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Original Article

Tissue Doppler Imaging of Left Atrial Appendage Predicts Successful Cardioversion in Patients with Atrial Fibrillation

Peggy M. Kostakou[1*], Elsie S. Tryfou[2], Vassilios S. Kostopoulos[3], Marianna Stamatelatou[3], Constantinos C. Mihas[4], Dimitrios S. Damaskos[5], Elias M. Tsougos[5], Christoforos D. Olympios[3], Nikos T. Kouris[3]

[1]Therapeutic Clinic of Athens University, Alexandra General Hospital, Greece

[2]Cardiology Department, General Hospital of Korinthos, Greece

[3]Cardiology Department, Thriassio General Hospital, Athens, Greece

[4]Internal Medicine Department, Kymi General Hospital, Evia, Greece

[5]6th Cardiology Department, Hygeia Hospital, Athens, Greece

[*]**Corresponding author:** Peggy M. Kostakou, Therapeutic Clinic of Athens University, Alexandra General Hospital, Greece.

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Abstract

Aims: Restoration of sinus rhythm in patients with Atrial Fibrillation (AF) prevents from thromboembolic events, decreases the risk for cardiomyopathy and improves quality of life. This study aimed to determine whether Tissue Doppler Imaging (TDI) during Transesophageal Echo (TEE) could predict successful electrical Cardioversion (CV) of AF lasting more than 48 hours but less than 6 months.

Materials and Methods: One hundred patients, 74 men and 26 women of mean age 64.7±9.8 years old with non-valvular AF were included. Pulse Wave (PW) Doppler velocities as well as TDI velocities of the medial and lateral walls of the Left Atrial Appendage (LAA) were recorded during TEE before cardioversion. Synchronized electrical cardioversion was occurred within 12 hours after TEE using 100-200 Joules. We also evaluated LA size and the global strain of LAA.

Results: Sinus rhythm restoration was succeeded in 80% of patients and maintained until discharge, 48 hours later. TDI velocities > 8cm/s were correlated with successful cardioversion (sensitivity 70% and specificity 63%) and were more predictive compared to PW Doppler velocities of > 40cm/s. TDI recordings at the medial LAA wall were more accurate, with less artefacts and better positioning of the sample volume. Global longitudinal strain was not significantly correlated with CV outcome.

Conclusion: Our results indicate that TDI velocities of the LAA walls more than 8cm/s could be used as a cut-off value predicting successful cardioversion of AF.

Keywords: Atrial Fibrillation; Electrical Cardioversion; Transoesophageal Echocardiography; Tissue Doppler Imaging; Strain

Abbreviations

AF: Atrial Fibrillation; **AUC:** Area Under The Curve; **CV:** Cardioversion; **DCCV:** Direct Current Cardioversion; **EF:** Ejection Fraction; **HF:** Heart Failure; **HFpEF:** Heart Failure with Preserved Ejection Fraction; **LA:** Left Atrium; **LAA:** Left Atrial Appendage; **LAVI:** Left Atrium Volume Index; **LVEF:** Left Ventricular Ejection Fraction; **PW:** Pulse Wave; **ROC:** Receiver Operated Characteristic; **STE:** Speckle Tracking Echocardiography; **TDI:** Tissue Doppler Imaging; **TEE:** Transesophageal Echo Cardiography; **TTE:** Transthoracic Echocardiography

Introduction

Atrial Fibrillation (AF) is the most common sustained arrhythmia [1] indicating a significant risk factor for stroke and other morbidities. In persistent AF, rhythm restoration leads to left ventricular function improvement [2], normalization of atrial and ventricular function [3], and consequently the reestablishment of atrium contraction improves Left Ventricular Ejection Fraction (LVEF) and maximal cardio competence [4]. Especially in Heart Failure (HF) patients, AF is the most frequent lingering arrhythmia, occurring in approximately one third of them [5,6], while those with concomitant HF and AF present worse prognosis than patients with HF only [7]. Especially patients in AF with rapid ventricular response and newly diagnosed HF, rhythm control strategy is highly recommended, since the cardiomyopathy due to the arrythmia could be a reparable reason for HF. Furthermore, Kelly et al showed recently that rhythm restoration in subjects of more than 65 years old suffering from HF with preserved ejection fraction (HFpEF) and AF, reduced 1-year all-cause mortality [8]. This is of great importance as until now, no therapy related to drugs has demonstrated better outcome in HFpEF.

In the AF-CDV Euro Heart Survey, AF Direct-Current Cardioversion (DCCV) leads to 75%-88% restoration of sinus rhythm of whom 70% kept this result over 12 months [9]. AF CV can be achieved by either pharmacologic or DCCV. DCCV is the most compelling method arresting AF momently [10]. In persistent AF where drugs are ineffective and can also be accompanied by side effects (bradycardia, ventricular proarrhythmia, acute heart failure), DCCV is the preferred treatment since CV seems to be occurred without danger associated with a reasonable risk when the appropriate anticoagulation treatment is followed [11].

Considering the electrical and anatomical remodeling of the atrium [12], during ongoing AF, an early CV seems mandatory. The predictive value of clinical and echocardiographic predictors of DCCV is far from optimal [13], so more precise predictors of DCCV are needed, besides the duration of AF or the Left Atrium (LA) diameter. The correlation of Left Atrial Appendage (LAA) emptying velocities, measured by Pulse Wave (PW) Doppler during Transesophageal Echocardiography (TEE), with DCCV of AF is long known [14]. LAA Tissue Doppler Imaging (TDI) during TEE estimates LAA myocardial contractility, assisting in the diagnosis of thrombus formation and the possibility of embolism [15] and determining the right time for DCCV [16]. To the same direction, several studies highlighted TDI use as an effective non-invasive method for the estimation of atrial function in case of AF and as a named indicator of mechanical remodeling predicting CV success [17-19]. Additionally, Farese et al showed that measurement of LAA wall TDI velocities by Transthoracic Echocardiography (TTE) may predict the development of paroxysmal AF [20]. Moreover TDI, having the intrinsic advantage to be a wave signal with increased amplitude with increased signal to noise proportion, can be handily perceived transthoracicly. The purpose of this study was to predict DCCV success by estimating TDI LAA velocities in AF subjects who underwent TEE directed DCCV.

Materials and Methods

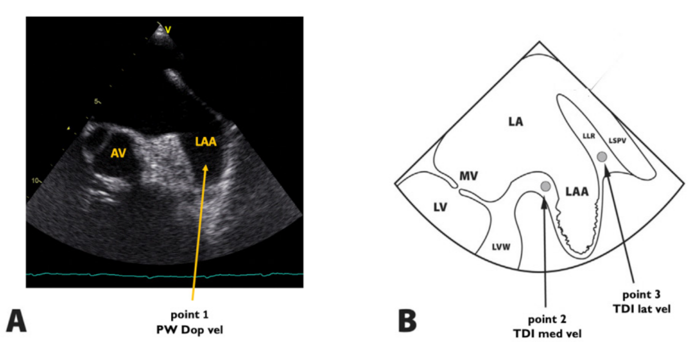
Study group

A total of 100 consecutive patients with optimal echo images, 74 men and 26 women with non-valvular AF lasting more than 48h and less than 6 months, were included. They were planned for TEE guided electrical DCCV. All 94 individuals were present for first time in order to undergo electrical CV, while none of them had put himself through ablation procedure previously. Patient demographic and clinical characteristics with patient medical history were recorded. Candidates with AF and thyroid disorders, valvular heart disease, acute coronary syndromes, acute myocarditis, pulmonary embolism, recent heart surgery, prosthetic valves, pericarditis, pericardial effusion, chronic obstructive lung disease, congenital heart disease, sick sinus syndrome and atrial thrombus formation found by TEE, were excluded from the study, but those with mild valvular heart disease were included in the protocol. Written consent about study protocol was given by each patient.

Since successful DCCV depends on several parameters like patient body habitus, position of defibrillation pads and the presence of antiarrhythmic drugs, patients with body mass index <18 or >35 kgr/m^2 were excluded from the study and a great effort was made in order to put the defibrillation pads at the appropriate position for every individual. Furthermore, all patients, proceeding to DCCV, were receiving full tolerable dose of b-blocker and amiodarone. After sinus rhythm recovery, the administration of b-blocker was continued (at full tolerable dose) while amiodarone administration was stopped one month later.

Echocardiography

TTE and TEE were performed within 12 hours before DCCV procedure in the Echo Lab of Thriassio General Hospital using standard commercial echocardiographic system (Vivid 7 GE full pack updated machine). The indication for TEE was to exclude intracardiac thrombus before DCCV and to evaluate LAA TDI velocities and it was performed using a 3-8MHz harmonics transducer. TTE measurements were obtained according to EACVI (European Association of Cardiovascular Imaging) recommendations [21], concerning LA Volume Index (LAVI), left ventricular end-diastolic and end-systolic diameter, left ventricular septal and posterior end-diastolic wall thickness. Ejection Fraction (EF) was estimated from the apical 4 chamber view via the Simpson´s biplane method. TEE was performed by an experienced echocardiographer after 6 hours of fast, following TTE. LAA thrombus was detected as a soft echo density in more than one view [22] and in this case patient was ruled out from the study. The LAA and LA were also screened for spontaneous echo contrast presence which was detected like spinning around smoke inside those cavities [23]. Mitral regurgitation evaluation was dependent on regurgitant jet area and its divergence by color flow Doppler imaging [24]. PW emptying velocities as well as TDI velocities of LAA medial and lateral walls were recorded during TEE. Peak LAA emptying velocity was calculated by PW Doppler at LAA orifice, as an average of three to five consecutive cycles [25] (Figure 1A, point 1). Finally, global longitudinal strain of LAA was evaluated off-line and correlated with the probability of successful cardioversion as well as the values of TDI and PW Doppler velocities.



AV: Aortic Valve, LA: Left Atrium, LAA: Left Atrium Appendage, LLR: Left Lateral Ridge, LV: Left Ventricle, LVW: Left Ventricle Wall, MV: Mitral Valve, LSPV: Left Superior Pulmonary Vein, PW Dop vel: Pulse Wave Doppler Velocity, TDI lat vel: Tissue Doppler Imaging Velocity of Lateral Wall, TDI med vel: Tissue Doppler Imaging Velocity of Medial Wall

Figure 1: Left atrial appendage structure with its basic segments in two-dimensions transesophageal echocardiography.

Left atrial appendage tissue Doppler imaging velocities

During TEE, from the mid esophageal four-chamber view, the multiplane angle was rotated forward towards the two-chamber view at 20˚- 40˚, and slightly withdrawing and turning the probe to the left leading to the recording of LAA orthogonal images. At this level, after adjusting the image depth to approximately 10 cm or less to maximize the LAA diameter, it was then carefully examined for thrombus with 80-100˚ vertical angulation while holding the LAA on the centerline of the image. LAA TDI was detected by depositing the Doppler cursor near LAA base, using a sample size of 2.5mm and cutting down progressively the angle between the interrogating beam and LAA long axis. In that way, TDI velocities of LAA medial and lateral walls were recorded. Peak TDI velocities (Figure 2) of medial (TDI med) and lateral (TDI lat) walls were measured within baso-medial appendage segment (Figure 1B-point 2) and within left lateral ridge near its bottom (Figure 1B-point 3), respectively [26-27].

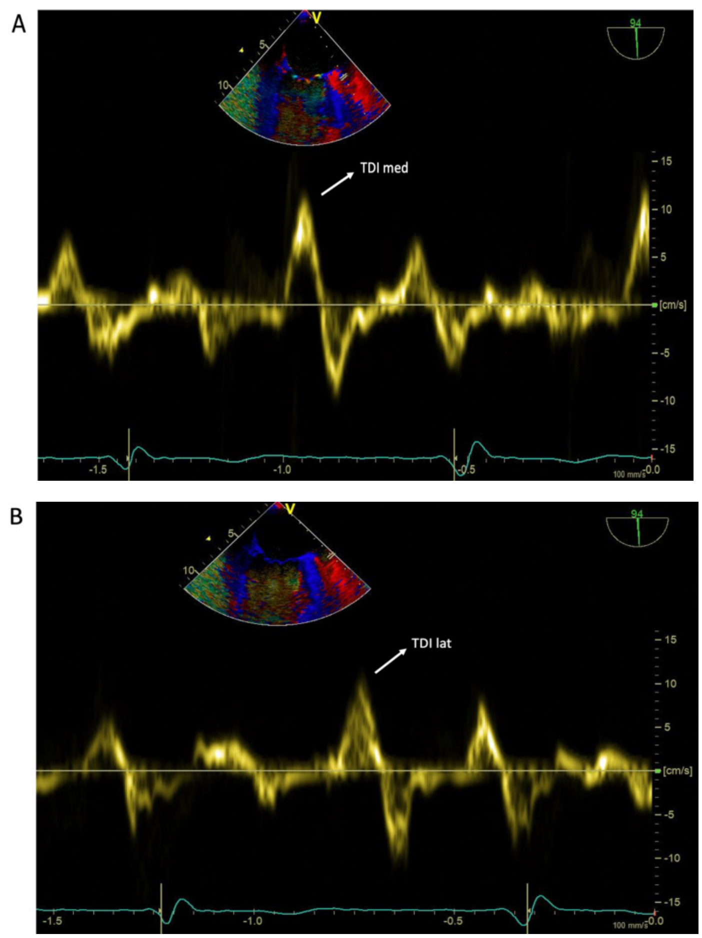


Figure 2: Tissue Doppler Imaging (TDI) velocities of A) medial wall and B) lateral wall in left atrial appendage during two-dimensions transesophageal echocardiography (TEE).

Cardioversion

DCCV was carried out in the coronary care unit after anesthesia with intravenous midazolam and an initial synchronized

DC shock of 100 Joules, progressively augmented to 200 to maximum 360 Joules, in order to be successful. The procedure was considered to be successful if sinus rhythm remained for at least 1 day and 6 months later. All patients followed the appropriate anticoagulation therapy before TEE which was expanded to 4 weeks in case of successful sinus rhythm reestablishment while in case of electrical CV failure, anticoagulation treatment was remained [28].

Statistical analysis

Quantitative variables are expressed as mean values ± Standard Deviations (SD). Qualitative variables are expressed as absolute and relative frequencies. Students't-tests were used in normally distributed variables for the comparison of means between two groups and the computation of effect sizes. Effect sizes of 0.2-0.5 are considered small, between 0.51-0.81 moderate and over 0.8 large. Pearson's or Spearman's correlation coefficients (r) were used to test the association of two continuous measures. Correlation coefficient between 0.1 and 0.3 are considered low, between 0.31 and 0.5 moderate and over 0.5 high. Receiver operated characteristic (ROC) curves, Areas under the Curve (AUC), and optimal cut-off values were calculated for selected variables. An AUC of 1 indicates perfect performance, while less than 0.5 indicates a performance that was not different from chance. Logistic regression analysis was also used to test the ROC analysis results. All p values reported are two-tailed. Statistical significance was set at 0.05 and analyses were conducted using SPSS statistical software (version 20).

Results

DCCV was performed in 100 patients (74 men and 26 women) with non-valvular atrial fibrillation within 24h after TEE. DCCV was successful in 80% of them and was maintained until discharge, with no side effects. Sinus rhythm restoration was obtained by synchronized DC shock of 100 Joules in 10%, 200 Joules in 75% and 360 Joules in 15% of patients. Six months after DCCV, sinus rhythm was remained in 75% of patients. The mean age of the patients was 64.7±9.8 years old with mean value of Left Ventricle Ejection Fraction (LVEF) and left atrium volume index (LAVI) of 46.4±8.2% and 47.3±12.9ml/m^2, respectively (Table 1).

	Minimum value	**Maximum value**	**Mean value**	**Std. Deviation**
AGE (YEARS)	42	87	64.74	9.77
TDI vel (cm/s)	4	17	9.64	2.751
TDImed vel (cm/s)	4	18	9.404	2.7576
TDIlat vel (cm/s)	3	18	9.142	3.031
PW Doppler vel (%)	14	85	49.08	17.883
LAVI (ml/m^2)	23	78	47.341	12.952
LVEF (%)	30	60	46.4	8.2
LVED (mm)	40	62	50.3	5.8

LAVI: Left Atrium Volume Index; **LVED:** Left Ventricle End-Diastolic Diameter; **LVEF:** Ejection Fraction of Left Ventricle; **TDI:** Tissue Doppler Imaging Velocity of Left Atrium Appendage Walls (mean value); **TDIlat vel:** Tissue Doppler Imaging Velocity of Lateral Wall of Left Atrium Appendage; **TDImed vel:** Tissue Doppler Imaging Velocity of Medial Wall of Left Atrium Appendage; **PW Doppler vel:** Pulse Wave Doppler Velocity of Left Atrium Appendage

Table 1: Baseline characteristics of patients with atrial fibrillation before electrical cardioversion.

On ROC curve analysis, TDI velocity (median value) was a significant predictor of sinus rhythm restoration (AUC=0.701, p=0.007) (Figure 3A). Particularly, TDI velocity »8cm/s predicted successful cardioversion with sensitivity 70% and specificity 63%. On the other hand, PW Doppler velocity >40cm/sec demonstrated sensitivity of 71.8% and specificity of 47.4%, while a value of >50cm/sec corresponded to sensitivity 57.7% and specificity 63.2% (Figure 3B). Therefore, TDI velocities were more predictive of a successful cardioversion compared to PW Doppler velocities of >40cm/s (p=0.015). Moreover, TDI recordings at the medial LAA were more accurate with less artefacts and better positioning of the sample volume than recordings at the lateral LAA. Finally, global longitudinal strain of LAA did not present any significant correlation with successful cardioversion (AUC=0.406, p=0.44) (Figure 3C).

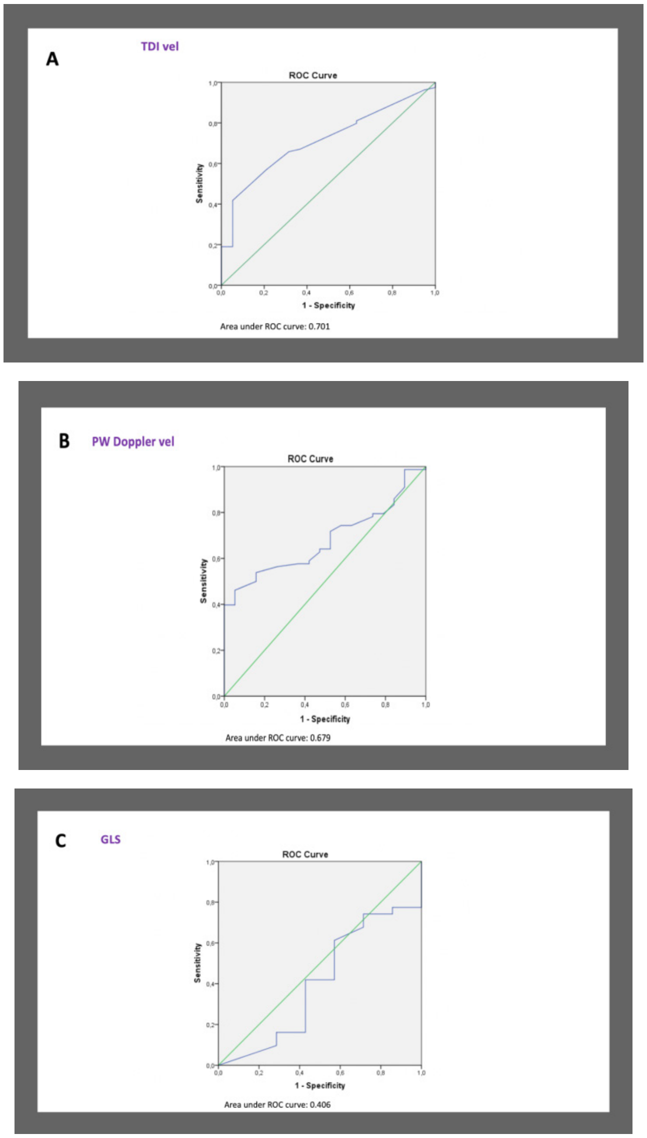


Figure 3: Receiver Operated Characteristic (ROC) analysis investigating the correlation between successful electrical cardioversion and: A. Tissue Doppler Imaging velocity of left atrial appendage walls (TDI vel), B. Pulse Wave Doppler velocity of left atrial appendage (PW Doppler vel), C. Global Longitudinal Strain of left atrial appendage (GLS).

No correlation was found between LVEF and successful DCCV (r<0.1), while moderate correlation between LAVI and successful DCCV (r=0.32, p=0.07) was revealed. Only low TDI values (<8cm/s) showed high negative correlation with successful DCCV (r=-0.645, p=0.007), while low PW values (<40cm/s) revealed low negative correlation with successful DCCV (r=-0.12, p=0.145). Maintenance of SR for 24 hours after successful DCCV was found to have low negative correlation only with TDI and LAVI (r=0.15, p=0.11 and r=0.11, p=0.2 respectively).

Discussion

In this study, we found that in patients with AF, TDI LAA velocities can predict successful DCCV and sinus rhythm recovery. Transthoracic DCCV is recognized as the cornerstone of rhythm-control strategy, being an effective treatment for sinus rhythm restoration and arresting progressive effects of AF, mainly the development of serious cardiomyopathy [29]. However, AF has a high recurrence rate which is defined by multiple factors such as the duration of AF and the size of LA. Catheter ablation for AF is characterized generally as a safe method and although there are few studies examining the favorable effect of CV in randomized populations as the elderly [30-31], it has not been looked into specifically in the population of AF patients with concomitant HFpEF [32], where no medical therapy appears to reduce mortality.

LAA flow velocity, which can mirror atrial contractility, constitutes an independent predictor and at the same time, the best discriminator of DCCV success [33]. LAA TDI and strain directly denotes LAA myocardial function and contributes to risk stratification of thrombus formation and possibility of embolism. This is of great importance, since risk factors for LA thrombus development are not fully comprehended and are not integrally equal to those for stroke appearance in AF patients [34]. Atrial thrombogenesis in AF subjects is based mainly on endocardial remodeling being the underlying pathophysiological mechanism [35], but also other mechanisms as oxidative stress and inflammation of fibrillating atrial tissue can contribute. To the same direction, coexistence of diseases or parameters such as ageing, diabetes mellitus, arterial hypertension or heart failure exert crucial effect. Previous conditions must be taken into account for all patients guided to electrical CV since this process may lead to thrombus formation and possible embolization [36].

Recently, Speckle Tracking Echocardiography (STE) is recognized as an important marker of LA and LAA mechanical function with two major disadvantages; difficulty, in several cases, to record optimal images particularly of LAA middle and distal segments but also lack of special software focused to investigate deformation mechanics of a much smaller cavity than left ventricle, such as LAA. Indeed, our study did not confirm any significant correlation of global longitudinal strain and successful DCCV. However, Di Salvo et al and Wang, et al. demonstrated that atrial strain and strain rate can forecast the possibility of sinus rhythm restoration [37,38]. It seems that, particularly in case of AF, the implementation of LAA wall STE must be examined to a larger extent. Also, there are controversial reports by several studies concerning LLA contractility as a predictor marker of successful DCCV in non-valvular AF disease [25,39-41]. Mitusch, et al. [25], found a significant difference in LAA peak emptying velocity of non-valvular AF individuals, comparing those with successful DCCV to those with unsuccessful one. However, the population of this study was heterogeneous since in the majority of its patients, LAA velocity was estimated exclusively after sinus rhythm restoration. Tabata, et al. [39], concluded that the duration of AF, the maximum LAA area and LAA emptying velocities before DCCV, predicted restoration of sinus rhythm for isolated AF but their findings were limited in a small number of patients. On the other hand, Perez, et al. [40], reported no correlation between LAA emptying velocities and DCCV result and similarly, Verhost, et al. [41], found no significant difference concerning LAA emptying velocities between successful and unsuccessful DCCV. By contrast Palinkas, et al. [14], examining a large group of patients using incisive excluding criteria, demonstrated that LAA emptying velocity by TTE can predict DCCV success adding significant prognostic value. Paraskevaidis, et al. [42], showed that TDI analysis of the mitral annulus during TTE at precardioversion time, anticipates AF recurrence. In fact, negative systolic wave velocity >5.25cm/sec indicated persistent AF or paroxysmal AF of more than 48h, leading after 1-year follow up to persistent AF. Velocities <5.25cm/sec corresponded to sinus rhythm or paroxysmal AF of less than 48h. Indeed, several studies demonstrated that higher LAA wall velocities can predict short-term or long-term success of DCCV while patients with a longer AF duration is associated with lower AF velocities [43-44]. Finally, LAA wall motion velocities could also be used to monitor changes in remodeling, as LAA wall contractility seems to be improved after percutaneous mechanical mitral commissurotomy [45], as well as after ablation of persistent AF [46]. Our study, which to our knowledge is the second published using TDI velocities of LAA during TEE, complemented the previous studies and showed additionally that measurement of LAA TDI velocities during TEE, probably even only this of medial wall, predicted effectually the outcome of DCCV compared to PW Doppler velocities. TDI of medial wall presents higher imaging quality, probably because imaging of lateral wall is impacted by shadowing artifacts across the LAA-pulmonary vein ridge (“coumadin ridge”).

Our results emphasize the importance of LAA wall motion contractility as an index of atrial fibrosis. Atrial fibrosis initiates atrial mechanical remodeling through the decrease of atrial contractility and the atrial enlargement, leading to high risk of recurrent AF [47]. The main advantage of using LAA wall motion, compared to other parameters of mechanical remodeling as left atrial ejection fraction and strain, is its reliability before DCCV especially during TEE. In our study, we concluded that TDI velocity and precisely a value > 8cm/sec can predict a successful DCCV. These findings could really enable a greater qualification of AF patients intending to undergo electrical rhythm control therapy. Especially for HFpEF patients, a group that no pharmacological agents have really demonstrated favorable prognosis, this is of great importance since the restoration of sinus rhythm could mean lower risk of mortality. Finally, these data could identify those patients with AF and lower TDI velocities who could benefit of supplementary medical antiarrhythmic therapy and keeping on anticoagulant strategy for a longer period after DCCV.

Conclusions

This study supports the aspect that markers of LA mechanical remodeling and especially TDI velocities of the LAA walls can be used for the prediction of sinus rhythm recovery after DCCV in AF patients. TDI-based technique is a less load dependent method providing supplementary information concerning atrial contractility, additionally to a conventional two-dimensions and Doppler flow echocardiography. Higher TDI velocities increased the likelihood of successful CV demarketing as the best cut-off value this of >8cm/sec.

Limitations

This study presented with some limitations concerning at first an observational study which includes a certain sample size of patients. Secondly at times, defibrillation threshold for atrial fibrillation DCCV can be related to patient body habitus, the position of defibrillation pads as it has already been referred and the parameter of patient age. Unfortunately, there is no homogeneity concerning the age of population in our study as it was very difficult to succeed it. On the other hand, maintenance of sinus rhythm may be influenced by other variables than the tested echocardiographic indices, such as glomerular filtration rate (GFR), and medications (b-blockers, eplerenone). Finally, we estimated AF duration retrospectively counted on patients’ statements. Since this is not a reliable strategy, we did not examine AF duration as an index of sinus rhythm recovery.

Conflict of Interest

The authors declare that there is no conflict of interest.

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