arrhythmic symptoms were eliminated, rate control and hemodynamics were enhanced, and susceptibility to systemic thromboembolic consequences was reduced. AF is treated with reestablishment of NSR (rhythm control) or keeping of controlled heart rate (rate control) depending on its symptoms[1-2]. NSR can be reestablished completely either by pharmacological cardioversion (CV) or electrical CV. In the Euro Heart Survey, the adequacy of CV was between 75-88%, and 70% of patients remained in NSR over 12 months[3]. Atrial remodeling (a change in atrial structure and function) has a significant role in the pathophysiology of supraventricular rhythm problems, including AF, other heart diseases like mitral valve abnormalities, heart failure, even ischemic cardiac disease, and channelo-pathies. There are three types of atrial tissue remodeling, 1-Electrical remodeling, 2-Structural remodeling and 3-Mechanical remodeling. So, many researchers are searching for imaging markers and laboratory markers of atrial remodeling that could help in assessing the clinical progression of

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atrial cardiomyopathies and its management[4]. There are several hypothesized clinical predictors and echocardiographic predictors of restoration of NSR and rhythm disorders recurrence in those patients undergoing successful elective CV of persistent AF. Short term and long-term keeping up of NSR is more in those patients with smaller size of left atrial (LA), shorter AF duration, intact function of left ventricular (LV) and absence of mitral valve defects[5,6]. Various researchers have reported potential clinical symptoms, imaging markers, and laboratory markers predicting NSR maintenance, after CV of AF[7-10]. We can use the echocardiography for measurement of LA emptying fraction (LA EF) to assess the mechanical function of the left atrium (LA) or left atrial appendage (LAA). It can further be assessed by estimation of blood inflow velocity through the mitral valve, speckle tracking echocardiography (STE), strain or strain rate by use of Tissue Doppler Imaging (TDI) and by measuring diastolic emptying velocity of left atrial appendage (LAAEV)[10-18].

Transesophageal echocardiography (TOE) has recently gained acceptance as a technique for guiding the care of patients with AF by evaluating the LAA, detecting thrombi, and allowing for an early CV55, 6. Moreover, the estimation of thromboembolic risk by measuring LAA diastolic velocities using TOE in persistent AF has become well accepted[7-9]. Recently studies have shown that long-term NSR keeping up, can be predicted before CV by evaluating LAA velocities[10,11].

METHODOLOGY

This prospectively study was conducted at Armed Forces Institute of Cardiology/National Institute of Heart Diseases Rawalpindi, Pakistan. A total 61 patients with AF duration >48 hours and <1 year. Clinical record including the duration of AF were taken from the patient's history record and further interviewing the patient in outdoor patient department (OPD). Duration of AF was further determined by asking the patient and by exploring all available past electrocardiograms (ECGs). The inclusion criteria were the symptomatic persistent atrial fibrillation for >7 days, the LV ejection fraction >40%, the really good anticoagulation (mostly with warfarin or novel oral anticoagulants like rivaroxaban, dabigatran and apixaban) for either ≥3 weeks duration before cardioversion and the oral antiarrhythmic mostly amiodarone for at least same duration. CV was achieved in all patients either DCCV (mostly) in emergency department or oral pharmacologic CV on OPD basis.

The exclusion criteria were no consent given to enroll in the study, age <18 years, no consent given for CV or TOE, bad quality of echocardiographic images, the presence of thrombus/clot in the LA or the LAA, the left atrial volume index LAVI a value of >40 ml/ m^2, and the acute heart failure, heart attack (acute myocardial infarction), previous history of pulmonary vein isolation for treatment of paroxysmal AF, anemia (hemoglobin <6.9 mmol/l), dys-thyroidism and cancer. All the enlist patients after CV, underwent about one-month follow-up for assessment of LAA function by re-assessing late diastolic emptying velocity of LAA and NSR maintenance. A 24 hour ambulatory electrocardiographic recording (Holter) was performed in all patients who had NSR on follow up ECG. Patients were further asked to contact to our department even earlier if they felt either palpitation or thought that atrial fibrillation had recurred.

Clinical records were taken on the day of CV and body surface area (BSA) was calculated from height and weight. CHA2DS2-VASC score and HAS-BLED scores were calculated on basis of age, sex, diabetes mellitus, hypertension, the history of coronary artery disease, intake of anticoagulants, liver and renal function tests, INR testsand the history of systemic thromboembolism or stroke or transient ischemic attack according to the current American heart association guidelines on persistent AF treatment.

BSA was required to index the volume of left atrium. Data of the accurate duration of current AF episode were enlisted only when patient could accurately tell it.After transthoracic echocardiography (TTE), TOE were performed inpatients having fasting of 4-6 hours and within 24 h before the CV attempt with the hospital available echocardiography Machine. During TTE, measurements were obtained in parasternal long-axis view using two-dimensional 2D and M-mode, according to the advice of the American Society of Echocardiography[11, 12]. Left ventricular ejection fraction (LVEF) were calculated with the Simpson's methodin apical 2, 4, and 5 chamber views. The left atrial volume (LAV) were measured in apical 4 and 2 chambers views. The LAV was measured on the frame of mitral valve closure, by tracing the inner line of the atrium and excluding the area under the valve annulus, LAA, and pulmonary veins. Then LAV was indexed to BSA (LAVI).

All DCCV were performed with anesthesia team cover under sedation in Emergency department. All DCCV were done with a biphasic defibrillator (with 200–300 J). If the first shock was not successful, the next shock energywas given with a higher energy (by 100 J) and if still failed then last shock was given at left side of antero-posterior position of chest. The successful cardioversion was defined as restoration of NSR and NSR maintenance for >24 hours. Patients with NSR, received anticoagulants as up-stream therapy for about 4 weeks and later on according to CHA2DS2_ VASC score but the antiarrhythmic drugs like amiodarone by clinical judgment.

During the TOE, images were taken by an experienced operator for the presence of intra-cardiac thrombus. During TOE, gain was adjusted to get the ideal images and to keep away of noiseartifacts. A clot was taken into consideration when a well all around, echo dense intra-cavity mass that was distinct acoustically from the underlying endocardial tissue, was recognized. Patients showing intra-cardiac thrombus or LA spontaneous echocardiographic contrast (intra-cavity twirling smoke like echo inside the left atrium or LAA) during TOE were excluded from the study. The LAA diastolic emptying velocity was acquired by pulsed-wave (PW) Doppler examination, about 1cm inside the orifice of the LAA with 30-60 Degree projection in mid esophageal view. The LAA mean diastolic emptying velocities of LAA were averaged with each RR interval of ECG forat least five cardiac cycles when were in AF and late diastolic emptying velocities were obtained when were in NSR. PW Doppler can be used to derive LAA flow velocities from any of the conventional imaging planes on TOE. A schematic illustration of typical quadriphasic flow pattern in patients when in NSR, is seen in figure.

In AF the flow design and amplitude is quite variable. Mostly, changing amplitude and regularity saw tooth waves are seen. So mean diastolic emptying velocities are taken to assess the function of LAA. Patients were followed-up about at one month after successful DCCV by performing ECG and measuring late diastolic emptying velocity of LAA by trans-esophageal echo (TOE). ECGs were recorded in order to record the keeping up of NSR or recurrence of AF. To prevent recurrence of AF the main drug therapy was amiodarone on follow up.

All data were expressed as means ± standard deviation (SD). Variables with categorical values were prescribed as counts and percentages. For comparing normally distributed variables Student's t-test was used. A *p*-value of 0.05 was considered statistically significant and all tests were two sided. The data analysis was performed by an SPSS-9 software.

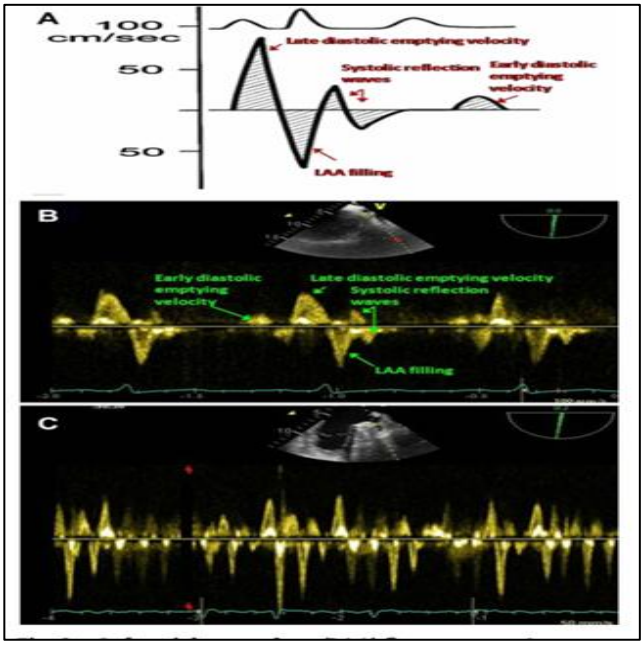

Figure: Left atrial appendage flow design (emptying and filling velocities) A): Schematic illustration showing different flow velocities during sinus rhythm. B): A well-illustrated pulsed-wave doppler tracing of LAA flow velocities in sinus rhythm. C): pulsed-wave doppler tracing of LAA flow velocities in atrial fibrillation.

RESULTS

We prospectively studied total 61 patients with AF lasting >48 h and <1 year. Out of these, successful CV either [electrical (n=48) or pharmacologic (n=8)], was achieved in 56 (91.8%) patients. Out of the 61 patients studied, 15 (24.59%) patients had previous history of episodes of AF and history of restoration of NSR by direct current cardioversion (DCCV) or pharmacological and now again they were in atrial fibrillation and 46 (75.4%) patients were having first time atrial fibrillation. Because patient generally did not know when their AF episodes were started, these data (known duration of AF) were available for only 49 (80.32%) patients and 12 (19.7%) were unaware of duration of AF.

The all patients were kept for one-month follow-up. At the end of the one-month period, all 56 (91.8%) patients were remained in NSR. Patients' demographic and clinical characteristics are shown in table-I. Out of 61 (100%) patients 37 (60.7%) were males and 24 (39.3%) were females. The mean value of age was 66.70 ± 11.36. The mean values of CHA2DS2-VASC (x/9),

Table-I: Socio-demographic characteristics.

Variables (n=61)	Frequency	Percentage
Age (year) (Mean ± SD)	66.70 ± 11.36	
CHA2DS2-VASC (x/9)	3.08 ± 1.00	
HAS-BLED (x/9)	0.80 ± 0.81	
LVEF (%)	53.66 ± 7.06	
LA SIZE (mm)	41.13 ± 2.1	
LAVI (ml/m²)	27.4 ± 3.53	
Pre-Cardio Version LAA mean diastolic emptying Velocity (cm/s)	23.70 ± 3.21	
Post-Carsio Version LAA late diastolic emptying Velocity (cm/s) At 1 Month	43.28 ± 8.44	
Gender		
Male	37	60.7
Female	24	39.3
Previous History of AFIB		
Yes	15	24.6
No	46	75.4
Duration		
Known	49	80.3
Unknown	12	19.7
Cardio Version		
Successful	56	91.8
Unsuccessful	5	8.2
Maintainence of Sinus Rhythm		
Yes	56	91.8%
Recurrence of AFIB	5	8.2%

HAS-BLED (x/9), LVEF (%), LA size (mm), LAVI (ml /m²), pre-cardioversion LAA mean diastolic emptying velocity (cm/s) and post-cardioversion LAA late diastolic emptying velocity (cm/s) at 1 month were 3.08 ± 1/9, 0.8 ± 0.81/9, 53.66 ± 7.06%, 41.13 ± 2.1mm, 27.4 ± 3.53 ml/m², 23.7 ± 3.21cm/s and 43.28 ± 8.44 cm/s respectively. Patients who were successfully cardioverted to NSR and were remained in NSR, were observed at about one month. On the basis of TTE parameters, patients who got successful cardioversion to NSR had lower LA parasternal diameter, LAVI and higher mean diastolic emptying velocity of LAA and good left ventricular ejection fraction (table-II).

According to the analysis, in all 61 patients with AF, the mean value of LAA mean diastolic emptying velocity was 23.70 ± 3.21cm/s, and in 56 patients

Table-II: Pre-cardio version LA diameter mm, LAVI ml/m², LVEF (%).

	Cardio Version	n (%)	Mean ± SD	*p*-value
Pre-cardio version LA diameter	Successful Unsuccessful	56 (91.8) 5 (8.2)	40.93 ± 2.11 mm 43.4 ± 0.89 mm	0.012
LAVI	Successful Unsuccessful	56 (91.8) 5 (8.2)	27.02 ± 3.338 ml/m² 32.2 + 1.789 ml/m²	0.001
LVEF	Successful Unsuccessful	56 (91.8) 5 (8.2)	53.89 ± 7.11 51 ± 5.47	0.38

(91.8%) with successful CV, the mean value of LAA mean diastolic emptying velocity was 24.07 ± 3.06 cm/ sec, that was high than of unsuccessful cardioversion patients having 19.60 ± 1.51 cm/s (table-III).

The late diastolic emptying velocity of LAA, when were remained in sinus rhythm at one month interval, was >40 cm/s with mean value of 45.39 ± 4.70 cm/s but the mean diastolic emptying velocity of LAA in patients who were having unsuccessful cardioversion and even at one month interval (when remained in Atrial fibrillation) was <20 cm/s with mean value of 19.60 ± 1.51 cm/s (table-IV).

The analysis has shown that mean LAA diastolic emptying velocity >20 cm/s was considered most predictor of one-month SR retention. Other predictors were AF duration of 1 week before CV, LA diameter <42 mm and use of antiarrhythmic drugs during AF and on follow-up. We enrolled patient with LVEF >40% and excluded patients with clot in LA or LAA and also presence of LA spontaneous echo contrast on TOE study.

Table-III: Pre-cardio version LAA mean diastolic emptying velocity cm/s.

	Cardio Version	n (%)	Mean ± SD	*p*-value
Pre-cardio version LAA mean diastolic emptying velocity	Successful Unsuccessful	56 (91.8) 5 (8.2)	24.07 ± 3.06 cm/s 19.60 ± 1.51 cm/s	0.002

Table-IV: Post-cardio version late diastolic emptying velocity/Mean diastolic emptying velocity of LAA at 1 month.

	Cardio Version	n (%)	Mean ± SD	*p*-value
Post-cardio version Late diastolic emptying velocity/ Mean diastolic emptying velocity of LAA at 1 month	Successful	56 (91.8%)	45.39 ± 4.70 cm/s	0.001
	Unsuccessful	5 (8.2%)	19.60 ± 1.51 cm/s	

DISCUSSION

Estimation of the mean diastolic LAA emptying velocity measured by pulse Doppler on TOE before CV treatment in patients with persistent AF can gives useful predicting information of successful CV to NSR and even development of clot in LAA.

Past research papers have found a link between LAA emptying velocity, LA size and AF duration and allthese are markers of long-term NSR maintenance[2]. However, there is clashing and scant data on the utility of diastolic LAA emptying velocity in predicting long-term preservation of NSR. The limited sample size and variable inclusion criteria of the past researches has resulted in mismatch of data[4,5].

In persistent AF, both the LA and the LAA undergo structural and histologic change over time (chamber enlargement, loss of myofibrils, discontinuity of sarcoplasmic reticulum and marked formation of collagen)[9].

These alarming degenerative alterations may produce atrial repolarization inhomogeneity, non-uniform anisotropy, or conduction slowness, and they are important factors in the pathophysiology of AF occurance [10]. With loss of contractile components of the LAA, it results in a loss of mechanical function and it is seen by low LAA flow velocities.

LIMITATION OF STUDY

The study involved a small number of patients and was limited to one location. The study sample may appear varied in terms of clinical factors such as AF duration, CV mode, and type of preventive antiarrhythmic medication, however this is due to the wide range of clinical situations encountered in hospital practice. It's worth noting that the length of follow-up has an effect on the rate of preserved NSR and, as a result, on the link between clinical parameters and outcomes. As a result, our findings may not be applicable over a longer period of time.

The LAA areas were not measured in our study due to the complicated three-dimensional structure of the LAA and these measurements are intrinsically prone to inter-observer variability. On the other hand assessment of LAA function by DTI during TOE, was simple to do, reproducible, and clinically relevant[7-9].

CONCLUSION

This study has identified those patients who had successful cardioversion to NSR and were remained in NSR for about one month among the patients having persistent AF with high LAA mean diastolic emptying velocity. As a result, it (LAA diastolic emptying velocity) can be used as a marker for mechanical remodeling and the maintenance of short- and long-term NSR following electrical cardioversion.

On the other hand, low mean diastolic LAA emptying velocity is of limi-ted utility in identifying individuals who will relapse again into AF though it can even predict the presence of a clot in the LAA when the levels are low.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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