Incremental Value of Right Atrial Strain Analysis to Predict Atrial Fibrillation Recurrence After Electrical Cardioversion

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Background: Although the assessment of left atrial (LA) mechanics has been reported to refine atrial fibrillation (AF) risk prediction, it doesn't completely predict AF recurrence. The potential added role of right atrial (RA) function in this setting is unknown. Accordingly, this study sought to evaluate the added value of RA longitudinal reservoir strain (RASr) for the prediction of AF recurrence after electrical cardioversion (ECV).

Methods: We retrospectively studied 132 consecutive patients with persistent AF who underwent elective ECV. Complete two-dimensional and speckle-tracking echocardiography analyses of LA and RA size and function were obtained in all patients before ECV. The end point was AF recurrence.

Results: During a 12-month follow-up, 63 patients (48%) showed AF recurrence. Both LASr and RASr were significantly lower in patients experiencing AF recurrence than in patients with persistent sinus rhythm (LASr, 10% ± 6% vs 13% ± 7%; RASr, 14% ± 10% vs 20% ± 9%, respectively; $P < .001$ for both). Right atrial longitudinal reservoir strain (area under the curve = 0.77; 95% CI, 0.69-0.84; $P < .0001$) was more strongly associated with the recurrence of AF after ECV than LASr (area under the curve = 0.69; 95% CI, 0.60-0.77; $P < .0001$). Kaplan-Meier curves showed that patients with both LASr ≤ 10% and RASr ≤ 15% had a significantly increased risk for AF recurrence (log-rank, $P < .001$). However, at multivariable Cox regression, RASr (hazard ratio, 3.26; 95% CI, 1.73-6.13; $P < .001$) was the only parameter independently associated with AF recurrence. Right atrial longitudinal reservoir strain was more strongly associated with the occurrence of AF relapse after ECV than LASr, and LA and RA volumes.

Conclusion: Right atrial longitudinal reservoir strain was independently and more strongly associated than LASr with AF recurrence after elective ECV. This study highlights the importance of assessing the functional remodeling of both the RA and LA in patients with persistent AF. (J Am Soc Echocardiogr 2023;36:945-55.)

Keywords: Speckle-tracking echocardiography, Atrial function, Right atrial strain, Right atrium, Atrial Fibrillation

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in adults.[1,2] It represents a major cause of mortality and morbidity, mainly related to embolic events, heart failure, sudden cardiac death, and noncardiac death.[1,2] Rhythm control therapy with electrical (ECV) or pharmacological cardioversion is recommended for symptomatic subjects to improve their quality of life.[1-3] However, recurrence of AF after cardioversion reaches up to 60% in the first 12 months.[1,2,4] Clinical factors such as older age, female sex, persistent AF, smoking, chronic obstructive pulmonary disease (COPD), chronic kidney disease, structural heart disease, heart failure, and previous cardioversion have been associated with an increased risk for AF recurrence after elective ECV.[1,2,5,6] In addition, the

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Conflicts of Interest: None.

This study was partially supported by the Italian Ministry of Health.

James D. Thomas, MD, served as guest editor for this report.

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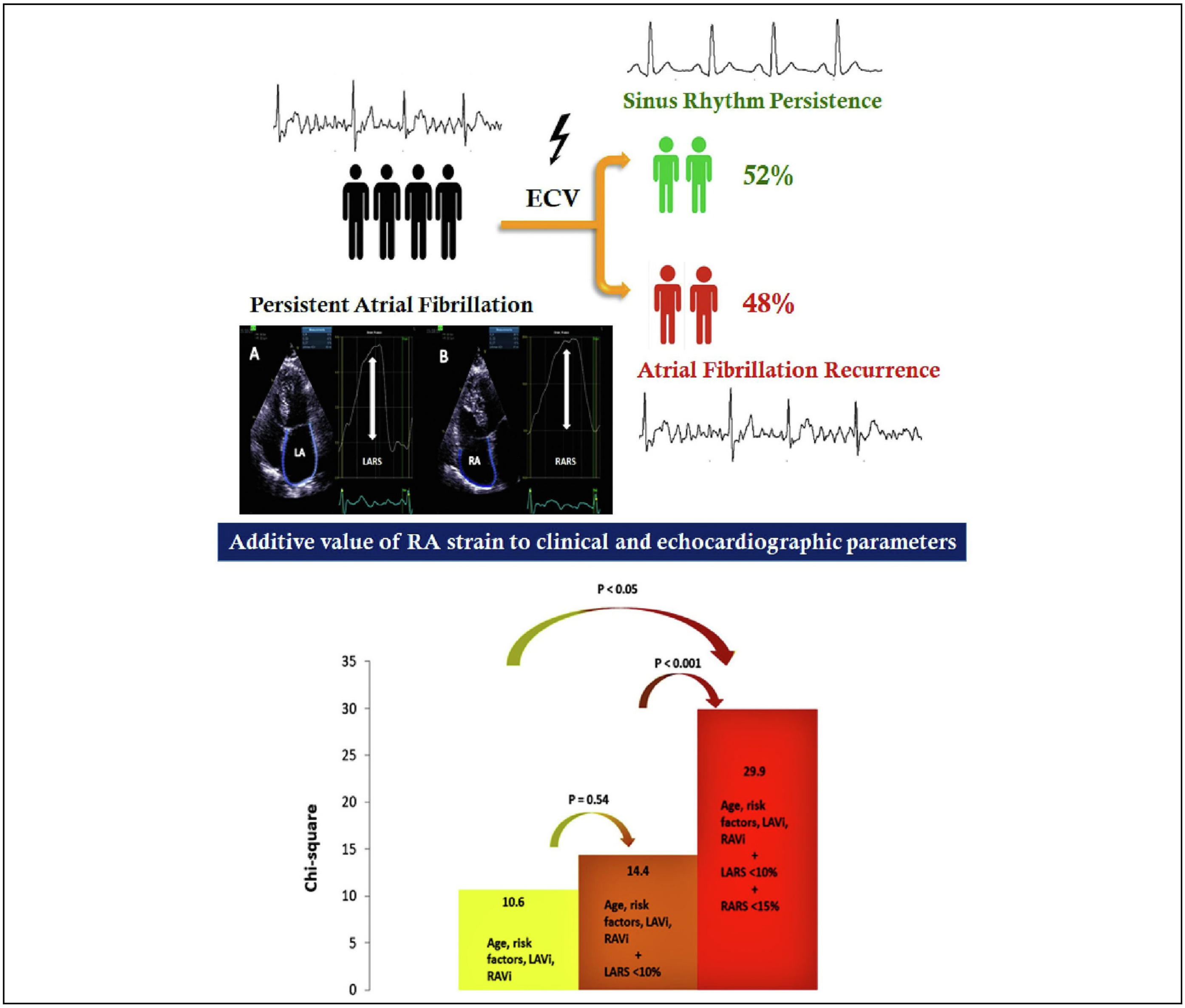
0894-7317/$36.00

https://doi.org/10.1016/j.echo.2023.05.011



Central Illustration The added role of right atrial strain over LA strain to predict AF recurrence after ECV

evaluation of left atrial (LA) volume and myocardial deformation by two-dimensional speckle-tracking echocardiography (2D-STE) has been shown to refine the prediction of AF recurrence after rhythm control strategy.[7,8] Recent findings suggest that AF could lead to several morphofunctional changes of both the left atrium (LA) and the right atrium (RA), a condition known as atrial cardiomyopathy, which could explain the progression of AF and the potential failure of the rhythm control strategy.[1,2,9] However, no study has evaluated the potential role of combining the right atrial (RA) and LA longitudinal myocardial deformation analysis by 2D-STE to predict AF recurrence after elective ECV. Accordingly, we sought to evaluate the relative value of LA longitudinal reservoir strain (LASr) and RA longitudinal reservoir strain (RASr) analysis by 2D-STE to predict AF recurrence after elective ECV.

METHODS

Study Population

We retrospectively analyzed echocardiographic studies obtained from clinically stable patients in AF scheduled for elective ECV between June 2020 and December 2021. Inclusion criteria were age >18 years and elective hospitalization for ECV of AF. Exclusion criteria were pregnancy, previous cardiac surgery, presence of a pacemaker or implantable cardioverter-defibrillator, more than moderate valvular regurgitation, severe aortic stenosis, systolic dysfunction of either the left (i.e., left ventricular [LV] ejection fraction [LVEF] <50%) or right ventricle (RV; i.e., tricuspid annular plane systolic excursion [TAPSE] <17 mm), poor apical acoustic window with inadequate images for 2D-STE analysis, hemodynamic instability

Abbreviations

2D = Two-dimensional

2D-STE = Two-dimensional speckle-tracking echocardiography

AF = Atrial fibrillation

AUC = Area under the curve

COPD = Chronic obstructive pulmonary disease

ECV = Electrical cardioversion

HR = Hazard ratio

LA = Left atrial, atrium

LASr = Left atrial longitudinal reservoir strain

LAVi = Left atrial volume index

LV = Left ventricular

LVEF = Left ventricular ejection fraction

OSAS = Obstructive sleep apnea syndrome

RA = Right atrial, atrium

RASr = Right atrial longitudinal reservoir strain

RAVi = Right atrial volume index

ROC = Receiver-operator characteristic

RV = Right ventricular, ventricle

RVFWLS = Right ventricular free-wall longitudinal strain

SR = Sinus rhythm

TAPSE = Tricuspid annular plane systolic excursion

requiring urgent ECV, unsuccessful ECV, early recurrent AF (defined as a relapse of AF within 1 minute after at least 2 sinus beats following the ECV),[10] AF recurrence post–ablation blanking period,[11] and lack of follow-up data. This retrospective analysis of clinically indicated echocardiographic studies data was approved by the Ethics Committee of the Istituto Auxologico Italiano, IRCCS (record 2021_05_18_13, approved on May 18, 2021). The need for patient written informed consent was waived due to the retrospective nature of the study. According to current privacy protection rules, data were anonymized before being included in the study database.

Atrial Fibrillation Clinical Management and Follow-Up

Restoration of the sinus rhythm (SR) was obtained through elective ECV. During ECV, patients were under deep sedation. All ECVs were performed using a biphasic defibrillator with the energy delivery selected on 150 to 200 Joules. After conversion to SR, optimization of medical therapy with class Ic/III antiarrhythmic drugs was left to the clinical judgment of the attending cardiologist.[1,2] All patients received appropriate oral anticoagulation 3 weeks before and at least 4 weeks after ECV according to their CHA_2DS_2-VASc and HASBLED risk scores.[1,2,12]

For the purposes of this retrospective analysis, we collected the patients' clinical data including age, sex, body mass index, hypertension, diabetes mellitus, dyslipidemia, smoking status, medical history of coronary artery disease or of thyroid dysfunction, chronic kidney disease, obstructive sleep apnea syndrome (OSAS), COPD, HASBLED and CHA_2DS_2-VASc scores, pharmacological treatment, and previous episode(s) of AF.

The primary end point was the evidence of new episodes of AF after the index ECV. Information concerning AF relapses was obtained at regular intervals (3, 6, and 12 months after the ECV) via review of electronic medical records of scheduled outpatient visits, 12-lead electrocardiograms, 24-hour ambulatory electrocardiographic monitoring, and hospital admission records. Assignment of clinical events was performed by physicians unaware of the patients' echocardiographic and clinical characteristics. Finally, in a subgroup of patients, we analyzed the echocardiographic exams obtained within 3 months after ECV.

TWO-DIMENSIONAL AND SPECKLE-TRACKING ECHOCARDIOGRAPHY

Image Acquisition

Comprehensive two-dimensional (2D) echocardiography and Doppler studies were performed prior to ECV (average time, 3 days before), using Vivid E9/E95 scanners (GE Vingmed) equipped with M5S and 4V probes. Left atrial volume was calculated using the biplane disk summation technique using dedicated, nonforeshortened LA apical 4- and 2-chamber views.[13] Right atrial volume was obtained from the RV-focused apical 4-chamber view using the single-plane area-length technique.[13,14] Left atrial and RA volumes were indexed to the body surface area to obtain the LA (LAVi) and RA (RAVi) volume indexes. Left ventricular systolic function was assessed using 2D biplane Simpson's LVEF.[13] Right ventricular (RV) functional assessment included both TAPSE and fractional area change.[15] Pulsed-wave spectral Doppler tracings of the mitral inflow and LV outflow were obtained from the apical 5-chamber view, with the sample volume at the tip of the mitral valve leaflets and at the LV outflow tract level, respectively. Pulsed-wave tissue Doppler imaging was used to obtain the myocardial velocities of the basal septal and lateral segments from the apical 4-chamber view. Continuous-wave Doppler was applied in the parasternal and apical 4-chamber views to record tricuspid regurgitation jet peak velocity.[16] Data sets were stored digitally and exported to a separate workstation for offline analyses.

Image Analysis

Digitally stored 2D echocardiography images and Doppler tracings were analyzed offline using EchoPAC 204 (GE Vingmed). Left ventricular global longitudinal strain and RV free-wall longitudinal strain (RVFWLS) were computed using dedicated speckle-tracking software packages (AFI and AFI RV, EchoPAC BT204, GE Vingmed) applied to LV apical 4- and 2-chamber and long-axis views, and RV-focused apical 4-chamber view, respectively.[17,18] Left atrial strain (Figure 1) was obtained from a dedicated apical 4-chamber view optimized to maximize LA size and using a dedicated software package (AFI LA, GE Vingmed).[18] The region of interest was adjusted according to the LA shape, avoiding the pulmonary veins and the LA appendage. The R wave on electrocardiography trace was used as the time reference to define the zero baseline for LA strain curves. The software then can calculate the LA longitudinal strain values for the reservoir, the conduit, and the contractile functions.[19] The measurements obtained from at least 5 consecutive cardiac cycles were averaged.[16] Right atrial strain (Figure 1) was measured using the same software package used for LA strain analysis. The region of interest was drawn on the RA walls using the RV focused apical 4-chamber view, optimized in terms of orientation, depth, and gain to maximize RA area and avoid RA foreshortening. Among the 3 atrial function components, we used the reservoir function because of its well-known clinical utility shown in previous reports[18] and the possible impairment of the conduit phases during AF.

HIGHLIGHTS

- LASr and RASr are associated with AF recurrence in AF patients undergoing ECV.
- RASr provides incremental prognostic value over LASr.
- Speckle-tracking evaluation of both atria is pivotal for a better risk stratification of AF patients

Reproducibility Analysis

Intra- and interobserver reproducibility of LASr and RASr was tested by computing intraclass correlations and coefficients of variation. Intraobserver variability was tested by reanalyzing 20 random data sets 1 month apart by the same researcher (V.C.) blinded to the initial measurements. The interobserver variability was tested by having the same data sets analyzed independently by a different researcher (N.R.) who was unaware of the results of the other.

Statistical Analysis

The Shapiro-Wilk test assessed the normal distribution of continuous quantitative variables. Continuous variables were presented as means with SD or median (interquartile range) for skewed variables. Categorical variables were presented as numbers with percentages. Comparisons of continuous variables were made with a Student's *t* test or Mann-Whitney *U* test and binomial variables with a chi-squared test as appropriate. Receiver-operator characteristic (ROC) curves were constructed to evaluate the performance of echocardiographic variables in predicting AF recurrence and to calculate optimal cutoff values, the specificity and sensitivity of the parameters in the prediction of AF recurrence, using Youden's index. To evaluate potential predictors of AF recurrence, univariable and multivariable Cox regression analyses were performed. Before multivariable analysis, to exclude any multicollinearity, preliminary analyses were performed by using the variance inflation factor, considering the values between 1 and 10 as the absence of collinearity. The results of the multivariable analysis are shown as the hazard ratio (HR) with the corresponding 95% CI. The incremental value of LASr and RASr was assessed in 3 modeling steps and was evaluated by comparing the additional percentage of increase of the chi-square value of combined models over the baseline model. The first step consisted of fitting a multivariate model 0, which included clinical variables, LAVi, and RAVi. Then LASr was included in the second step and RASr in the third step. Kaplan-Meier survival curves were used to evaluate the AF-free survival rate, and comparisons between groups were performed using the log-rank test. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 28.0 (IBM) and MedCalc 20 (MedCalc Software). A 2-sided significance level of $P < .05$ was considered statistically significant.

RESULTS

Baseline Characteristics

From a total of 190 patients that were screened in our study, 20 were excluded because of incomplete or inadequate transthoracic echocardiography data sets, 5 were excluded because of the presence of cardiac implantable electronic devices, 16 were excluded for lack of follow-up data, and 17 were excluded because of severe mitral and/or tricuspid regurgitation. Finally, 132 patients were included in the study cohort. The distribution of LASr and RASr in the study population is shown in Supplemental Figure 1.

Table 1 summarizes the main clinical, demographic, and echocardiographic characteristics of the study population. During the follow-up period of 12 months, 63 patients (48%) experienced AF recurrence. Patients who experienced AF recurrence had similar age, sex, and body mass index distribution as patients with persistent SR (Table 1). Similarly, the prevalence of smoking, hypertension, thyroid dysfunction, diabetes, chronic kidney disease, smoking, OSAS, COPD, history of ischemic heart disease, and previous AF episodes or catheter ablation for AF was similar between the 2 groups (Table 1). The use of flecainide was significantly more frequent ($P < .05$) in patients who did not experience AF recurrence, whereas no significant differences between the 2 groups were found in the use of beta-blockers, amiodarone, direct oral anticoagulants, and vitamin

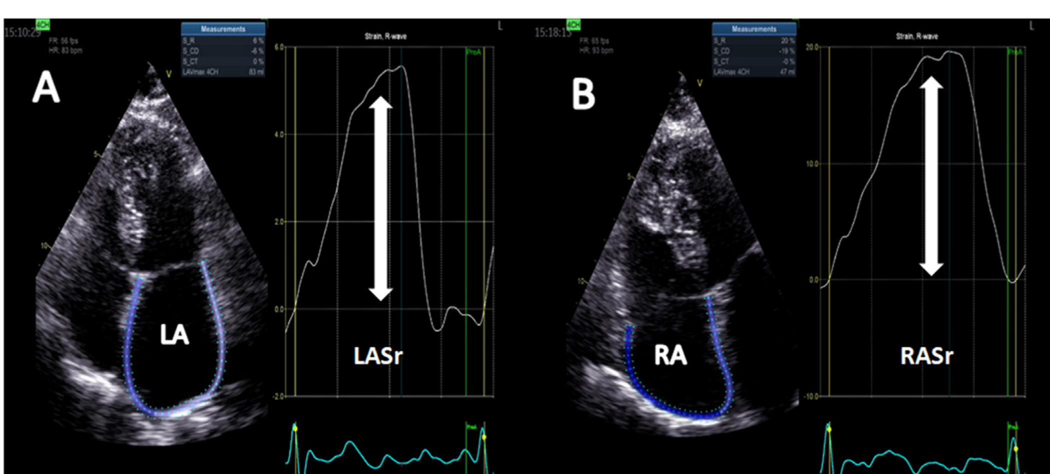


Figure 1 Left atrial and RA strain curves obtained from 2D-STE. **(A)** Automated tracking of the LA myocardium in the 4-chamber view. **(B)** Automated tracking of the RA myocardium in the RV-focused apical 4-chamber view. *LAVmax* 4CH, Single-plane atrial maximal volume in 4-chamber apical view; *S-CD*, conduit longitudinal strain; *S-CT*, contraction longitudinal strain; *S-R*, reservoir longitudinal strain.

Table 1 Clinical and echocardiographic parameters of the study population

	Total (n = 132)	No AF recurrence (n = 69)	AF recurrence (n = 63)	P
Age, years	72 ± 10	71 ± 10	73 ± 10	.108
Gender, male	73 (55)	41 (59)	32 (51)	.321
Body mass index ≥ 30 kg/m^2	17 (13)	8 (11)	9 (14)	.664
Heart rate, bpm	86 ± 22	83 ± 18	88 ± 26	.490
Systolic blood pressure, mm Hg	135 ± 18	134 ± 16	137 ± 19	.393
Diastolic blood pressure, mm Hg	83 ± 11	83 ± 12	84 ± 11	.368
Hypertension	108 (81)	59 (86)	49 (77)	.433
Diabetes mellitus	14 (11)	8 (11)	6 (9)	.747
Smoking	32 (24)	19 (27)	13 (21)	.357
OSAS	17 (13)	8 (11)	9 (14)	.664
COPD	12 (9)	5 (7)	7 (11)	.454
Chronic kidney disease stage IV/V	3 (2)	1 (1)	2 (3)	.506
Thyroid dysfunction	29 (22)	13 (19)	16 (25)	.382
Coronary artery disease	14 (11)	8 (11)	6 (9)	.682
Previous AF episodes	58 (44)	26 (38)	32 (51)	.129
Previous AF catheter ablation	15 (11)	5 (7)	10 (15)	.142
Beta-blockers	89 (67)	44 (64)	45 (71)	.351
Flecainide	30 (22)	22 (32)	8 (13)	**.0089**
Amiodarone	37 (28)	22 (32)	15 (24)	.304
Direct oral anticoagulants	114 (87)	58 (84)	56 (88)	.542
Vitamin K antagonists	4 (3)	2 (3)	2 (3)	.926
CHA_2DS_2-VASC	3 ± 1	3 ± 1	2.5 ± 1	.373
HASBLED	1 ± 0.7	1 ± 1	0.9 ± 0.8	.591
LV end-diastolic volume, mL/m^2	57 ± 17	57 ± 16	56 ± 17	.207
LV end-systolic volume, mL/m^2	27 ± 14	27 ± 13	26 ± 15	.379
LVEF, %	54 ± 10	54 ± 10	54 ± 11	.820
LV global longitudinal strain, %	14 ± 5	14 ± 5	14 ± 4	.596
E wave, cm/sec	89 ± 21	87 ± 19	89 ± 23	.531
E’ septal, cm/sec	9 ± 3	9 ± 3	9 ± 3	.162
E’ lateral, cm/sec	11 ± 3	12 ± 3	11 ± 4	.360
E/e’	9 ± 4	9 ± 3	10 ± 5	.202
TAPSE, mm	19 ± 4	20 ± 4	19 ± 4	.052
RV fractional area change	41 ± 8	42 ± 8	40 ± 8	.229
Systolic pulmonary artery pressure, mm Hg	33 ± 9	34 ± 9	32 ± 8	.162
RVFWLS, %	19 ± 6	20 ± 6	18 ± 6	**.036**
LA volume, mL/m^2	50 ± 15	48 ± 14	53 ± 16	.060
LA reservoir strain, %	12 ± 7	14 ± 7	10 ± 6	**<.001**
RA volume, mL/m^2	35 ± 14	33 ± 13	37 ± 15	.059
RA reservoir strain, %	17 ± 10	20 ± 9	14 ± 10	**<.001**

Data are presented as mean ± SD or n (%).
In bold are the statistically significant differences between patients with AF recurrences and no AF recurrences.

K antagonists (Table 1). As expected, both LASr (10% ± 6% vs 14% ± 7%) and RASr (14% ± 10% vs 20% ± 9%) were significantly lower in the group that experienced AF recurrence (Table 1, $P < .001$). Conversely, both RAVi and LAVi were similar between patients who maintained the SR and those who experienced AF recurrence. Finally, no significant differences were found among the other echocardiographic parameters of LV and RV function, except for RVFWLS magnitude, which was lower in the group with AF recurrence (Table 1, $P < .05$).

Predictors of AF Recurrence After Elective ECV

At Cox regression univariable analysis, including clinical and echocardiographic parameters, only LASr (HR = 2.21; 95% CI, 1.32-3.68; $P = .002$) and RASr (HR = 3.69; 95% CI, 2.09-6.52), $P < .0001$) were associated with the recurrence of AF (Table 2). The ROC curve analysis showed that RASr (area under the curve [AUC] = 0.77, 95% CI, 0.69-0.84, $P < .0001$) was more strongly associated with the recurrence of AF than LASr was (AUC = 0.69; 95% CI, 0.60-0.77, $P < .0001$; Figure 2).

Table 2 Univariate and multivariate analyses of associations with AF recurrence after ECV

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Clinical parameters:				
Age, years	1.02 (0.98-1.05)	.15		
Heart rate, bpm	1.01 (0.99-1.02)	.23		
Systolic blood pressure, mm Hg	1.00 (0.98-1.02)	.46		
Diastolic blood pressure, mm Hg	1.00 (0.97-1.02)	.96		
Hypertension	0.78 (0.42-1.49)	.47		
Diabetes mellitus	0.92 (0.40-2.21)	.92		
OSAS	1.1 (0.54-2.12)	.78		
Body mass index, kg/m^2	0.95 (0.52-1.74)	.89		
Thyroid dysfunction	1.22 (0.98-2.17)	.49		
Echocardiographic parameters:				
LV end-diastolic volume, mL/m^2	0.99 (0.99-1.00)	.25		
LV end-systolic volume, mL/m^2	0.99 (0.99-1.00)	.42		
LVEF, %	1.00 (0.99-1.00)	.99		
E wave, cm/sec	1.00 (0.99-1.01)	.53		
E' septal, cm/sec	0.93 (0.85-1.03)	.21		
E' lateral, cm/sec	0.97 (0.89-1.04)	.41		
LV global longitudinal strain, %	0.99 (0.99-1.00)	.28		
TAPSE motion, mm	0.95 (0.89-1.01)	.10		
RV fractional area change	0.98 (0.94-1.01)	.15		
Free wall longitudinal strain, %	0.99 (0.99-1.00)	.27		
LA volume, mL/m^2	1.01 (0.99-1.03)	.08		
LA reservoir strain <10%, n (%)	2.21 (1.32-3.68)	**.002**	1.33 (0.74-2.39)	.38
RA volume, mL/m^2	1.01 (0.99-1.03)	.11		
RA reservoir strain <15%, n (%)	3.69 (2.09-6.52)	**<.0001**	3.26 (1.73-6.13)	**<.001**

In bold are the statistically significant figures.

The optimal threshold values with the highest sensitivity and specificity were 15% for RASr (sensitivity = 76%, specificity = 75%) and 10% for LASr (sensitivity = 71%, specificity = 62%). Patients with LASr < 10% and RASr < 15% had a significantly higher risk of experiencing a recurrence of AF (log-rank P < .001 for both; Figure 3). However, the Kaplan-Meier curves for the RASr thresholds had a higher χ^2 at the log-rank discrimination analysis than the LASr threshold value (χ^2 = 36.400 vs χ^2 = 15.218).

Patient subgroups having both LASr ≥ 10% and RASr ≥ 15% had comparatively higher AF-free survival than patients with both LASr < 10% and RASr < 15% (log-rank P < .001; Figure 4).

A multivariable Cox regression analysis selected RASr < 15% (HR = 3.26; 95% CI, 1.73-6.13; P < .001) as the only independent variable associated with the recurrence of AF (Table 2). The additive prognostic value of RASr was further evaluated along with previously reported clinical and echocardiographic parameters using a hierarchical model χ^2 analysis. The addition of RASr < 15% to a basal model including age, risk factors for AF, LAVi and RAVi, and LASr < 10% significantly improved the model (P < .001), showing increased prognostic value for AF recurrence (Figure 5).

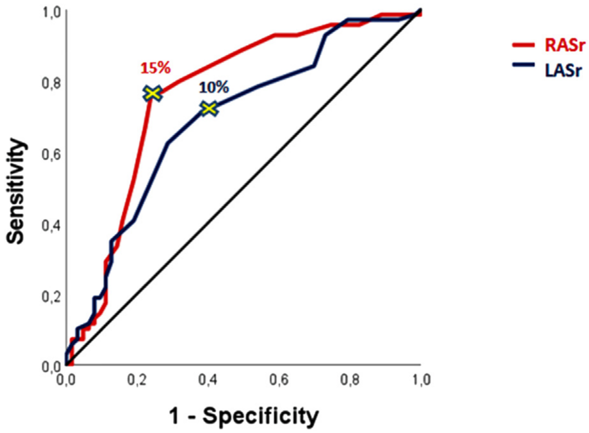


Figure 2 Receiving operator curves of LASr and RASr to identify values associated with early AF recurrence after ECV.

Comparison of Atrial Strain Parameters Pre- and Post-ECV

Sixty-two of the participants (47%) underwent echocardiography within 3 months after ECV (median 44 days, interquartile range, 16-86). Patients who maintained SR (45/62) after ECV increased LASr and RASr values compared to pre-ECV values (19.4% ± 5.6% vs 11.5% ± 4.2% and 27.1% ± 7% vs 17.5% ± 6%, $P < .0001$, respectively). Conversely, in patients with early AF relapse (17/62) there was no significant change in LASr and RASr between the studies obtained before and after the elective ECV values (11.5% ± 5.9% vs 9.8% ± 6.2%, P = .15, and 14.2% ± 7.7% vs 12.2% ± 6.4%, P = .08, respectively; Figure 6). After a follow-up period of 9 months, 10 of the 45 patients (22%) in SR experienced AF recurrence. Patients who maintained SR had a greater increase in atrial strain magnitude values (+8.5% ± 4.2% for LASr and +10.9% ± 4.9% for RASr, $P < .0001$) compared with patients with AF recurrence (+4.5% ± 1.4% for LASr and +4.1% ± 4.4% for RASr, $P < .0001$; Figure 6). The ROC curve analysis showed that the diagnostic accuracy of LASr and RASr, measured pre-ECV (during AF) and post-ECV (in SR), to identify AF recurrence post-ECV was better only for RASr (AUC = 0.74 vs 0.51, $Z = 3.9$, $P < .05$). Conversely, no difference was observed for LASr (AUC = 0.69 vs 0.52, $Z = 0.85$, $P < .39$).

Inter- and Intraobserver Reproducibility

Intra- and interobserver agreements for LASr and RASr measures were good, with intraclass correlation coefficients of 0.94 (95% CI, 0.80-0.98) and 0.897 (95% CI, 0.45-0.99) for LASr and 0.95 (95% CI, 0.83-0.97) and 0.88 (95% CI, 0.34-0.97) for RASr, respectively.

DISCUSSION

The present study demonstrates the role of RASr measured by 2D-STE before elective ECV to predict AF recurrence in patients with restored SR. The main findings of our study can be summarized as the following: (1) in patients with AF undergoing elective ECV, both LASr and RASr are associated with AF recurrence; (2) among the clinical and the echocardiographic parameters measured before elective ECV, RASr was the strongest parameter associated with AF recurrence and had additional prognostic power over LASr; and (3) the change in magnitude of LASr and RASr from pre-to post-ECV is associated with the recurrence of AF during follow-up (Central Illustration).

Atrial Remodeling as a Hallmark Phenomenon of AF Progression

Despite extensive research, the mechanisms underlying AF remain incompletely understood. Initiation of AF is generally sustained by rapidly discharging drivers.[1,2,20] The pulmonary veins have been identified as the main AF trigger site,[20] and their isolation is associated with higher rates of AF freedom in patients with both paroxysmal and persistent AF.[21] Recent reports suggest that the mechanisms underlying the perpetuation of AF could be related to a progressive electroanatomical remodeling of the atria, including modification of ionic currents, calcium handling, and wall fibrosis, potentially leading to multiple functional reentry circuits varying in time and space.[22] As a direct consequence, persistent AF is associated with a shift in the pathophysiological paradigm of AF, pointing out the central role of atrial substrates, a concept known as atrial cardiomyopathy.[9] As a marker of this process, in persistent AF, the atria become larger, and the myocardium of the atrial wall is less prone to deform compared with the atria of patients with paroxysmal AF.[22,23] This fibrotic remodeling involves both the LA and the RA, as

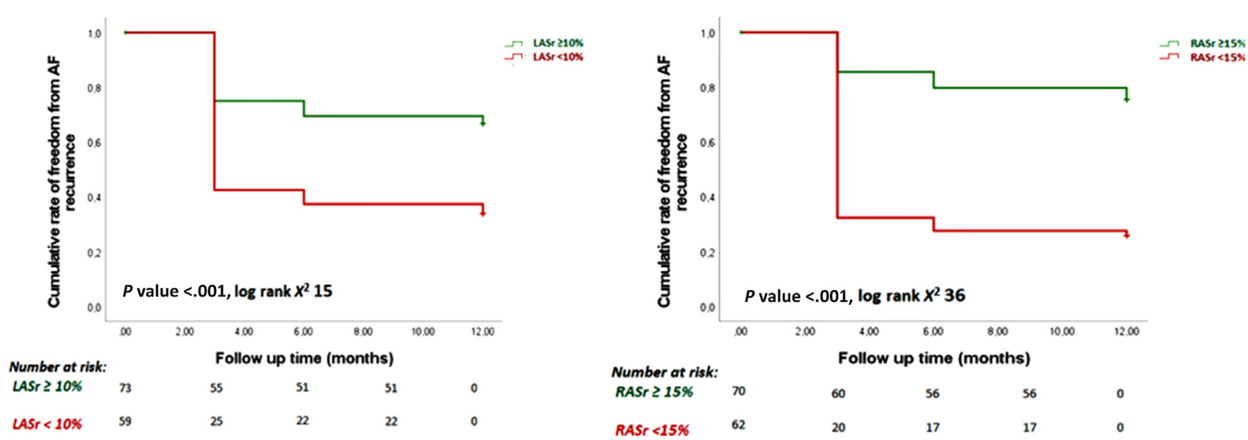


Figure 3 Atrial fibrillation recurrence freedom according to LASr and RASr. Kaplan-Meier plots of patients grouped according to the threshold levels of left (*left panel*) and right (*right panel*) values of reservoir longitudinal strain identified by the ROC curve analyses.

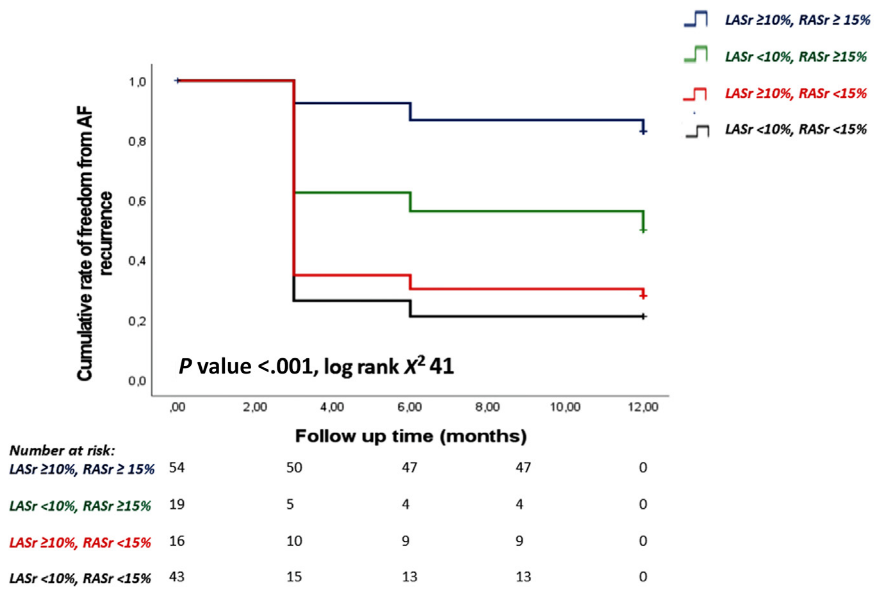


Figure 4 Additive prognostic value of RASr. Kaplan-Meier plots of 4 subgroups of patients grouped according to LASr and RASr values below or above the threshold values identified by the ROC curve analyses.

demonstrated by late gadolinium enhancement cardiac magnetic resonance,[24] which identified a similar amount of LA and RA fibrosis in AF patients undergoing pulmonary vein isolation. Accordingly, the identification of atrial fibrosis could be crucial to stratify the risk of AF progression and address patient management.[25] In recent years, the use of 2D-STE of the LA has proven to be a reliable surrogate of atrial fibrosis by showing a good correlation with both histology[26,27] and regional late gadolinium enhancement findings.[24,28]

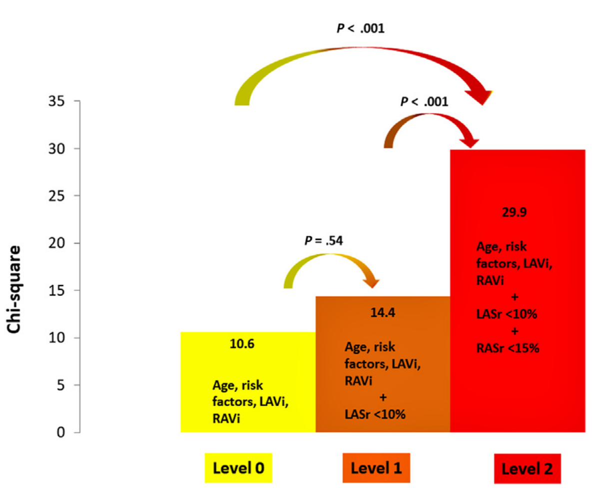


Figure 5 Incremental prognostic value of LASr and RASr over clinical risk factor for AF recurrence after cardioversion and atrial volumes. Level 0: Multivariable basal model including age, clinical risk factors for AF recurrence (see text), LAVi, and RAVi. Level 1: Addition of LASr on level 0. Level 2: Addition of RASr on level 1. The bar graphs show the chi-squares of the resulting models at each level.

The Added Value of RA Strain to Predict AF Recurrence

Although LAVi has been demonstrated to be a valuable predictor of AF both in the general population[29] and in patients undergoing either ECV[30] or catheter ablation,[31] in our sample LAVi was not associated with recurrence of AF after elective ECV. Conversely, LASr < 10% was associated with AF recurrence. In line with this, a previous study demonstrated that LASr independently predicted AF recurrence after ECV, with a cutoff value of 10.75%.[32] The lack of predictive power of LAVi in our population could be explained by the ability of LASr to detect subclinical impairment of the LA myocardium regardless of the LA size.[33]

The role of the RA geometry and mechanics in the pathogenesis, progression, and treatment of AF has been less examined. Recent reports suggest that RAs remodel similarly to LAs and that the RA size could have an additional role in AF recurrence. Right atrial volume index by cardiac magnetic resonance was independently associated with incident AF in patients without cardiovascular disease in the Multi-Ethnic Study of Atherosclerosis.[34] Akutsu *et al.*[35] demonstrated that both LA and RA enlargement (>99 mL and >87 mL, respectively), measured with 64-slice multidetector computed tomography, was associated with AF recurrence after catheter ablation, and the combined value of both atrial volumes had additive prognostic power. Takagi *et al.*[36] showed that RA remodeling, defined as an RA volume of 111.5 mL measured with computed tomography, was the strongest predictor of recurrence after AF catheter ablation, regardless of AF type (paroxysmal vs persistent). Luong *et al.*[37] showed that RAVi had a superior ability to predict AF recurrence at 6 months after ECV, with a cutoff value of 42 mL/m^2. In another study,[38] RAVi was the only independent predictor of early AF recurrence (<3 months). Right atrial volume and mechanics evaluated with 2D and three-dimensional echocardiography showed a higher association with AF episodes in patients with atrial septal defect undergoing percutaneous closure compared with LA indices.[39] A RAVi > 38 mL/m^2 and RASr < 11% were independent predictors of postoperative AF

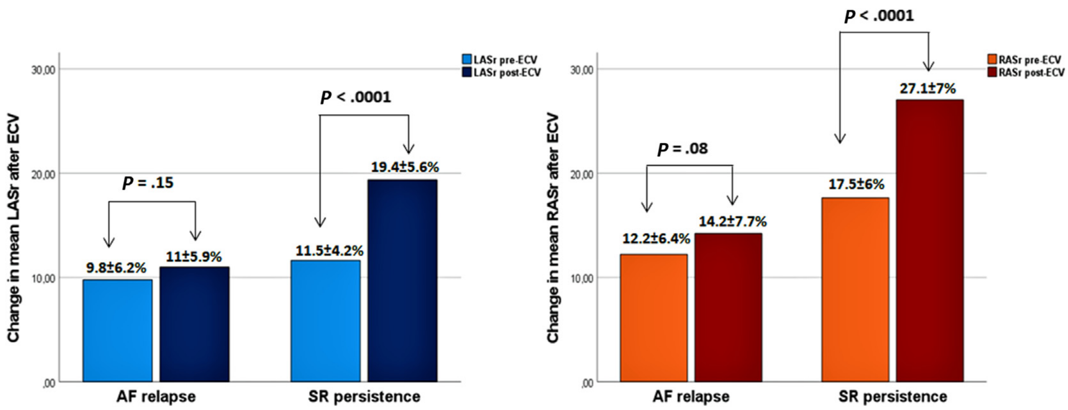


Figure 6 Comparison of mean LASr (*left panel*) and RASr (*right panel*) before and after ECV.

development in 142 consecutive patients who underwent coronary artery bypass surgery.[40] Right atrial booster strain function was predictive of SR maintenance for up to 1 year in patients with paroxysmal AF.[41] Recently, a study performed using cardiac magnetic resonance[42] in patients affected by paroxysmal/persistent AF who underwent pulmonary vein isolation showed that the RA undertook a progressive remodeling process from healthy individuals to persistent AF characterized by enlargement and deformation. Moreover, atrial remodeling involved simultaneously both the RA and the LA. In accordance with the previously reported studies, our patients who experienced AF recurrence had a more unfavorable RA remodeling, characterized by larger RA volume and lower RA strain values, compared with patients who maintained SR. However, at multivariable regression analysis, RASr < 15% showed the strongest statistical power to predict AF recurrence after ECV, irrespective of the value of LASr.

Clinical and Technical Implications

Although atrial remodeling is a well-known risk factor for AF recurrence, the current AF treatment strategy does not include it in the decision-making process.[1,2] However, atrial remodeling has been shown to involve both the LA and RA in a similar way.[24] As pointed out in our paper, in patients with AF undergoing ECV, the combined analysis of LASr and RASr had an additional impact on predicting AF recurrence. Another important aspect to highlight is that 2D-STE analysis of atrial strain during AF may give different results compared with measurements obtained after the restoration of SR. Several data suggested that during AF, atrial strain values are lower than control values.[43,44] However, LASr performed in AF has been shown to yield valuable prognostic information about AF relapses and the refinement of thromboembolic risk.[43,45] Moreover, after successful cardioversion from persistent AF to SR, atrial mechanics appears compromised, a process defined as "atrial stunning."[43,44] Impairment of LA mechanics is at a maximum immediately after cardioversion and improves progressively within 4 to 6 weeks.[43,44] However, this phenomenon is highly variable depending on the duration of the preceding AF, the atrial size, and the coexistence of structural heart disease.[43,44] Indeed, in our study we showed that during follow-up, patients who maintained SR after ECV had a higher increase of LASr compared with patients who experienced AF relapses. In line with this, Shaikh *et al.*[44] revealed that change in LASr after ECV was significantly higher among individuals who remained in SR when compared with individuals with recurrent AF (+3.6% ± 1.1% vs +0.4% ± 0.8%, $P = .02$). These data suggest that the analysis of the change of atrial strain values from pre- to post-ECV could also play a prognostic and therapeutic role in patients with persistent AF by identifying patients at higher risk of AF recurrence. Therefore, according to our data, a comprehensive approach including pre-ECV LASr and RASr and the evaluation of their absolute change post-ECV (in patients with restored SR) could contribute to a more personalized management of the patients by identifying patients who may need a closer follow-up, implant of a loop recorder, and prescription of specific antiarrhythmic drugs.

Study Limitations

Several limitations of our study should be acknowledged. First, this is a single-center retrospective study performed on a selected relatively small group of hemodynamically stable patients. We included only patients with persistent AF that underwent complete 2D and 2D-STE before elective ECV. Strain values are influenced by the temporal definition of end systole and end diastole; therefore, since the echocardiographic exams were performed during AF, to obtain an optimal definition of atrial deformation mechanics we selected examinations with a minimum frame rate of 50 frames/sec.[17,46] The second limitation concerns the lack of a continuous monitoring device during follow-up that could have resulted in unnoticed asymptomatic AF episodes. Therefore, further prospective studies with continuous monitoring during a prolonged follow-up (>1 year) are needed to confirm our results. Moreover, we cannot rule out that these patients were a subgroup of cases with high AF recurrence rate. The third limitation is the heterogeneous drug treatments after ECV. In our study, patients treated with flecainide were more likely to maintain SR. Since flecainide is administered in patients without coronary artery disease,[1,2] a population at higher risk for AF relapses, its use may have slightly influenced our results. Finally, RASr was measured by a software package designed for LA strain analysis applied to the RA. However, we have recently demonstrated that the measurements obtained by this software package yield accurate results.[19]

CONCLUSION

In our patients affected by AF who underwent successful SR restoration by elective ECV, RASr was a better predictor than LASr of AF recurrence during follow-up. Our findings support the need to assess the size and deformation parameters of both the atria, to better stratify the risk of AF recurrence after ECV, and to tailor AF management to patient characteristics.

REVIEW STATEMENT

Given his role as *JASE* Associate Editor, Luigi P. Badano, MD, had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to James D. Thomas, MD.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.echo.2023.05.011.

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