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Epicardial Fat Volume as a New Imaging-Based Feature Associated with Risk of Recurrence after Pulmonary Veins Ablation in Atrial Fibrillation

Emanuel Blîndu[1,2], Szilamér Korodi[3,4], Lehel Bordi[1,2,3], István Kovács[1,2,3], Imre Benedek[1,2,3]

[1] Center of Advanced Research in Multimodality Cardiac Imaging, Cardio Med Medical Center, Târgu Mureș, Romania
[2] Clinic of Cardiology, Emergency Clinical County Hospital, Târgu Mures, Romania
[3] "George Emil Palade" University of Medicine, Pharmacy, Science and Technology, Târgu Mureș, Romania
[4] Clinic of Cardiology, Emergency County Hospital, Miercurea Ciuc, Romania

CORRESPONDENCE

Szilamér Korodi
Str. Doctor Dénes László nr. 2
530173 Miercurea Ciuc, Romania
Tel: +40 266 324 193
E-mail: szilamerkorodi@yahoo.com

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Emanuel Blîndu • Str. 22 Decembrie 1989 nr. 76, 540124 Târgu Mureș, Romania. Tel: +40 265 217 333, E-mail: emi.blindu@yahoo.com

Lehel Bordi • Str. Gheorghe Marinescu nr. 38, 540138 Târgu Mureș, Romania. Tel: +40 265 215 551, E-mail: bordi_lehel@yahoo.com

István Kovács • Str. Gheorghe Marinescu nr. 38, 540138 Târgu Mureș, Romania. Tel: +40 265 215 551, E-mail: kov_istvan@yahoo.com

Imre Benedek • Str Gheorghe Marinescu nr. 38, 540139 Târgu Mureș, Romania. Tel: +40 265 215 551, E-mail: imrebenedek@yahoo.com

ABSTRACT

Background: Atrial fibrillation (AF), a common arrhythmia in clinical practice, is associated with a high rate of complications and an increased risk for thromboembolic events. Pulmonary vein ablation is a new therapeutic option to cure AF; however, it remains associated with a high rate of recurrence. In this study we aimed to identify the clinical characteristics and imaging-based features that may predict the risk of recurrence after pulmonary veins ablation in atrial fibrillation. **Materials and method:** Twenty-four patients with paroxysmal and persistent AF, who underwent radiofrequency catheter ablation and a 12-month follow-up were included in the study. Group 1 included 8 patients with AF recurrence, and group 2 included 16 patients with no AF recurrence. In all cases, cardiovascular risk factors, ejection fraction, left atrial diameter, atrial volumes, and epicardial fat volume were analyzed. **Results:** CT analysis revealed that patients with AF recurrence presented a significantly larger mean index of left atrial volume (59.57 ± 8.52 mL/m2 vs. 49.99 ± 10.88 mL/m2, p = 0.04), right atrial volume (58.94 ± 8.37 mL/m2 vs. 43.21 ± 6.4 mL/m2, p<0.0001), and indexed bi-atrial volume (118.5 ± 15.82 mL/m2 vs. 93.19 ± 16.42 mL/m2, p = 0.005). At the same time, CT analysis of the epicardial adipose tissue volume indicated that patients with AF recurrence have a larger amount of epicardial fat than those without AF recurrence (176.4 ± 100.8 mL vs. 109.8 ± 40.73 mL, p = 0.02). **Conclusion:** Left atrial diameter, indexed atrial volumes, and epicardial fat volume may be used as factors to identify patients at risk for developing recurrence after pulmonary vein ablation.

Keywords: AF recurrence, pulmonary vein ablation, indexed atrial volumes, epicardial adipose tissue

INTRODUCTION

Atrial fibrillation (AF) is the most common type of atrial rhythm disturbances, being associated with an increased risk for thromboembolic complications and heart failure. The increased incidence of this rhythm disorder can be attributed to an increased life expectancy and to a higher rate of predisposing factors. Although AF is not life-threatening, it significantly influences the quality of life through a series of anatomical and hemodynamic changes. A study published in 2014 has shown that AF affects 8 million patients in Europe, and these numbers are expected to increase to about 18 million by 2060, with higher incidence and prevalence rates in developed countries.[1] Estimates suggest a prevalence of AF of approximately 3% among adults aged 20 years or older, with a higher prevalence in the elderly and in patients with obesity, high blood pressure, heart failure, ischemic heart disease, valvulopathy, diabetes, or chronic kidney disease.[2–4] As the incidence of AF continues to increase, it is very important to identify therapies that are safe and effective, improving patients' symptoms and daily life.

Radiofrequency pulmonary vein (PV) ablation is a novel and complex procedure that has encountered increasing interest in the last decade. The exponential development of new techniques and the innovation of existing ones are reflected in clinical practice in a continuously increasing number of PV ablation procedures performed. This also leads to an increasing need to establish predictive factors for the success of PV ablation in AF.[5] To date, the success rates of ablation are not very satisfactory, reaching only 70% in patients with paroxysmal AF and 60% in patients with persistent AF.[6] Recurrences still remain a common problem after the ablation, affecting quality of life through symptomatic episodes and high readmission rates. The recurrence rate after AF ablation has been reported up to 45% in a study published in 2017.[7] Therefore, there is considerable clinical interest to identify factors that can predict the success of PV ablation, in order to develop personalized therapeutic strategies for each patient.

Several clinical characteristics have been described as being associated with an increased recurrence rate after ablation procedures such as age, gender, comorbidities (hypertension, obesity, diabetes mellitus, heart failure), or imaging-derived features of cardiac volumes, mainly the diameter or volume of the left atrium.[7–15] More recently, the amount of epicardial adipose tissue, assessed either by its thickness via echocardiography, or by its volume via cardiac computed tomography (CT), has been described as a reliable predictor for the risk of AF development or recurrence.[16,17] Given the heterogeneous clinical profile of patients with AF or with AF recurrence after PV isolation, identification of those factors that can predict maintenance of sinus rhythm after ablation could help the clinicians to better select the patients for this complex and expensive procedure. Furthermore, an optimal patient selection for interventional AF therapies could reduce the costs of care and avoid to expose them to unnecessary interventions.

In the present study, we sought to identify clinical and imaging-based predictors for the risk of recurrence at one year following radiofrequency catheter ablation in patients with paroxysmal and persistent atrial fibrillation.

MATERIALS AND METHOD

We analyzed 24 patients with paroxysmal and persistent AF, who underwent radiofrequency catheter ablation in the 2015–2018 period. All patients underwent radiofrequency ablation for AF using the PV isolation method and presented to follow-up at 1, 3, 6, and 12 months after the intervention. Prior to the procedure, all patients underwent contrast-enhanced cardiac CT for assessment of left and right atrial volumes, as well as for quantification of the epicardial adipose tissue using manual tracing.

Patients were divided into two groups, according to the presence or absence of AF recurrence during follow-up. Group 1 included 8 patients who presented AF recurrence in the first year after ablation, and group 2 included 16 patients without any sign of recurrence during the 12-month follow-up.

The study was approved by the Ethics Committee of the institution where the procedures were performed and was conducted in compliance with the ethical principles stated in the Declaration of Helsinki. All patients gave informed consent for their participation in the study.

Ablation Protocol

After venous access using the Seldinger technique, one sheath was placed in the left femoral vein and two sheaths in the right femoral veins. A 6F decapolar diagnostic catheter was placed in the coronary sinus, one non-steerable sheath was used for positioning the mapping catheter (Lasso) and the other steerable sheath for placing an externally irrigated contact force-sensing ablation catheter. Interatrial septal puncture was performed using transesophageal echocardiography guidance. 3D electroanatomically mapping of the left atrium and PVs was performed using the EnSiteTM NavXTM system, EE3000

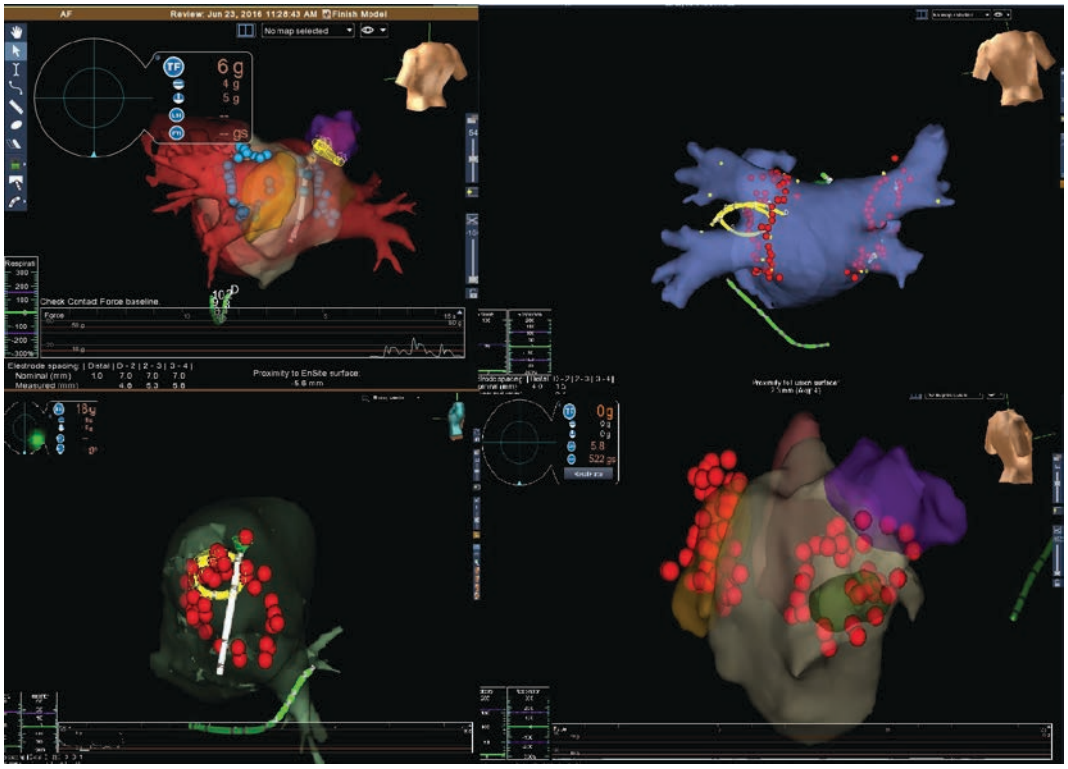

FIGURE 1. 3D maps of the left atrium and PVs. The red tags represent ablation points around the right and left pulmonary veins' ostia. The yellow catheter is the Lasso catheter, positioned in pulmonary vein. The green catheter is placed in the coronary sinus

version (St. Jude Medical, St. Paul, MN, USA), associated with advanced techniques of fusion imaging, fusing 3D mapping images with those acquired by CT. After inserting the mapping catheter in the ostium of the PV, radiofrequency catheter ablation was initiated in order to isolate the PVs. Ablation was performed by applying a 30 W energy and a 10 to 30 g pressure with temperature adjusted at 50 °C, using an irrigated contact force-sensing catheter positioned on the left atrial wall. A PV was considered electrically isolated when no electrical potentials were identified or when a successful PV potential dissociation was demonstrated.

CT Analysis

The cardiac CT acquisition was performed using 64- and 128-slice CT (Somatom Sensation 64-slice CT, Somatom Definition 128-slice CT, Siemens Healthcare, Germany), and the Syngo.via Frontier software (Siemens Healthineers, Erlangen, Germany) was used for image post-processing. Quantification of epicardial fat volume was performed by tracing and manually adjusting epicardial contours, as part of postprocessing protocols. Adipose tissue was identified using the attenuation references between –190 and –30 Hounsfield units. Atrial endocardial profiles were traced semi-automatically on the axial slices.

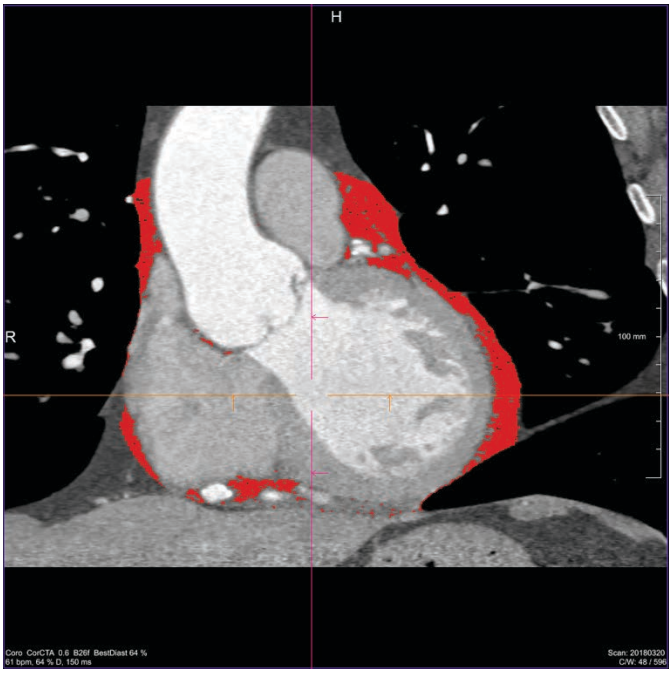

FIGURE 2. Exemplification of epicardial adipose tissue quantification using native CT

TABLE 1. Baseline characteristics of the study population

Age (years)	57.25 ± 11.72
Gender, male, n (%)	14 (58.33%)
History	
Hypertension, n (%)	17 (70.83%)
Diabetes, n (%)	7 (29.16%)
Dyslipidemia, n (%)	5 (20.86%)
Obesity, n (%)	12 (50%)
Clinical characteristics	
eGRF (mL/m²/min)	79.85 ± 17.51
Ejection fraction (%)	53.21 ± 5.09
Left atrium (mm)	41.54 ± 6.43
Heart failure, n (%)	10 (41.66%)
CAD, n (%)	10 (41.66%)
AF type	
Persistent AF	10 (41.66%)
Indexed atrial volume	
LAVI (mL/m²)	58.18 ± 10.98
RAVI (mL/m²)	48.45 ± 10.41
BAVI (mL/m²)	101.6 ± 20.02
Epicardial fat volume (mL)	132 ± 72.14

Atrial volumes were calculated by the software, interpolating the endocardial tracings. Indexed atrial volumes were calculated by indexing atrial volume to body surface area. Body surface area was calculated using the DuBois formula after recording height and weight.

Statistical analysis

Statistical analysis was performed using GraphPad Prism 7 (GraphPad Software, San Diego, CA, USA). Quantitative data were expressed as mean ± standard deviation, and data were compared using Student's t test or the Mann-Whitney test when appropriate. Qualitative values were expressed as integer values and percentages, and the difference between groups was analyzed using the Chi2 test or its appropriate variants. The threshold for statistical significance was set at an alpha of <0.05.

RESULTS

Baseline characteristics of the study lot, including demographic data, medical history, comorbidities, and clinical and imaging features of the 24 patients included in the study are listed in Table 1.

There were no statistically significant differences between the two groups in respect to age, gender, or cardiovascular risk factors (Table 2). There was no significant difference between the study groups regarding the left ventricular ejection fraction evaluated by 2D echocardiography (51.88 ± 6.55% vs. 53.88 ± 4.28%, p = 0.3); however, clinical symptoms of heart failure were significantly more frequent in patients with AF recurrence following ablation (p = 0.03). Also, left atrium diameter was significantly larger in patients with AF recurrence after catheter ablation (p = 0.04) (Table 2).

CT analysis revealed that patients with AF recurrence presented a significantly larger mean index of left atrial volume (LAVI) (59.57 ± 8.52 mL/m² vs. 49.99 ± 10.88 mL/m², p = 0.04). Also, the indexed right atrial volume (RAVI) and the indexed bi-atrial volume (BAVI) were higher in the group with AF recurrence (58.94 ± 8.37 mL/m² vs. 43.21 ± 6.4 mL/m², p <0.0001 for RAVI and 118.5 ± 15.82 mL/m² vs. 93.19 ± 16.42 mL/m², p = 0.005 for BAVI). Figure 3 indicates the difference between the groups in respect to anatomic features as assessed by cardiac CT, namely calculated indexes of atrial volumes.

At the same time, CT analysis of the epicardial adipose tissue volume indicated that patients with AF recurrence have a larger amount of epicardial fat compared with patients without recurrence (176.4 ± 100.8 mL vs. 109.8 ± 40.73 mL, p = 0.02). Figure 4 represents the difference between the groups in respect to the volume of epicardial fat as computed by CT.

TABLE 2. Clinical and echocardiographic features associated to AF recurrence after ablation

	AF recurrence n = 8	No AF recurrence n = 16	p value
Heart failure, n (%)	6 (75%)	4 (25%)	0.03
Left atrium (mm)	45.25 ± 5.14	39.69 ± 6.33	0.04
LAVI (mL/m²)	59.57 ± 8.52	49.99 ± 10.88	0.04
RAVI (mL/m²)	58.94 ± 8.37	43.21 ± 6.74	<0.0001
BAVI (mL/m²)	118.5 ± 15.82	93.19 ± 16.42	0.005
Epicardial fat volume (mL)	176.4 ± 100.8	109.8 ± 40.73	0.02

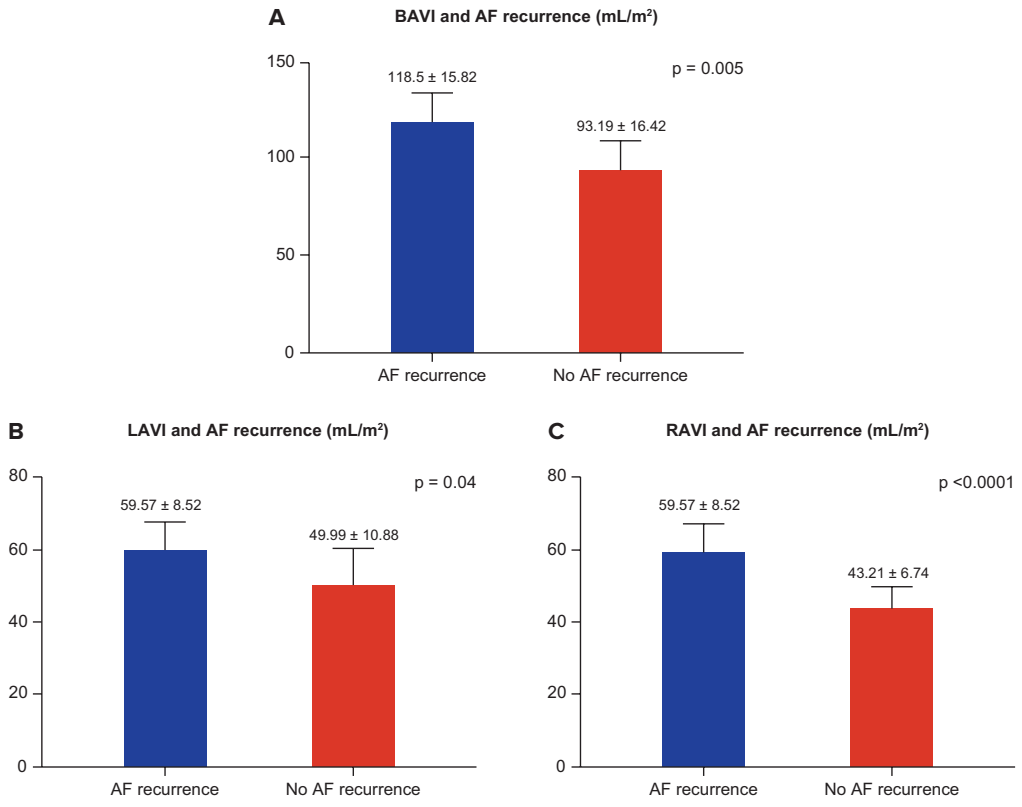

FIGURE 3. Atrial volumes and risk of recurrence after AF ablation. **A** – Bi-atrial indexed volume in the study groups; **B** – Right indexed atrial volume in study groups; **C** – Left indexed atrial volume in the study groups

DISCUSSIONS

AF is a disease with a high prevalence and is associated with increased mortality and morbidity. PV catheter ablation has emerged as a first-line treatment option, especially in cases resistant to antiarrhythmic medication.[18] Immediate success rates have been achieved using PV catheter ablation, but maintaining long-term sinus rhythm in these cases still remains a challenge. Given the average success rates, it is necessary to investigate factors associated to a lower risk of recurrence, which may facilitate a proper selection of patients for ablation. In the last years, several studies have tried to identify predictive factors for a favorable long-term outcome, but reliable markers predicting the maintenance of sinus rhythm have not been identified.[9,19,20] The contribution of this study relies on the description of the role of new imaging-based features associated with the risk of AF recurrence, such as LAVI, RAVI, BAVI, and the volume of epicardial adipose tissue, along with other factors investigated also in other studies, such as AF type, cardiovascular risk factors, left atrium diameter, ejection fraction, and renal function.

Our study aimed to identify new predictive factors for the risk of recurrence based on the differences between patients who presented AF recurrence and those who maintained sinus rhythm. The results of this study indicate that the diameter of the left atrium, the presence of heart failure, atrial volumes, and the amount of epicardial adipose tissue are predictive factors for the risk of arrhythmia recurrence at one year after radiofrequency ablation of AF.

The link between the enlargement of the left atrium and the recurrence of AF is still controversial. In the long term, an enlarged left atrium leads to cardiac remodeling,

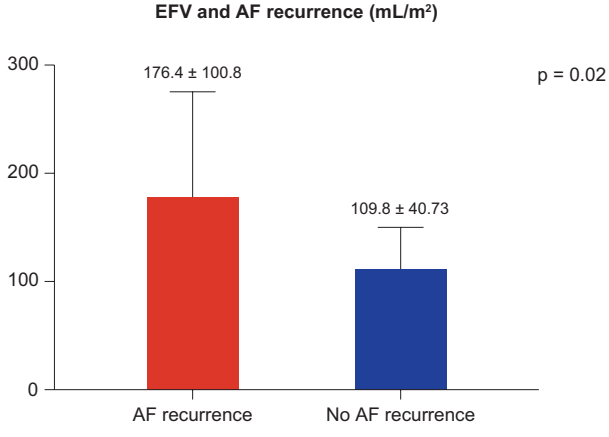

FIGURE 4. Epicardial fat volume in the study groups

manifested by reduced myocardial tissue and increased fibrosis. The increased diameter of the left atrium, reflecting diastolic dysfunction and increased filling pressure due to atrial remodeling, contributes to the vulnerability of atrial myocytes to arrhythmia.[9] As it has been shown that the size of the left atrium is an important factor in the occurrence and maintenance of AF, this could be used in the same way to predict the recurrence after intervention. In a meta-analysis on risk factors for recurrence of post-ablation arrhythmias, an increased diameter of the left atrium was found to have predictive value for AF recurrence.[13] In our study, patients who had maintained sinus rhythm had a significantly smaller left atrium diameter compared to patients with recurrence.

AF and heart failure are two linked conditions, each one predisposing to the other one, and are associated with considerable mortality and morbidity. Important changes in the prevalence of AF in patients with heart failure have been observed, AF occurrence being directly linked to the severity of heart failure, from less than 10% in patients with NYHA class I to almost 50% in patients in NYHA class IV.[21] In a recent study, patients with heart failure had an increased susceptibility to develop recurrences, compared to patients with normal left ventricular function. The main limitation for using left atrial diameter as a measure of the risk of recurrence relies on its representation as a one-dimensional value, which can underestimate or overestimate the true size of the atrium. Therefore, assessment of the atrial volume, especially body surface-related volume, is indicated for a more precise assessment of the left atrium, having a superior predictive value.[15] Comparing atrial volumes between the two groups, we observed that patients with AF recurrence had significantly larger left, right, and bi-atrial indexed volumes than patients who maintained sinus rhythm during follow-up. A number of studies found LAVI to be predictive of AF recurrence, but no consensus was reached on the predictive cut-off value.[15,22] At the same time, there are few data regarding the effect of an increased right atrial volume on the risk of AF recurrence after PV isolation. Given that ablation targets the myocardial tissue surrounding the PV, the right atrium remains "untreated", thus maintaining an increased risk of recurrence in patients with a higher right atrial volume. In one study it was found that RAVI has predictive value only for early recurrences of AF, while LAVI has predictive value in recurrences at one year.[23]

Epicardial adipose tissue is a special type of fat located in the space between the myocardium and the visceral pericardium. This tissue is not just an anatomical depot of fat, but also an active tissue that secretes cytokines and pro-inflammatory hormones, being involved in the pathogenesis of both structural heart disease and the coronary heart disease independent of body mass index.[24] Several studies have evaluated the association between pericardial fat and AF and have shown that an increased volume of pericardial adipose tissue, independent of intrathoracic or intraabdominal adipose tissue, results in a higher risk of AF.[16,17] Another important observation is that in patients with persistent AF, the volume of pericardial adipose tissue is higher than in patients with paroxysmal AF or in patients with sinus rhythm.[25] Several studies have shown that following PV ablation, patients with increased epicardial fat volume had more frequent recurrences, regardless of body mass index and body surface area.[26–28] In this paper, the volume of epicardial adipose tissue was determined using computed tomography, and a lower epicardial fat volume was associated with maintenance of the sinus rhythm one year after the intervention.

CONCLUSIONS

AF is a common disorder in clinical practice and is often characterized by recurrences. Therefore, the identification of particular features that can predict the maintenance of sinus rhythm after PV ablation represents an important goal in clinical practice, allowing a more appropriate patient selection. This study shows that left atrial diameter, indexed atrial volumes, and epicardial fat volume may be used as reliable indicators of the risk to develop AF recurrence after pulmonary vein ablation.

CONFLICT OF INTEREST

Nothing to declare.

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