Global atrial longitudinal strain is a powerful predictor of atrial fibrillation ablation outcomes in patients with normal echocardiographic images.

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Abstract

Background: Speckle tracking echocardiography (STE) with recent standardized left atrial (LA) deformation allows for the assessment of various LA function parameters. Proper qualification for catheter ablation (CA) for atrial fibrillation (AF) is still an issue. We aimed to assess the value of detailed evaluations of LA function parameters in patients without abnormal baseline standard echocardiography to predict the outcomes after CA for AF.

Methods: We studied 84 patients (59% males, mean age 57.3±9.4 years) with nonvalvular paroxysmal AF who underwent CA and had normal preprocedural echocardiographic examinations. Peak longitudinal LA strain (LAS) and strain rate (LASR) during the reservoir (r), conduit (cd) and contraction (ct) phases were measured by STE. AF recurrence was confirmed by serial 4-7 day Holter ECG monitoring during a 12-month follow-up period. Three definitions of ablation success were used: complete success – freedom from symptomatic and asymptomatic AF without antiarrhythmic drug therapy (AA), success on AA – freedom from any AF with continued AA and partial success – clinically relevant reduction of the symptoms. The remaining patients were classified as having ablation failure.

Results: Complete success was achieved in 37 (45.1%) patients, success on AA in 7 (8.5%) patients, and partial success in 11 (13.4%) patients. Altogether, 55 (67.1%) patients benefited from CA. The remaining 27 (32.9%) patients were classified as having CA failure. In the multivariate logistic regression analysis, only global LASr was identified as an independent predictor of AF recurrence after CA (OR [95% CI]: 1.27 [1.136-1.423], $p<0.0001$). The receiver operating characteristic analysis identified LASr as a powerful parameter for predicting the outcome after CA with an area under the curve (AUC) of 0.8548. When CA success was defined as all patients who benefited from CA, the multivariate logistic regression analysis also showed that only global LASr was an independent predictor of whether patients would benefit from CA (OR [95% CI]: 1.44 [1.207-1.716], $p<0.0001$)

Conclusions: In patients with paroxysmal AF and normal standard echocardiographic assessments, LA strain analysis is crucial for selecting the best candidates for catheter ablation. LA reservoir strain is the only echocardiographic parameter that is an independent predictor of either complete success or clinical benefits from catheter ablation.

Background

Catheter ablation (CA) for atrial fibrillation (AF) is an established therapeutic option; however, the efficacy of CA is suboptimal [1, 2]. Proper patient selection for this invasive procedure improves the results of intervention and is therefore one of the most debated topics in this field [3-7]. Multiple factors like left atrial (LA) diameter, volume, and strain, as well as parameters of left ventricular (LV) systolic and diastolic function have been shown to have predictive value in assessing CA efficacy [8], however small sample sizes of the studies as well as heterogeneity of the studied populations and echocardiographic methods suggest the need for further studies. Especially in patients with not enlarged LA dimensions and normal diastolic as well as systolic LV function, the prediction of arrhythmia recurrence remains a challenge.

We hypothesized that a detailed estimation of LA function is crucial for the proper selection of candidates for CA. Speckle tracking echocardiography (STE) provides an opportunity to estimate various LA parameters and assess LA function [9, 10]. However, variability among the different imaging techniques, modes of strain analysis and types of software used in published studies precludes a meaningful comparison of the results. Recently, the standardization of LA deformation using STE was developed [11].

The aim of our study was to assess the value of a detailed assessment of LA function parameters for patients without abnormal baseline standard echocardiographic findings in predicting the outcome after CA for AF.

Methods

Study population

We prospectively screened 208 consecutive patients with AF admitted to our institution between July 2011 and January 2014 for CA. The inclusion criteria were: non valvular AF without structural heart disease and first-time CA. The exclusion criteria were severe valvular heart disease according to ESC guidelines [12], a left ventricular ejection fraction (LVEF) <40% and poor-quality two-dimension (2D) echo images precluding visualization of the LA wall. One hundred and six patients were excluded from the analysis due to prior CA (47), no possibility to continue follow-up (34), uninterpretable echo images (9), an LVEF <40% (9), congenital heart disease (2), severe mitral regurgitation (2) and LA appendage (LAA) occluder (1). Out of the 102 remaining patients, 18 patients with AF during the analysis were excluded, and finally, the data from 84 patients with sinus rhythm were analyzed. All patients underwent transthoracic and transesophageal echocardiography (TTE and TEE, respectively) within 24-48 hours before CA. The study was approved by the local ethics committee (approval number 58/PW/2011). All patients gave written informed consent to participate in the study.

Echocardiography

Transthoracic echocardiography was performed using Vivid 9 (GE Medical System, Horten, Norway, 2010). The cardiac dimensions were measured in accordance with the recommendations for cardiac chamber quantification by echocardiography in adults [13].

The following LV parameters were assessed: LV end-diastolic (LVEDd) and end-systolic (LVESd) diameters; LV ejection fraction (LVEF) was calculated by Simpson's biplane method. The LA diameter (LAd) was measured at end-systole in the parasternal long-axis view. The LA volume (LAV) was calculated from the apical 4-chamber (4C) and 2-chamber (2C) views using biplane area-length method. The LAV index was defined as the LA volume divided by the body surface area (BSA). Mitral flow velocities (E and A) were assessed by pulsed-wave Doppler (PW) from the apical 4C view. Tissue Doppler imaging (TDI) was used to measure velocities of the early (e') and late (a') diastolic phases at the mitral annular septal and lateral corners. The E/e' ratio was calculated by dividing E by the average of the septal and lateral e' velocities.

Peak longitudinal LA strain (LAS) and strain rate (LASR) during the reservoir (r), conduit (cd) and contraction (ct) phases were measured by STE (Figure 1). The images in the apical 4C and 2C views images were obtained with a frame rate set between 60 and 80 frames per second. Loops of 3 cardiac cycles were stored digitally and analyzed offline with software (EchoPac, GE Healthcare) by an experienced echocardiographer. Briefly, the LA endocardium was manually traced in the 4C and 2C views to create a region of interest (ROI) composed of six segments in each view. After segmental tracking quality analysis with the possibility of manual adjustments to the ROI, the software generated strain curves for each atrial segment. The LA global longitudinal strains for each LA phase were calculated by averaging the values observed in all LA segments. We set the zero strain point as the time from the beginning of the QRS wave. The LA stiffness index (LAstf) [14], the ratio of E/e' to LASr, was calculated. The reproducibility of 2D STE was tested in 18 randomly selected patients [15]. LA strain was reanalyzed at least 3 months later in 18 patients by the same observer to evaluate intraobserver variability. To evaluate interobserver variability, a second experienced observer analyzed the same data and was blinded to the other observer's results. All LAS measurements were analyzed according to the recent consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging [11].

All patients underwent TEE within 24-48 hours before the CA procedure. TEE was performed according to the standard practice guidelines using Vivid 9 (GE Medical System, Horten, Norway, 2010) with 6T and 6TC multiplane TEE probes [16,17]. The LA appendage velocity (LAAv) was recorded by placing the PW Doppler gate within 1 cm of the LAA orifice.

Catheter ablation procedure

Patients underwent radiofrequency (RFCA) or cryoballoon (CB) ablation, which were performed according to widely accepted protocols [3]. Allocation to RF or CB ablation was random. To rule out the presence of a LA thrombus, patients underwent TEE within 24 hours prior to the procedure or intracardiac echocardiography at the beginning of the procedure. Point-by-point pulmonary vein isolation (PVI) using RF energy was performed after double transseptal puncture using irrigated ablation catheters (Thermocool SF or Thermocool SmartTouch ST), a LASSO catheter and the CARTO 3 system (Biosense Webster, USA). CB PVI was performed using a single transseptal puncture. A steerable 15 Fr sheath (FlexCath Advance, Medtronic, Minnesota, USA) was positioned in the left atrium and an inner lumen mapping catheter for PV potential recordings (Achieve, Medtronic, Minnesota, USA) was advanced in each PV ostium. A 28 mm CB (Arctic Front or Arctic Front Advance, Medtronic, Minnesota, USA) was used.

The goal of ablation was to achieve of PVI. The procedures were performed under mild conscious sedation and on uninterrupted anticoagulation. One or two days after the ablation procedure, all patients underwent TTE to assess pericardial effusion.

Follow-up

The follow-up lasted for one year. Patients were seen in the outpatient clinic 3, 6 and 12 months after CA and underwent serial 4-7 day Holter ECG monitoring (DMS 300-4A, DM Software, Nevada, USA). The recurrence of arrhythmia was defined as AF or atrial tachycardia (AT) that lasted at least 30 seconds and was documented on standard ECG or during Holter ECG monitoring. Three definitions of ablation success were used: (1) complete success – freedom from symptomatic and asymptomatic AF without antiarrhythmic drug therapy (AA); (2) success on AA – freedom from any AF but with continued AA; and (3) partial success – clinically relevant reduction of the symptoms, which was defined as an ≥1 improvement in the EHRA class in spite of the presence of AF recorded on ECG or during Holter ECG monitoring that did not require another ablation procedure. The remaining patients were classified as having ablation failure.

Statistical analysis

Continuous and normally distributed variables were expressed by the mean ± standard deviation, and categorical data were expressed by the number and percentage. A comparison of the parametric values between two groups was performed using the two-tailed Student's t-test. Categorical variables were compared using the X^2 test. Multiple linear regression analyses were performed to examine the independent predictors of CA efficacy. The impact of LA function parameters on CA success was evaluated with multivariate regression analysis. Intra and inter-observer reproducibility was computed by coefficient of variability (COV) and intra-class correlation coefficient (ICC) with 95% confidence interval. Statistical analysis was performed using SAS 9.2 (NC, USA) software.

Results

Patient characteristics

The study group consisted of 84 patients (59 % males, mean age 57.3±9.4 years) with paroxysmal AF who were in sinus rhythm during the analysis and had normal baseline echocardiographic parameters. There were no significant differences in clinical characteristic between subgroups except age. The complete success group was younger than the remaining patients (53.4±11.1 vs 60.6± 6.4, p=0.001) and CA failure subgroup (53.4±11.1 vs 61.9± 6.5, p=0.0003). Table 1 summarizes the baseline demographic and clinical parameters of the studied population.

The echocardiographic parameters indicated not enlarged LV dimensions, normal LV systolic and diastolic function as well as not enlarged LA dimensions.

Procedural data

RFCA was performed in 50 (59.5%) patients, and CB was performed in 34 (40.5%) patients. There were no differences in the baseline demographic, clinical and echocardiographic parameters between the RFCA and CB subgroups except for LAVindex (34.0±10.9 vs 27.5±6.5 mL/m², p=0.0012) and LAScd (-14.1±5.2 vs -16.7±5.6%, p=0.0433). Complete PVI was achieved in all patients (all PV isolated), and there were no major complications other than local hematoma.

Follow-up results

A one year follow-up period was completed for 82 patients, and 2 patients were lost to follow-up. The outcomes of catheter ablation according to the various definitions is shown in Figure 2.

Complete success (no AF/AT and no AA) was achieved in 37 (45.2%) patients, success on AA was achieved in 7 (8.5%) patients, and partial success was achieved in 11 (13.4%) patients. Altogether, 55 (67.1%) patients benefited from ablation. The remaining 27 (32.9%) patients were classified as having ablation failure. There were no significant differences in the ablation outcomes between patients treated with RFCA and those who underwent CB.

Echocardiographic parameters identifying patients with complete success of ablation

Table 2 shows a comparison of the echocardiographic parameters between patients with completely successful ablation and the CA failure. There were numerous echocardiographic variables that were significantly different between the two patient groups (Table 2).

In the multivariate logistic regression analysis, only global LASr was identified as an independent predictor of AF recurrence after CA (odds ratio [95% CI]: 1.27 [1.136-1.423], p<0.0001). Age, DM, LAVindex, mitral E, e', a', E/e', global LASr, LAstf, global LAScd, global LASct, global LASRr, global LASRct and LAAv were included into the model. Table 3 shows univariate and multivariate predictors of CA success.

The receiver operating characteristic analysis identified LASr as a powerful parameter for predicting the outcome after CA, with an area under the curve (AUC) of 0.8548 (Figure 3). Parameters of LA volume (LAVindex) and LV diastolic function (E/e') were less accurate for predicting AF recurrence after CA, with an AUC of 0,626 and 0,643 respectively (Figures 4 and 5, table 3).

Prediction CA success in subgroup with not enlarged LA

Out of the whole study group with the average LAVi of 31.4± 10.0 ml/m2, 31 (37%) patients had dilated LA. We repeated all calculations after excluding these patients. Again, the receiver operating characteristic identified global LASr and LASct as the most powerful parameters for predicting CA success with an AUC of 0.914 and 0.917 respectively (Table 4)

Accuracy of LASr for predict complete success of CA

A global LASr >28% had a high positive predictive value (PPV) with an acceptable negative predictive value (NPV) to determine the complete success of CA (Table 5).

Echocardiographic parameters separating patients who benefited from ablation versus those who had procedure failure

Table 6 shows a comparison of the echocardiographic parameters between patients who benefited from ablation (complete success, success on AA and partial success) and those who had CA failure.

When CA success was defined as all patients who benefited from ablation (complete success, success on AA and partial success), the multivariate logistic regression analysis also showed that global LASr was the only independent predictor that identified these patients (odds ratio [95% CI]: 1.44 [1.207-1.716], $p<0.0001$). The receiver operating characteristic analysis identified LASr as a powerful parameter for identifying patients who benefited from ablation with an AUC of 0.9248 (Figure 6)

A global LASr >23% had a high positive predictive value (PPV) to determine whether patients would benefit from CA (Table 7).

LA strain feasibility. Intra-observer and inter-observer variability for LA strain

During the screening nine out of 208 patients (4.3%) had poor-quality 2D echo images precluding visualization of the LA wall. Out of images initially classified as interpretable, the measurement of LA strain was not feasible in three (3.6%) out of 84 included patients.

Eighteen patients were randomly identified for intra-observer and inter-observer agreement. LA strain had very good reproducibility (table 8)

Discussion

The major finding of our study is that out of the many echocardiographic variables that describe LA function, LASr is the most useful parameter in predicting the outcome of CA for paroxysmal AF in patients with normal echocardiographic images.

Multiple factors have been shown to be predictors of AF recurrence after CA. Previous reports demonstrated that LA enlargement is a strong predictor of AF recurrence after CA [18]. LA enlargement provides robust information on the severity of AF, although using this parameter has limitations. The LA volume can increase in patients with diastolic dysfunction, patients with bradycardia, and trained athletes and can decrease as a result of therapy with diuretics. In the present study, there was a significant difference in LAV between the CA failure and complete success subgroups, although the multivariate analysis did not identify LAV as an independent predictor of AF recurrence after CA. Our study group consisted mainly of patients with normal LA dimensions, fifty three (63%) of them had not enlarged ($\leq$34 mL/m^2) LA, which suggests that these patients had early stage AF. Nevertheless complete CA success was observed in only part of the group, what indicates that thorough LA function assessment is crucial in selecting patients for CA. Out of various LA function parameters these reflecting LA compliance which is altered by LA fibrosis were the most accurate for predicting CA outcome.

It has been shown that increased LA fibrosis which can be present in not enlarged left atria and in patients with lonely AF, was significantly associated with AF recurrence post CA [4]. Echocardiography with the use of advance imaging techniques allows for the evaluation of the properties and function of the LA wall and therefore may be used in the diagnosis of LA fibrosis. A reduced LAS during the reservoir phase has been shown to correlate with histopathological alterations of the LA wall and the degree of fibrosis estimated by late gadolinium enhancement magnetic resonance imaging (LGE-MRI) [4]. We also previously showed that LASr and LAstf correlated well with the extent of LA fibrosis assessed invasively using electroanatomical mapping and found stronger associations between low atrial potential areas and the parameters characterizing LA diastolic function (LASr, LAstf) than between the same areas and the parameters characterizing LA systolic function (LASct, LAAv, A, a') [15].

The LA mechanics in predicting the outcome after CA in patients with AF have been analyzed in several studies. Recently, Koca et al reported that LA global longitudinal strain (LA-GLS) and LAV index were independent parameters predicting AF recurrence after cryoablation with the cutoff value of 18.1%, LA-GLS had sensitivity of 92.6% and specificity of 85.7% to predict AF recurrence [19]. The optimal cutoff value in our study for prediction of benefit from CA was 23% (84.6% sensitivity and 92.6% specificity) and for prediction of complete success of CA - 28% (79.1% sensitivity and 83.8% specificity). Moreover, Koca et al did not take into consideration the complexity of the LA function and out of LA deformation parameters only reservoir strain was analyzed.

Consistent with previous results, our study indicates that LASr has a high prognostic value as a predictor of AF recurrence after CA [20]. Ma XX et al analyzed in the meta-analysis clinical relevance of LA strain to predict recurrence of AF after CA in eight studies and documented the usefulness of LA strain in identifying patients with high risk of AF recurrence after CA. Results obtained in the present study are confirmatory, although out of eight analyzed studies, six included patients both with paroxysmal and persistent AF. During AF, LA function during the reservoir and conduit phases is severely impaired, and systolic function does not exist: hence a reduction in LASr is observed during AF. Reduced LAS in AF occurs mainly due to atrial mechanical function impairment (lack of systole, impairment of diastole), rather than as a reflection of atrial wall properties. We previously reported no significant relationships between low atrial potential areas and echocardiographic LA function parameters in patients examined during AF [15]. The present study included only patients with sinus rhythm during the analysis.

Two studies included in the above-mentioned meta-analysis investigated patients with paroxysmal AF, however there are some differences when comparing with our study. Hwang et al demonstrated that lower LA systolic strain was strongly associated with AF recurrence after CA [21] however LA strain cutoff was not reported. Moreover the study group included only 40 patients and follow-up lasted 9 months therefore some episodes of AF might have been missed. Morris et al showed that both LA myocardial diastolic dysfunction expressed by global LA strain during LV systole (LAGLS) and systolic dysfunction expressed by LA strain rate during LV late diastole could be useful in distinguish patients with high or low risk of recurrence of AF after CA and found LAGLS 18,8% to be cut-off value [22]

Although LAS has been widely used in clinical studies, there were inconsistencies and pitfalls with these assessments. Recently, the standardization of LA deformation using STE has been developed [11] and can shed new light on the results of previous studies. The present study was performed in accordance with the consensus document established by the EACVI/ASE/Industry Task Force. There have been reports that segmental basal LAS [23] or lateral LAS [24] could be useful predictors for AF recurrence after CA, whereas the interpretation of LAS as global strain rather than as segmental strain is currently recommended [11]. Moreover, at the present time, we are able to use echocardiographic reference ranges for normal LA function parameters, taking into account age and sex [25]. In the present study, the values of LAScd and LASct were within normal values, whereas the LASr value was lower than normal.

The success rate of CA of AF depends on many factors, including the definition used for a successful procedure. In the literature, this definition is variable [26]. The strictest definition is the lack of recurrence of any AF or AT during long-term ECG recordings and frequent ECG monitoring with no AA therapy. This definition is the most ambitious goal of CA, and patients fulfilling this definition have probably reduced or even no risk of thrombo-embolic complications as well as no risk of proarrhythmic effects of AA. The identification of such “super responders” would therefore be of great value. On the other hand, it is unrealistic to expect that all patients with apparently successful CA of AF will be completely free from AF recurrence during follow-up, especially when using the very strict 30 second definition of AF. Moreover, in patients with a CHA2DS2VASc >1, stopping of anticoagulation is currently not recommended, irrespective of the results of CA [3]. Thus, the identification of a broader cohort of patients who benefit from CA of AF is also clinically important. We therefore defined four types of CA results (Fig. 2). First one is strict - no AF recurrence off AA. The second is less strict and includes also patients with no AF recurrences but on AA. We are not able to say what was the reason for continuation of AA since the treatment was left to the discretion of attending physician. However these patients had no AF recurrences after ablation and thus, AA were not introduced because of AF recurrence. We speculate that the most frequent reason for not withholding AA after ablation was patient's or attending physician desire to continue this treatment because of fear of AF recurrence but this is only our speculation. However, since these patients had improvement and no AF recurrences, we classified them as “benefited from ablation”. When we used another, strict definition – “complete success”, these patients were included in the group called “remaining patients”.

Moreover, in every day practice there is a group of patients who do have recurrences of AF following ablation, however, episodes are rare, less symptomatic or shorter. These patients feel better than before the procedure which is, for example, depicted as the reduction in the EHRA class. Therefore, we assumed that it would be justified to identify such a group of patients as partial success (third definition of success used in our study) and include them in the efficacy analysis in two different ways.

Our study shows that modern echocardiography can be effectively used to identify responders to CA of AF, irrespective of the definition of efficacy. This finding suggests that a detailed echocardiographic assessment prior to CA of AF may play a major role in selecting patients for this procedure.

In recent years, there has been a growing interest in atrial cardiomyopathy in patients with AF [27]. Structural fibrotic changes in LA can be present at the very early stage of the disease, and traditional echocardiographic images can be normal. Currently, we are able to use many echocardiographic tools to evaluate LA function. There is a need to determine a simple and reproducible parameter to indicate the best candidate for invasive procedure of CA. We showed that LASr has a high predictive value for patients with sinus rhythm and normal echocardiographic images.

LIMITATIONS

First, the study group was relatively small, and duration of follow-up is relatively short. However, the follow-up period was completed in 98% of patients and the number of patients was sufficient to perform meaningful statistical analysis.

Second, there were some difficulties in obtaining high-quality LA images for speckle tracking analysis to estimate the strain rate in all patients. Due to the difficulties with obtaining accurate estimation of LASRcd on the strain rate curves, we decided to exclude this parameter from the analysis.

Third, although we performed three 4-7 days Holter ECG recordings during a one-year follow-up and patients were frequently seen in the outpatient clinic, we might have missed silent episodes of AF because no long-term continuous ECG recordings, such as implantable loop recorders, were used. Finally, we used two techniques for CA of AF – RFCA and CB, which might have influenced the results. However, the outcomes of CA of AF were similar in both groups and there were only a few minor differences in the baseline echocardiographic parameters between the two groups.

Conclusions

In patients with AF without abnormal standard echocardiographic assessments, LAS analyses are crucial in selecting candidates for CA. LASr is the only echocardiographic parameter that is an independent predictor of either complete success or clinical benefits from CA.

Declarations

Ethics approval and consent to participate: The study was approved by the local ethics committee (approval number 58/PW/2011). All patients gave written informed consent to participate in the study.

Consent for publication: Not applicable

Availability of data and material: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: All authors have nothing to declare in relation to the study

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Authors' contributions: EPP collected, analyzed and interpreted the patient data and was a major contributor in writing the manuscript. JB contributed to the conception of the work and performed the catheter ablation. PK contributed to the conception of the work, was a contributor in writing the manuscript. BZ collected, analyzed and interpreted the patient data, contributed to the conception of the work, was a contributor in writing the manuscript and substantively revised the work. All authors read and approved the final manuscript.

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Abbreviations

2C - apical 2-chamber

2D - two-dimension

4C - apical 4-chamber

AA - antiarrhythmic drug therapy

AF - atrial fibrillation

ASE - American Society of Echocardiography

AT - atrial tachycardia

AUC - area under the curve

BSA - body surface area

CA - catheter ablation

CB - cryoballoon ablation

COV - coefficient of variability

EACVI - European Association of Cardiovascular Imaging

EHRA - European Heart Rhythm Association

ESC - European Society of Cardiology

ICC - intra-class correlation coefficient

LA - left atrial

LA - left atrial appendage

LAAv - left atrial appendage velocity

LAd - left atrial diameter

LAS - left atrial strain

LAScd - left atrial conduit strain

LASct - left atrial contractile strain

LASr - left atrial reservoir strain

LASR - left atrial strain rate

LASRcd - left atrial conduit strain rate

LASRct - left atrial contractile strain rate

LASRr - left atrial reservoir strain rate

LAstf - left atrial stiffness index

LAV - LA volume

LGE-MRI - late gadolinium enhancement magnetic resonance imaging

LVEDd - left ventricular end-diastolic diameter

LVEF - left ventricular ejection fraction

LVESd - left ventricular end-systolic diameter

NPV - negative predictive value

PPV - positive predictive value

PVI - pulmonary vein isolation

PW - pulsed-wave Doppler

RFCA - radiofrequency ablation

ROC - receiver operating characteristic

ROI - region of interest

STE - speckle tracking echocardiography

TDI - Tissue Doppler imaging

TEE - transesophageal echocardiography

TTE - transthoracic echocardiography

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Tables

Table 1. Demographic and clinical parameters of the studied population.

Clinical characteristic	Study group N=84	Complete success N=37 (45.1%)	Remaining patients N=45 (54.9%)	Complete success vs remaining patients p	CA failure N=27 (32.9%)	Complete success vs CA failure p
Men n (%)	59 (70.2%)	28 (75.7%)	30 (66.7%)	0.37	17 (63.0%)	0.27
Age [years]	**57.3±9.4**	**53.4 ± 11.1**	**60.6 ± 6.4**	**0.001**	**61.9 ± 6.5**	**0.0003**
BMI [kg/m^2]	29.8 ± 4.0	29.5 ± 3.4	30.1 ± 4.5	0.53	29.5 ± 29.9	0.99
Duration of AF [years]	5.0 [2.7-10.0]	5.8 [3.0 – 10.0]	4.0 [2.0 – 10.0]	0.743	6.0 [3.0 -10.0]	0.65
DM	11 (13.1%)	2 (5.4%)	7 (15.6%)	0.17	5 (18.5%)	0.12
CAD	5 (6.1%)	3 (6.7%)	2 (5.4%)	1.00	1 (3.7%)	1.00
Arterial hypertension	37 (44%)	17 (45.9%)	20 (44.4%)	0.89	12 (44.4%)	0.91
CHA2DSVASc	1 [0 – 2]	1 [0 – 1]	1 [0 – 1]	0.11	1 [0 – 2]	0.14
Hyperlipidemia	37 (44.0%)	14 (37.8%)	22 (48,9%)	0.32	12 (44.4%)	0.60
Heart rate [beats/min]	59.0 ± 9.8	59.9 ± 10.3	58.2 ± 9.1	0.51	60.5 ± 12.1	0.38
Systolic BP [mmHg]	132.4 ± 11.8	133.0 ± 10.9	131.8 ± 12.8	0.64	132.4 ± 10.9	0.83
Diastolic BP [mmHg]	84.8 ± 6.9	84.7 ± 6.7	85.0 ± 7.3	0.83	84.3 ± 6.5	0.67
Bblokers	41 (48.8%)	19 (51.3%)	22 (48.9%)	0.82	15 (55.6%)	0.74
AA	13 (15.5%)	3 (8.1%)	10 (22.2%)	0.08	4 (14.8%)	0.44
ACE-I	40 (47.6%)	17 (45.9%)	22 (48.9%)	0.79	13 (48.1%)	0.86

Abbreviations: CA - cathether ablation, BMI – body mass index, AF - atrial fibrillation, DM - diabetes mellitus, CAD - coronary artery disease, BP - blood pressure, AA - antiarrhythmic therapy, ACE-I - angiotensin converting enzyme inhibitor
Values are expressed as the mean ± SD and range or number and (%).

Table 2. Echocardiographic parameters – comparison between patients with complete success and the CA failure

Parameter	Whole study group N=84	Complete success group N=37 (45.1%)	CA failure N=27 (32.9%)	p
LVEF [%]	66.1±6.4	66.2±7.3	66.3±5.4	0.94
IVSDd [mm]	11.4±1.8	11.2±1.8	11.4±1.6	0.57
LAd [cm]	38.6±0.5	38.0±4.0	39.0±5.0	0.57
LAV index [ml/m2]	**31.4±10.0**	**28.8±8.4**	**35.3±12.1**	**0.020**
Mitral E [cm/s]	**68.9±17.3**	**65.0±19.0**	**76.0±14.0**	**0.013**
Mitral A [cm/s]	57.4±19.8	58±20.0	56.0±24	0.74
e' [cm/s]	9.2±2.1	9.6±2.1	8.7±1.7	0.06
a' [cm/s]	**8.2±2.1**	**8.7±2.1**	**7.3±2.1**	**0.009**
E/e'	**7.9±2.7**	**7.1±2.5**	**9.2±2.73**	**0.002**
Global LASr [%]	**27.2±8.4**	**32.5±6.4**	**19.1±6.7**	**<0.0001**
LAstf	**0.36±0.29**	**0.23±0.11**	**0.59 ± 0.40**	**<0.0001**
Global LAScd [%]	**13.92±7.06**	**-17.99 ± 5.03**	**-10.56 ± 4.14**	**<0.0001**
Global LASct [%]	**11.95±1.13**	**-14.50 ± 4.68**	**-8.51 ± 4.17**	**<0.0001**
Global LASRr [s^{-1}]	**1.04±0.32**	**1.24 ± 0.21**	**1.02 ± 0.23**	**0.0004**
Global LASRct [s^{-1}]	**1.39±0.48**	**-1.58 ± 0.47**	**-1.13 ± 0.44**	**0.0005**
LAAv [m/s]	**0.66±0.24**	**0.74±0.25**	**0.58±0.21**	**0.010**

Abbreviations: LVEF – left ventricular ejection fraction, IVSDd – interventricular septum diastolic diameter, LAd – left atrial diameter, LAV – left atrial volume,
LASr – left atrial reservoir strain, LAstf – left atrial stiffness index,
LAScd – left atrial conduit strain, LASct – left atrial contractile strain, LASRr – left atrial reservoir strain rate, LASRrct – left atrial contractile strain rate LAAv – left atrial appendage velocity
The rest of the abbreviations are the same as in table 1. Values are expressed as the mean ± SD.

Table 3. Univariate and multivariate predictors of CA success.

Parameter	Univariate analysis			Multivariate analysis		
	OR [95% CI]	AUC	p	OR [95% CI]	AUC	p
Age	**0.908 [0.853-0.966]**	**0.703**	**0.002**			
DM	0.310 [0.060-1.595]	0.551	0.161			
LAVindex	**0.951 [0.905-0.999]**	**0.626**	**0.0470**			
Mitral E	0.083 [0.006-1.206]	0.613	0.068			
e’[*100]	1.24 [0.969-1.591]	0.625	0.088			
a’	1.236 [0.984-1.552]	0.626	0.068			
E/e’	**0.809[0.674- 0.970]**	**0.643**	**0.022**			
Global LASr	**1.255[1.132-1.391]**	**0.849**	**<0.0001**	**1.27[1.136-1.423]**	**0.855**	**<0.0001**
LAstf [*10]	**0.484 [0.321-0.729]**	**0.787**	**0.0005**			
Global LAScd	**1.307 [1.144-1.493]**	**0.797**	**<0.0001**			
Global LASct	**1.249 [1.108-1.407]**	**0.759**	**0.0003**			
Global LASRr [*10]	**1.438[1.129–1.832]**	**0.716**	**0.003**			
Global LASRct	**0.177 [0,055-0.571]**	**0.698**	**0.004**			
LAAv [*10]	**1.358 [1.097-1.680]**	**0.682**	**0.005**			

*rescaled to interpret odds ratio

Abbreviations are the same as in tables 1 and 2

Table 4: The ROC analysis in predicting CA succes in subgroup with not enlarged LA

Parameter	All n=53 ≤34 mL/m2	Complete success group N=28 (68.3%)	CA failure N= 13(31.7%)	Odds ratio	AUC	p
LVEF [%]	65.6±6.3	66.2 7.4	63.4±2.4	1.09 [0.96-1.23]	0.576	0.195
IVSDd [mm]	11.5±1.9	11.2±1,8	11.3±1.7	0.97 [0.67-1.41]	0.526	0.874
LAd [cm]	3.8±0.4	3.7±0.4	3.7±0.4	1.45 [0.28-7.47]	0.537	0.654
Mitral E [cm/s]	0.64±0.16	0.61±0.18	0.68±0.11	0.06 [0.001-4.61]	0.643	0.206
Mitral A [cm/s]	0.56±0.15	0.55±0.14	0.54±0.18	1.47 [0.02-128.1]	0.518	0.866
e' [cm/s][*100]	0.09±0.02	0.10±0.02	0.08±0.01	1.40 [0.96-2.05]	0.702	0.081
a' [cm/s]	**8.6±2.0**	**8.9±2.0**	**7.3±2.1**	**1.49 [1.02 – 2.2]**	**0.702**	**0.038**
E/e'	7.35±2.72	6.7±2.6	8.5±3.0	0.78 [0.61- 1.01]	0.696	0.057
Global LASr [%]	**29.0±8.3**	**33.4±6.3**	**19.7±7.5**	**1.35 [1.12-1.62]**	**0.914**	**0.002**
LAstf [*10]	**0.27±0.16**	**0.21±0.11**	**0.43±0.20**	**0.39 [0.21-0.74]**	**0.893**	**0.004**
Global LAScd [%]	**-15.6±6.0**	**-18.3±5.3**	**-9.4±4.3**	**1.60 [1.19-2.15]**	**0.917**	**0.002**
Global LASct [%]	**-13.5±4.8**	**-15.1±4.7**	**-10.3±4.9**	**1.24 [1.04-1.47]**	**0.762**	**0.014**
Global LASRr [s^{-1}] [*10]	1.21±0.22	1.26±0.21	1.11±0.21	1.54 [0.95-2.49]	0.732	0.077
Global LASRct [s^{-1}]	-1.56±0.46	-1.67±0.48	-1.37±0.48	0,27 [0.05-1.38]	0.648	0.116
LAAv [m/s] [*10]	0.67±0.25	0.76±0.26	0.59±0.23	1.37 [0.93-1.91]	0.668	0.064

*rescaled to interpret odds ratio

Abbreviations are the same as in table 2

Table 5. Accuracy of LASr for predicting complete success of CA

LASr [%]	Accuracy (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
>23%	71.2 (61.3–81.1)	53.5 (38.6–68.4)	91.9 (83.1–100.0)	88.5 (76.2–100.0)	63.0 (50.1–75.9)
>26%	73.8 (64.2–83.4)	65.1 (50.9–79.3)	83.8 (71.9–95.7)	82.4 (69.6–95.2)	67.4 (53.9–80.9)
>27%	78.8 (69.8–87.8)	74.2 (61.1–87.3)	83.8 (71.9–95.7)	84.2 (72.6–95.8)	73.8 (60.5–87.1)
>28%	**81.2 (72.6–89.8)**	**79.1 (66.9 –91.3)**	**83.8 (71.9 –95.7)**	**85.0 (73.9 –96.1)**	**77.5 (64.6 –90.4)**
>29%	73.7 (64.1–83.3)	79.1 (66.9–91.3)	67.6 (52.5–82.7)	73.9 (61.2–86.6)	73.5 (58.7–88.3)

Abbreviations: PPV – positive predictive value, NPV – negative predictive value

Table 6. Echocardiographic parameters – comparison between patients who benefited from ablation and those who had CA failure

Parameter	Whole study group N=84	Benefited from CA N=55 (67.1%)	Had CA failure N=27 (32.9%)	p
LVEF [%]	66.1±6.4	66.2±6.9	66.3±5.4	0.918
IVSDd [mm]	11.4±1.8	11.4±1.9	11.4±1.6	0.981
LAd [cm]	38.6±0.5	39.0±4.0	39.0±5.0	0.811
LAV index [ml/m2]	31.4±10.0	29.3±8.3	35.3±12.1	0.026
Mitral E [cm/s]	68.9±17.3	66.0±18.0	76.0±14.0	0.008
Mitral A [cm/s]	57.4±19.8	58.0±18.0	56.0±24	0.654
e' [cm/s]	9.2±2.1	9.5±2.0	8.7±1.7	0.067
a' [cm/s]	8.2±2.1	8.7±1.9	7.3±2.1	0.004
E/e'	7.9±2.7	7.2±2.4	9.2±2.73	0.001
Global LASr [%]	27.2±8.4	31.0±6.2	19.1±6.7	<0.0001
LAstf	0.36±0.29	0.24±0.11	0.59±0.40	0.0002
Global LAScd [%]	13.92±7.06	-17.27±4.63	-10.56±4.14	<0.0001
Global LASct [%]	11.95±1.13	-13.89±4.47	-8.51±4.17	<0.0001
Global LASRr [s^{-1}]	1.04±0.32	1.21±0.22	1.02±0.23	0.0011
Global LASRct [s^{-1}]	1.39±0.48	-1.54±0.44	-1.13±0.44	0.0005
LAAv [m/s]	0.66±0.24	0.69±0.25	0.58±0.21	0.054

Abbreviations: the same as in Table 2

Table 7. Accuracy of LASr for predicting whether patients would benefit from CA

LASr [%]	Accuracy (95% CI)	Sensitivity (95% CI)	Specifciity (95% CI)	PPV (95% CI)	NPV (95% CI)
>22%	85.0 (77.2–92.8)	65.4 (47.1–83.7)	94.4 (88.3–100)	85.0 (69.4–100)	85.0 (76.0–94.0)
>23%	**90.0 (83.4–96.6)**	**84.6 (70.7–98.5)**	**92.6 (85.6–99.6)**	**84.6 (70.7–98.5)**	**92.6 (85.6–99.6)**
>24%	88.7 (81.8–95.6)	84.6 (70.7–98.5)	90.7 (83.0–98.4)	81.5 (66.9–96.1)	92.4 (85.3–99.5)
>26%	82.5 (74.2–90.8)	88.5 (76.2–100)	79.6 (68,9–90.3)	67.6 (51.9–83.3)	93.5 (86.4–100)
>28%	75.0 (65.5–84.5)	88.5 (76.2–100)	68.5 (56.1–80.9)	57.5 (42.2–72.8)	92.5 (84.3–100)

Abbreviations: the same as in Table 3

Table 8. Intra- and inter-observer reproducibility

	Intra-Observer		Inter-Observer	
	COV (%)	ICC (95% CI)	COV (%)	ICC (95% CI)
LASr 4C	3.1%	0.995 [0.992-0.998]	4.3%	0.993 [0.988-0.996]
LASr 2C	2.5%	0.998 [0.996-0.999]	2.9%	0.997 [0.995-0.999]
LASct 4C	4.6%	0.995 [0.992-0.998]	4.7%	0.995 [0.991-0,997]
LASct 2C	3.4%	0.997 [0.995-0.998]	2.9%	0.998 [0.996-0.999]

Abbreviations: COV - coefficient of variability, ICC - intra-class correlation, CI - confidence interval.

Figures

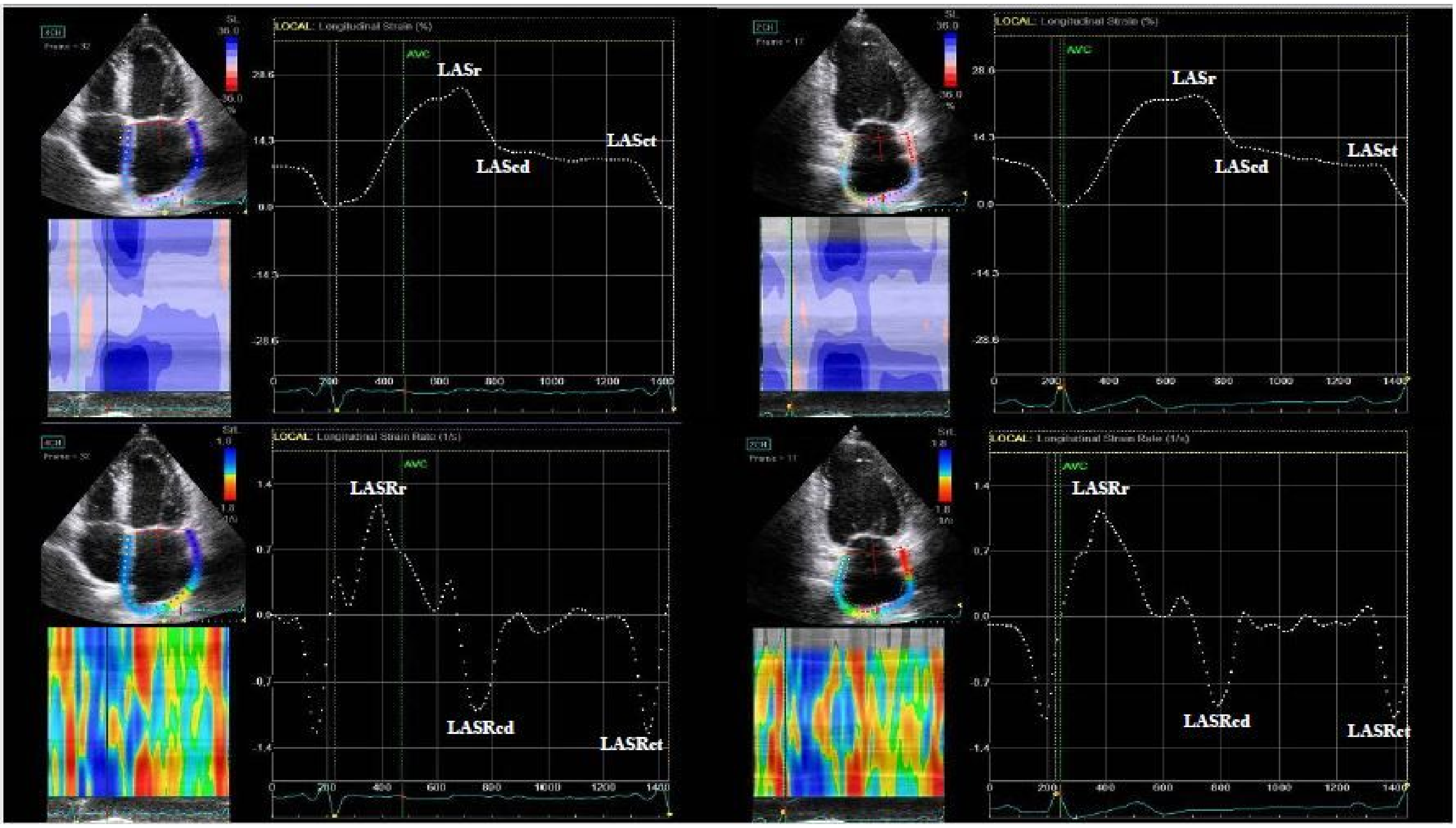

Figure 1

Measurment of peak longitudinal LA strain (LAS) and strain rate (LASR) during the reservoir (r), conduit (cd) and contractile (ct) phases obtained from the apical four chamber (left panel) and two chamber (right panel) views

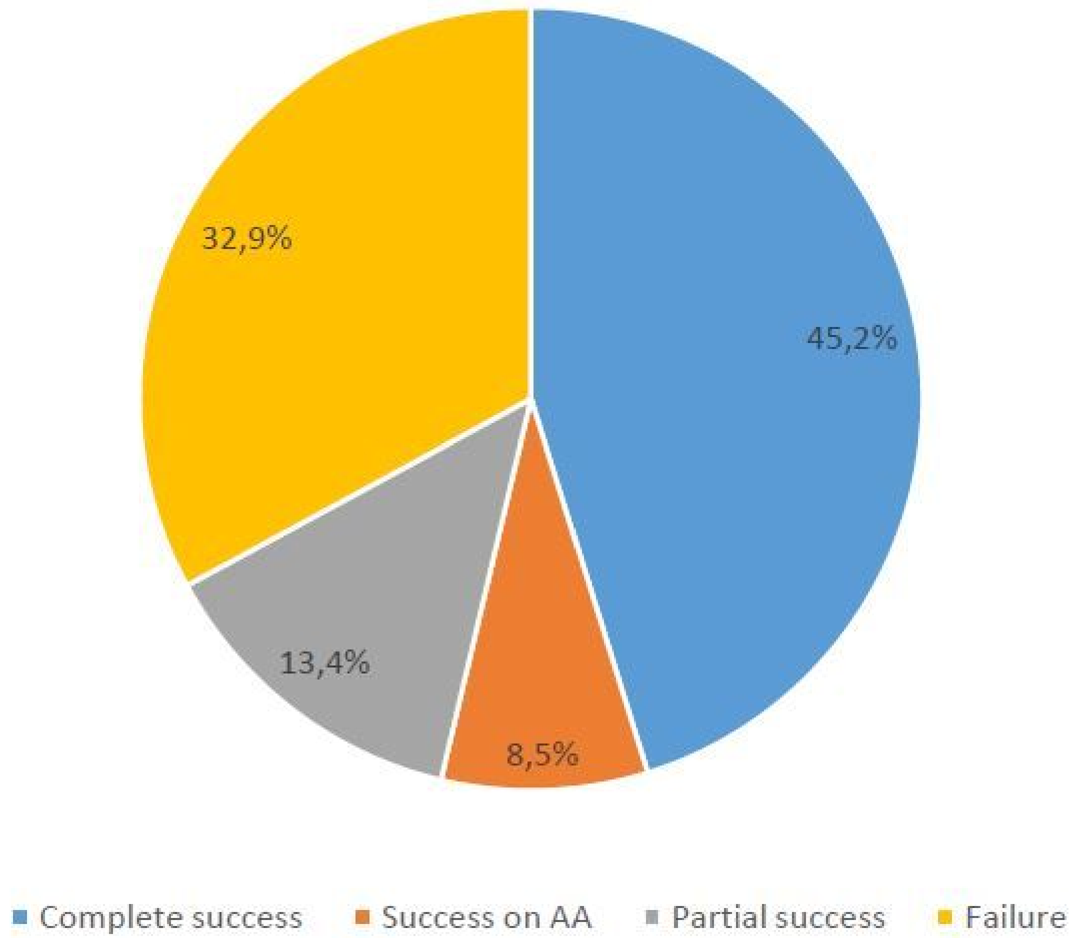

Figure 2

Catheter ablation (CA) outcomes according to the various definitions. (AA) - antiarrhythmic drug therapy

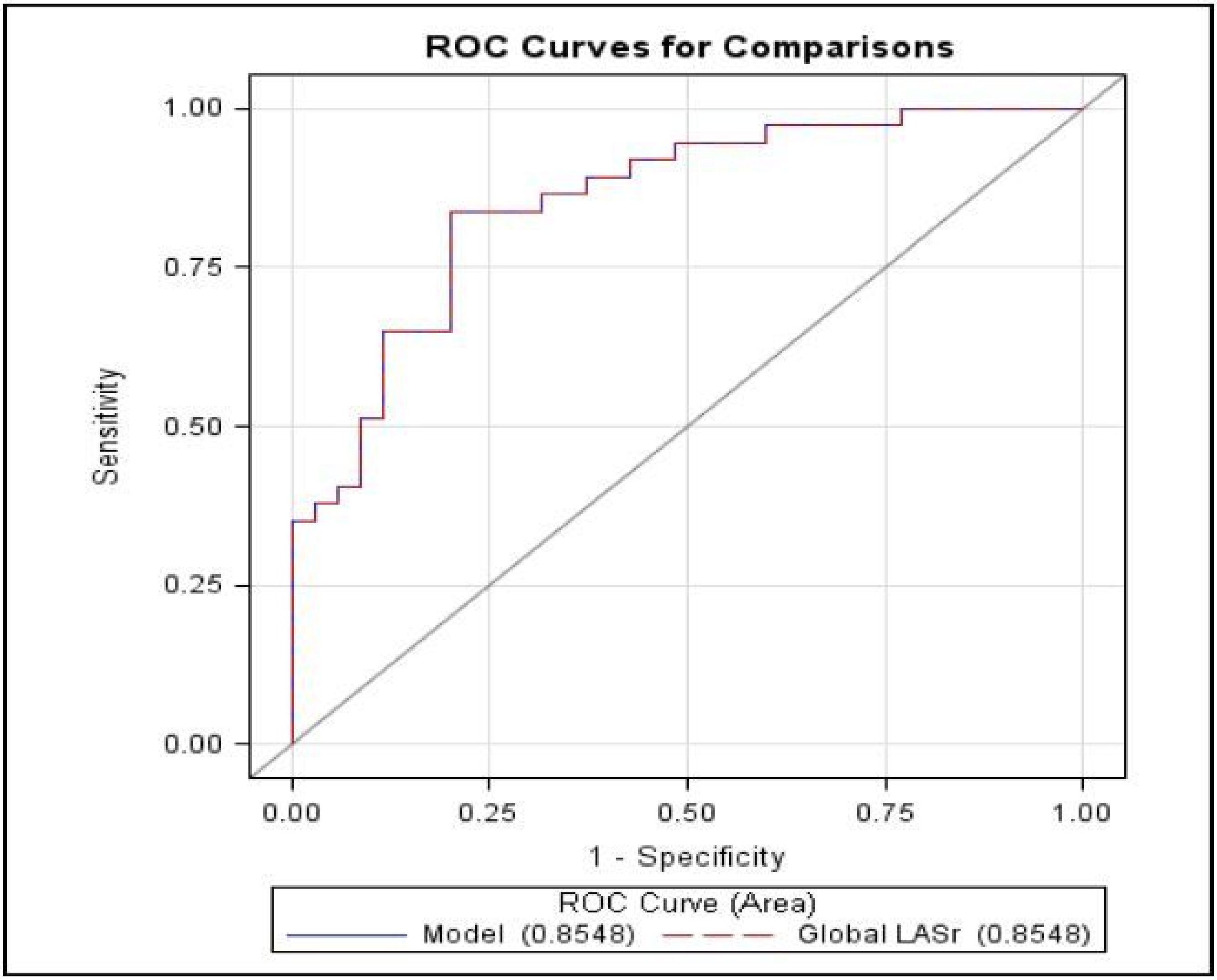

Figure 3

ROC curve for predicting the recurrence of AF after catheter ablation

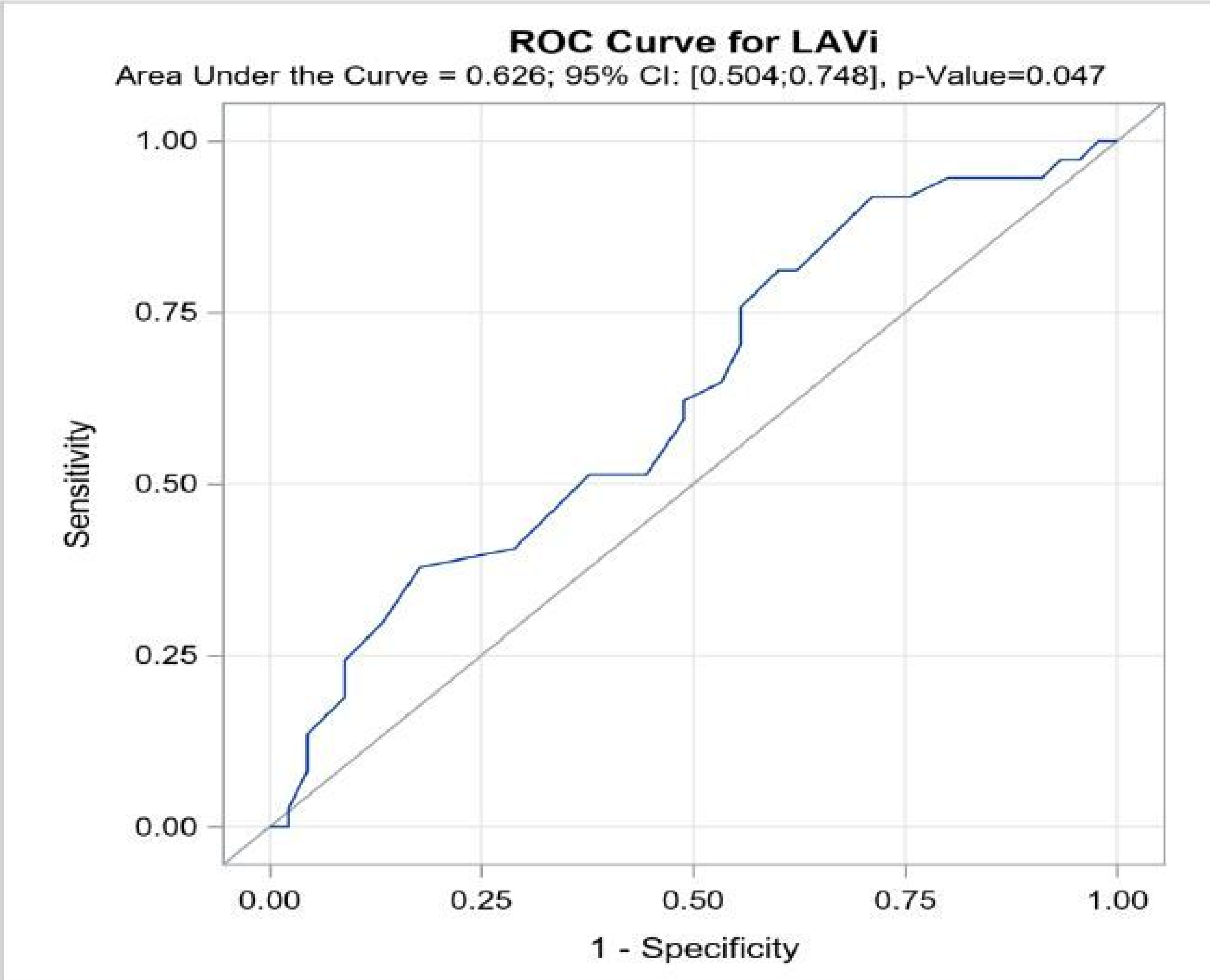

Figure 4

ROC curve for LAVindex in prediction catheter ablation success

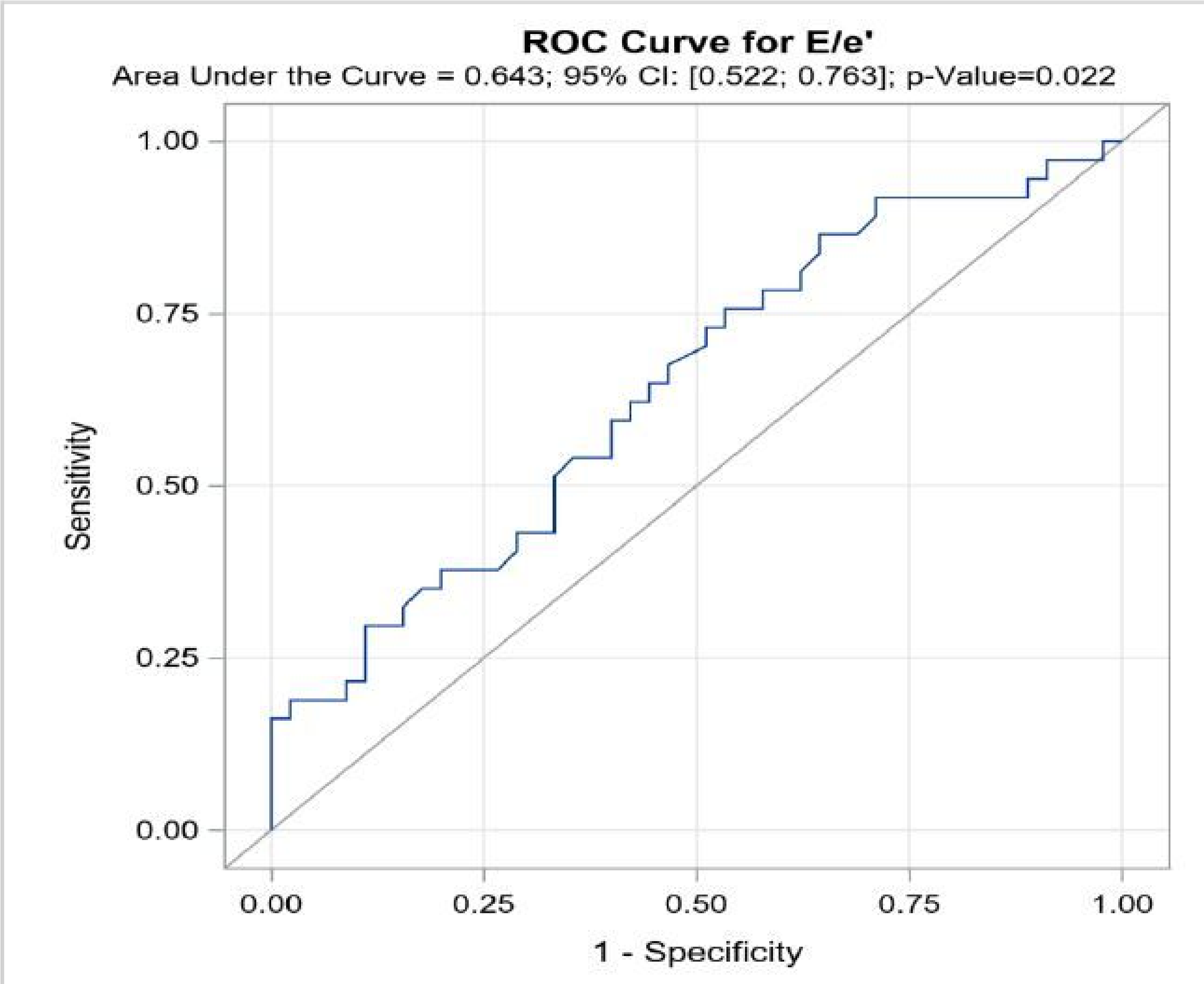

Figure 5

ROC curve for E/e' in prediction catheter ablation success

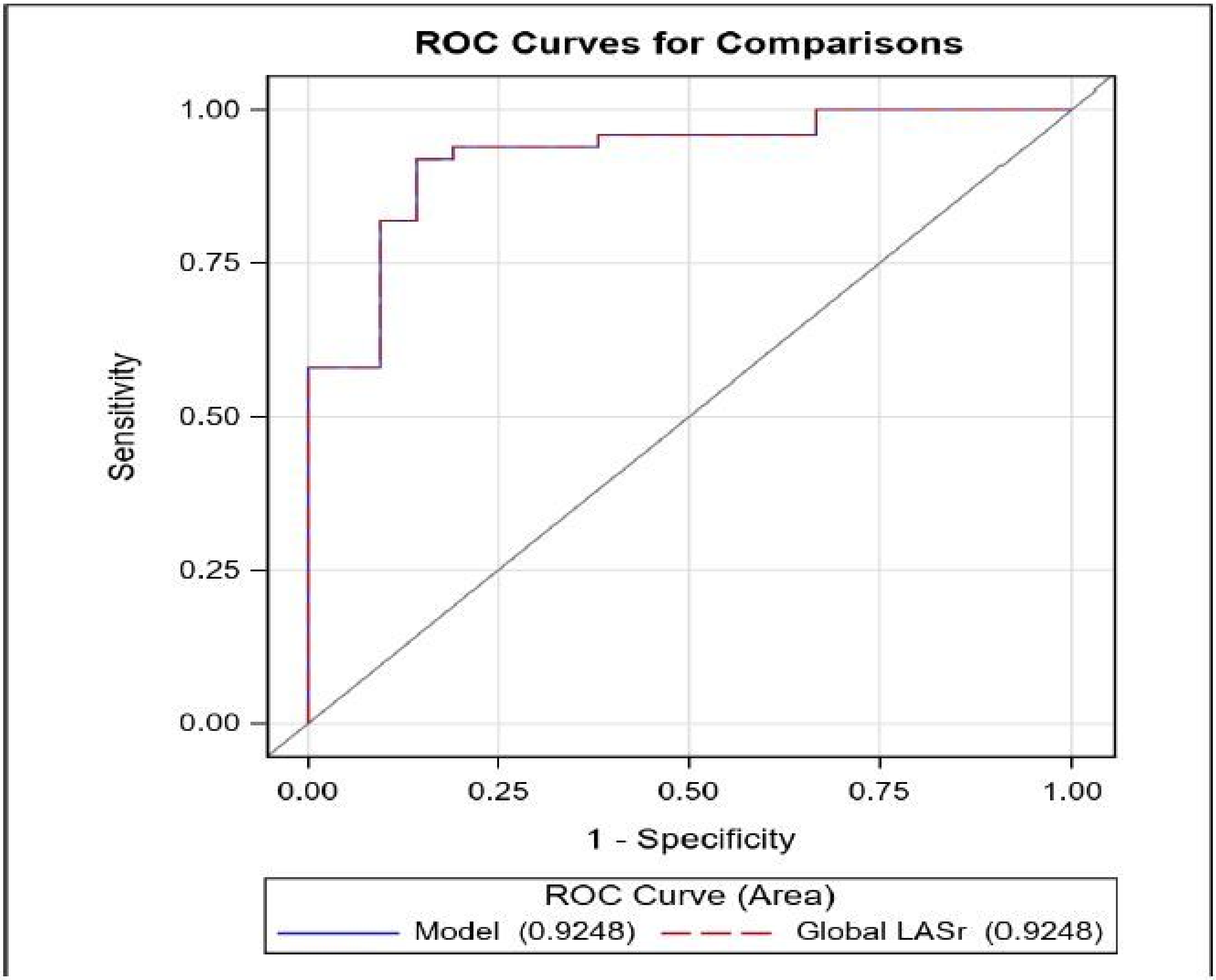

Figure 6

ROC curve for predicting whether patients would benefit from catheter ablation