sciendo

Journal of Cardiovascular Emergencies 2023;9(2):24-31
DOI: 10.2478/jce-2023-0004

ORIGINAL RESEARCH

Left Atrial Volume Quantified by MSCT Predicts Emergency Hospitalizations for AF and Arrhythmia Recurrence after Catheter Ablation

László-Lehel Bordi[1,2,3], Diana Opincariu[1], Theodora Benedek[1,2,3], István Kovács[1,2,3], Zsolt Parajkó[1,2], Emese Márton[1,2], Renáta Gerculy[1,2], Imre Benedek[1,2,3]

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

ABSTRACT

Introduction: This study aimed to investigate the correlation between multislice computed tomography (MSCT)-derived parameters characterizing atrial enlargement and the frequency of emergency hospitalizations after catheter ablation for atrial fibrillation (AF). **Methods:** The study included 52 patients with paroxysmal or persistent AF, who presented criteria for interventional rhythm control strategies and underwent MSCT evaluation prior to ablation. **Results:** The majority of emergency hospital admissions were due to heart failure caused by high-frequency arrhythmia (90.33%), or by cardioembolic complications, causing acute stroke (9.67%). The number of emergency referrals was significantly increased in cases of moderately enlarged left atrial volume (69.23%), and re-admission was necessary for over three quarters of the patients with highly enlarged left atrial volume (76.92%, p = 0.02). The average recurrence rate of AF following ablation therapy was 28.84% during the one-year follow-up, being 0% for volumes <71.33 mL, 32% for volumes between 71.33 mL and 109.5 mL, and 53.84% for volumes >109.5 mL (p = 0.01). **Conclusion:** A large volume of the left atrium, determined by MSCT, is associated with a higher risk of emergency rehospitalizations following catheter ablation of AF.

Keywords: atrial fibrillation, emergency hospitalization, ablation, recurrence, left atrium volume

ARTICLE HISTORY

Received: April 6, 2023
Accepted: April 28, 2023

CORRESPONDENCE

Diana Opincariu
Str. Gheorghe Marinescu nr. 50
540139 Târgu Mureș, Romania
Tel: +40 372 653 100
Email: diana.opincariu@yahoo.ro

INTRODUCTION

Atrial fibrillation (AF) usually begins with rare and short episodes, which become longer and more frequent as the disease progresses.[1] Patients who develop long-standing, persistent AF respond increasingly poorly to antiarrhythmic treatment and have worse outcomes.[2] An important goal of treatment is to restore and maintain sinus rhythm in order to prevent the rapid progression of the disease and the development of potential complications. Besides

László-Lehel Bordi: Str. Gheorghe Marinescu nr. 50, 540139 Târgu Mureș, Romania. Tel: +40 372 653 100, Email: bordi_lehel@yahoo.com
Theodora Benedek: Str. Gheorghe Marinescu nr. 50, 540139 Târgu Mureș, Romania. Tel: +40 372 653 100, Email: theodora.benedek@gmail.com
Isván Kovács: Str. Gheorghe Marinescu nr. 50, 540139 Târgu Mureș, Romania. Tel: +40 372 653 100, Email: kov_istvan@yahoo.com
Zsolt Parajkó: Str. Gheorghe Marinescu nr. 50, 540139 Târgu Mureș, Romania. Tel: +40 372 653 100, Email: p_zsolt92@yahoo.com
Emese Márton: Str. Gheorghe Marinescu nr. 50, 540139 Târgu Mureș, Romania. Tel: +40 372 653 100, Email: emese.marton92@gmail.com
Renáta Gerculy: Str. Gheorghe Marinescu nr. 50, 540139 Târgu Mureș, Romania. Tel: +40 372 653 100, Email: gerculy_renata@yahoo.com
Imre Benedek: Str. Gheorghe Marinescu nr. 50, 540139 Târgu Mureș, Romania. Tel: +40 372 653 100, Email: imrebenedek@yahoo.com

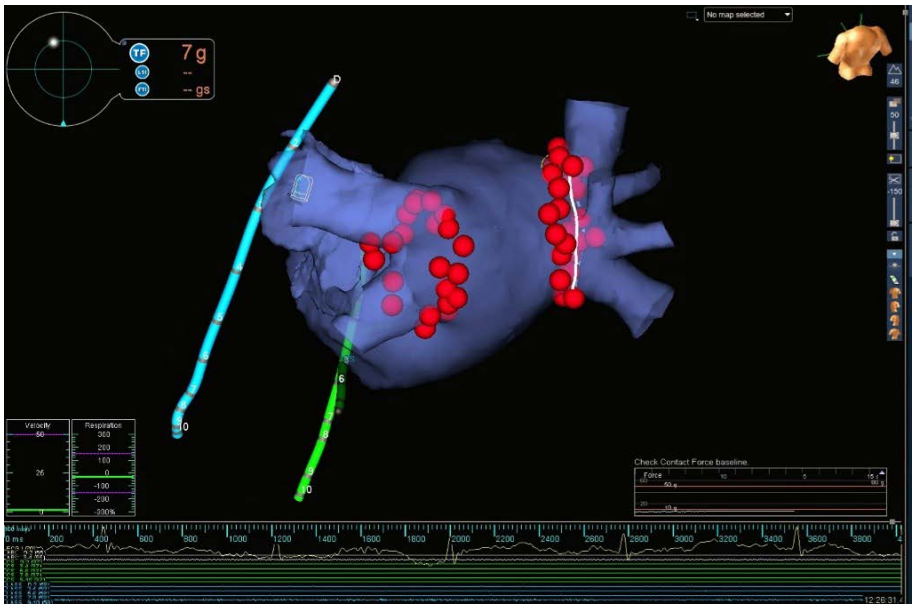

FIGURE 1. Pulmonary vein isolation by radiofrequency using Ensite NavX system

antiarrhythmic medication, catheter ablation is one of the most important elements of an effective therapeutic strategy.[3]

The adequate assessment of left atrial (LA) size and function can provide relevant information for clinicians in the treatment and prognosis of the disease. Several studies have demonstrated that LA enlargement is correlated with the incidence of AF,[4] heart failure,[5] and ischemic stroke.[6] Numerous clinical and imaging parameters have also been correlated with LA enlargement, which leads to the appearance and recurrence of AF.[7] However, few studies have examined these parameters in relation to different degrees of LA enlargement determined by multislice computed tomography (MSCT) and the clinical outcome of these patients.

The aim of this study was to investigate the correlation between LA volume determined by MSCT and various cardiovascular risk factors and imaging parameters. We also examined the correlation between the degree of LA enlargement and the frequency of emergency hospitalizations. Furthermore, we investigated the recurrence rate of AF following ablation treatment, as well as the impact of invasive treatment on the emergency hospitalization rate of the patients.

MATERIAL AND METHODS

STUDY POPULATION AND END-POINTS

In this single-center observational, ambidirectional cohort study, we included 52 patients with paroxysmal or persistent AF, who presented criteria for interventional rhythm control strategies and consented to participate in the one-year follow-up at the Cardiology Clinic of the Emergency Clinical Hospital of Târgu Mureș, Romania. For each patient, medical history, baseline clinical, laboratory and imaging characteristics, as well as procedural and follow-up data were recorded. We excluded patients with chronic AF, LA larger than 136 milliliters, acute coronary syndrome in the last 30 months, suspected hyperthyroidism as the cause of AF, malignant tumors or autoimmune diseases, and allergy to iodine-based contrast agents.

At baseline, we recorded demographic data (gender, age, weight), cardiovascular risk factors, and data from the patients' medical history regarding emergency hospitalizations for left ventricular failure due to AF and for rhythm and rate control strategies from the last 2 years prior to presentation. We performed general laboratory tests, ECG, echocardiography, and MSCT on all patients. Afterwards, pulmonary vein (PV) isolation was performed for every patient using cryo- or radiofrequency ablation, and all study subjects were followed up for 1 year. Figure 1 shows the image of the left atrium after successful ablation by radiofrequency.

STUDY END-POINTS

- emergency hospitalizations for left ventricular (LV) dysfunction triggered by high-frequency arrhythmia, transient ischemic attack or ischemic stroke of cardioembolic origin occurring before catheter ablation;

- recurrent emergency hospitalization for LV dysfunction triggered by high-frequency arrhythmia, transient ischemic attack or ischemic stroke of cardioembolic origin after ablation;
- rhythm and rate control strategies used before catheter ablation;
- recurrence of AF after catheter ablation during the one-year follow-up.

CARDIOVASCULAR IMAGING EVALUATION

We performed an echocardiographic examination before the procedure, as well as at 6 and 12 months after ablation, using a Vivid E9 echocardiography device (General Electric Vingmed Ultrasound, Horten, Norway). We measured LV dimensions and ejection fraction, LA diameter, as well as valvular morphology and function using standard 2D parasternal long and short axis views, as well as apical 4-chamber and 2-chamber views. The anteroposterior diameter of the LA was measured during end-systole of the LV. The LV end-diastolic diameter (LVEDD) and end-systolic diameter (LVESD) were measured in parasternal long axis, and the LV ejection fraction (LVEF) was calculated using Simpson's method based on apical 4-chamber and 2-chamber views.

LA, PV anatomy, coronary artery reconstruction, and calcium scoring were quantified with cardiac CT. Imaging data was acquired with 128-slice CT scanner (Somatom Definition 128-slice CT, Siemens Healthcare, Germany), using a retrospective ECG-gated, contrast-enhanced acquisition protocol. The coronary calcium score (CCS) was evaluated in each coronary artery using the Singo.via Frontier software. The artery was selected by determining its proximal and distal ends, and the volume of calcified plaque was calculated for each artery. These volumes were summed to obtain the total plaque volume, which was used to create the total CCS. The calcium detected by the software was verified manually to ensure accurate identification.

LA volume (LAV), which included the LA appendage but excluded the PV, was measured in the ventricular end-diastolic phase. The LAV was obtained by summing the volumetric measurements of the region of interest on sequential axial slices that were 2 mm thick, using a semi-automated volumetric software. The LAV was measured from the mitral valve orifice to the roof of the LA (Figure 2).

Based on LAV, the study population was divided into tertiles, more specifically into three groups: group 1, with LAV <71.33 mL (n = 13), group 2 with LAV 71.33¬¬–109.5 mL (n = 26), and group 3 with LAV >109.5 mL (n = 13). First, we studied the association between LA enlargement and various cardiovascular risk factors and imaging parameters. Next, we examined the relationship between the rate of emergency hospitalizations and the degree of LA enlargement. Then, we examined the incidence of AF recurrence and the changes in emergency care following ablation therapy.

FIGURE 2. Left atrium reconstruction using MSCT

STATISTICAL ANALYSIS

Statistical analysis was performed using GraphPad Prism 7.0.0 software (GraphPad Software, San Diego, CA, USA). One-way ANOVA test was used to compare the data between the three groups, and the difference between groups was analyzed using the Chi-squared test or its corresponding variants. Continuous variables are presented as mean ± standard deviation (SD), and qualitative categorical data are presented as numbers and percentages. The significance level was set at $p < 0.05$.

RESULTS

PATIENT DEMOGRAPHICS

The study included 52 patients with AF who underwent ablation treatment. The mean age of the patients was 57.33 ± 9.37 years, with a higher prevalence of males (61.63%). Among the cardiovascular risk factors, hyper-

TABLE 1. Demographic parameters, cardiovascular risk factors, and medical history of the study participants

Variable	Group 1 (<71.33 mL) (n = 13	Group 2 (71.33–109.5 mL) (n = 26)	Group 3 (>109.5 mL) (n = 13)	Total	p value
Age, years	56.31 ± 9.92	57.31 ± 9.307	58.38 ± 9.588	57.33 ± 9.37	0.8
Gender, male, n (%)	10 (76.92%)	13 (50%)	9 (69.23%)	32 (61.53%)	0.2
Cardiovascular risk factors and medical history					
Hypertension, n (%)	9 (69.23%)	19 (73.07%)	9 (69.23%)	37 (71.15%)	0.9
Dyslipidemia, n (%)	6 (46.15%)	15 (57.69%)	7 (53.84%)	27 (51.92%)	0.4
Obesity, n (%)	4 (30.76%)	10 (38.46%)	5 (38.46%)	7 (13.46%)	0.8
Smoking, n (%)	3 (23.07%)	2 (7.69%)	2 (15.38%)	19 (36.53%)	0.4
Diabetes, n (%)	3 (23.07)	2 (7.69%)	2 (15.38%)	7 (13.46%)	0.4
Stroke n (%)	0 (0%)	3 (11.53%)	0 (0%)	3 (5.76%)	0.2
Coronary artery disease n (%)	2 (15.38%)	2 (7.69%)	1 (7.69%)	5 (9.61%)	0.7
Pulmonary disease n (%)	0 (0%)	3 (11.53%)	0 (0%)	3 (5.76%)	0.2
Type of atrial fibrillation					
Paroxysmal AF, n (%)	7 (53.84%)	11 (42.3%)	5 (38.46%)	23 (44.23)	0.7
Persistent AF, n (%)	6 (46.15%)	15 (57.69%)	8 (61.53%)	29 (55.76%)	0.7

tension (71.15%) and dyslipidemia (51.92) were the most common. The types of AF were almost equally distributed, with 23 patients (44.23%) having paroxysmal and 29 patients (55.76%) having persistent AF. Baseline and clinical characteristics of the study participants are presented in Table 1.

Demographic and clinical data, the distribution of age, gender, cardiovascular risk factors, and types of AF were similar among the three groups. Stroke and pulmonary diseases occurred exclusively in group 2 (with moderate LA enlargement), in 3 patients (11.53%), but the difference was not significant statistically compared to the other groups.

TABLE 2. Imaging characteristics derived from echocardiography and cardiac CT

Variable (mean ± SD)	Group 1 (<71.33 mL) (n = 13	Group 2 (71.33–109.5 mL) (n = 26)	Group 3 (>109.5 mL) (n = 13)	p value
LVEDD, mm	50.15 ± 4.05	49.81 ± 9.98	51.61 ± 4.44	0.6
LVESD, mm	32.69 ± 4.30	33.27 ± 6.07	34.62 ± 4.38	0.6
LVS thickness, mm	11.46 ± 1.27	11.73 ± 1.51	11.92 ± 1.6	0.7
PW thickness, mm	10.54 ± 1.26	10.77 ± 1.65	11.62 ± 1.75	0.1
LVEF, %	53.08 ± 4.53	51.85 ± 6.46	54.15 ± 3.36	0.2
RV diameter, mm	33.54 ± 4.48	36.08 ± 4.06	37.85 ± 5.95	0.09
LA diameter, mm	38.15 ± 5.9	43 ± 6.07	47 ± 4.37	0.001
E, cm/sec	76.69 ± 19.67	75.5 ± 20.13	63.69 ± 16.4	0.1
A, cm/sec	64.92 ± 19.84	67.5 ± 16.68	73.15 ± 17.07	0.4
DT, msec	173.3 ± 25.71	195.7 ± 43.4	218.2 ± 31.39	0.02
CS total, IU	30.42 ± 30.46	67.96 ± 89.31	149.9 ± 130.2	0.02
CS ADA, IU	14.6 ± 17.36	32.61 ± 54.15	37.07 ± 38.89	0.2
CS LCX, IU	5.32 ± 9.88	10.25 ± 18.85	25.35 ± 26.07	0.1
CS RCA, IU	11 ± 10.64	27.05 ± 46.57	92.92 ± 81.16	0.01
RAV, mL	57.33 ± 13.93	71.17 ± 11.29	91.39 ± 24.23	<0.0001

LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVS, left ventricular septum; PW, posterior wall; LVEF, left ventricular ejection fraction; RV, right ventricle; LA, left atrium; E, mitral early diastolic velocity; A, mitral late diastolic velocity; DT, deceleration time; CS, calcium score; ADA, anterior descendent artery; LCX, circumflex artery; RCA, right coronary artery; RAV, right atrial volume.

TABLE 3. Hospitalization rate and therapeutic strategies in the study groups

Variable	Group 1 (<71.33 mL) (n = 13	Group 2 (71.33–109.5 mL) (n = 26)	Group 3 (>109.5 mL) (n = 13)	p value
Emergency hospitalization, n (%)	4 (30.76%)	18 (69.23%)	10 (76.92%)	0.02
Recurrent emergency hospitalization, n (%)	0 (0%)	9 (34.61%)	5 (38.46%)	0.03
Pharmacologic cardioversion, n (%)	3 (23.07%)	12 (46.15%)	5 (38.46%)	0.37
Electric cardioversion, n (%)	2 (15.38%)	6 (23.07%)	8 (61.53%)	0.01
AF recurrence after ablation, n (%)	0 (0%)	8 (32.00%)	7 (53.84%)	0.009

IMAGING CHARACTERISTICS DERIVED FROM ECHOCARDIOGRAPHY AND CARDIAC CT

The analysis of echocardiographic parameters revealed that the LA diameter presented a significant correlation with LAV increase in the three study groups (38.15 ± 5.9 vs. 43 ± 6.07 vs. 47 ± 4.37, p = 0.001), and in cases of larger LAV, a higher prevalence of LV diastolic dysfunction was observed. The imaging parameters of the study groups are presented in Table 2.

Right atrial volume (RAV) measured with MSCT also demonstrated a significant correlation with LAV, increasing proportionally with LAV (57.33 ± 13.93 mL vs. 71.17 ± 11.29 mL vs. 91.39 ± 24.23 mL, p <0.0001). Total CCS was significantly higher in group 3 (30.42 ± 30.46 vs. 67.96 ± 89.31 vs. 149.9 ± 130.2, p = 0.02). Similarly, the separated analysis of right CCS was significantly higher in group 3 (11 ± 10.64 vs. 71.17 ± 11.29 vs. 91.39 ± 24.23, p = 0.01). However, there were no significant differences between groups with regards to the separate analysis of calcium burden in the left anterior descendant and left circumflex arteries.

STUDY END-POINTS

The majority of emergency hospital admissions of the study participants were due to heart failure caused by high-frequency arrhythmia (90.33%) and in 3 cases (9.67%) due to cardioembolic complications causing acute stroke. We found that the number of emergency admissions were significantly increased in cases with moderately increased LAV (69.23%) and were necessary for over three quarters of the patients with highly increased LAV (76.92%) (p = 0.02). Similarly, the rate of recurrent emergency hospital admissions was significantly higher in the second and third LAV tertiles (p = 0.03).

Analyzing the therapeutic strategies, we found that pharmacological cardioversion occurred more frequently in group 2, with a rate of 46.15%, but did not show a significant difference compared to the other two groups (p = 0.3). In contrast, the need for electric cardioversion showed a significant increase proportional to LA enlargement, reaching 61.53% in cases with larger atrial volumes (p = 0.01).

The recurrence rate of AF following ablation therapy was 28.84% during the one-year follow-up. Ablation success rate was also significantly correlated with atrial volumes. The recurrence rate of AF was 0% for volumes of 71.33 mL, 32% for volumes between 71.33 and 109.5 mL, and 53.84% for volumes above 109.5 mL (p = 0.01). A comparison of emergency hospitalizations and therapeutic strategies is presented in Table 3.

During the one-year follow-up, we found that due to the low recurrence rate, hospitalization rates decreased significantly in all three patient groups following ablation therapy.

DISCUSSION

To determine the prognosis and appropriate treatment for AF, accurate determination of LA size and function can provide essential information for clinicians. Multimodal imaging can allow a comprehensive assessment of the anatomy and function of the LA in patients with AF, including a detailed evaluation of the PVs and LA.[8] Several studies have demonstrated that the most accurate and reliable method for determining the volume of the LA is MSCT examination.[9–11] Based on previous research, in the present study we measured LA volumes using MSCT and divided the patients into three groups based on the size of the average volumes.

Examining the demographic data and cardiovascular risk factors, the study population did not show any significant differences that would be related to LA enlargement. Hypertension, which can be one of the main drivers of LA dilatation and seems to be associated with higher AF progression,[12] was the most commonly observed risk factor, but there were no significant differences in its prevalence among the patient groups. Diabetes and obesity occurred

in smaller and equal proportions. Recently, Nicolaou *et al.* described that patients with paroxysmal AF and metabolic syndrome had an increased LA diameter, and in hypertensive patients, obesity was an important covariate of LA size.[13] Another study, published by Ayer *et al.*, demonstrated that obesity can be an independent predictor of LA size.[14]

Stroke occurred in the medical history of 11.53% of participants, and all cases were found in the group with moderately enlarged LA. There were no significant differences between groups, although this may be attributed to the relatively small sample size. Previous studies conducted on large populations have found evidence linking LA dilatation to the incidence of stroke, regardless of diagnosed AF.[6,15]

M-mode echocardiography is a commonly used and easy method to measure the LA diameter. However, it is controversial whether it shows a good correlation with LA volume determined by MSCT, given that LA has an asymmetrical shape and enlargement occurs unevenly due to the physical limitations of the spine and sternum.[16,17] Therefore, 2D echocardiography may allow for a more accurate determination of LA volume. In our study, although we had a limited sample size, the LA diameter showed a significant correlation with LA volume determined by MSCT ($p = 0.001$).

Another significant echocardiographic parameter was diastolic dysfunction, which showed a higher prevalence with increased atrial volume. This relationship may be based on the interaction between the LA and LV. While the LA acts as a reservoir during LV systolic phase, in the late diastolic phase, the LA is responsible for the inflow of blood into the LV, overriding LV resistance. Based on these mechanical correlations, LA size may play an important role in the development of LV diastolic dysfunction.[18,19] Park *et al.* reported that LA volume was strongly correlated with the degree of diastolic dysfunction.[20]

Several mechanisms have been described regarding the possible association between coronary artery stenosis and the risk of AF, but the exact pathogenic processes of how coronary artery calcification leads to the development of AF are not fully understood.[21] We know that in ischemic heart disease, a high CCS correlates well with subclinical inflammatory processes that can lead to myocardial damage and atrial inflammation.[22] Inflammatory markers change the structural and electrical properties of the LA, leading to the formation of micro-reentry circuits, thereby favoring atrial dilation and the appearance of AF.[23,24] Our study supports this hypothesis, as we found a significant association between a high CCS and larger atria ($p = 0.01$). We also observed that calcification at the level of the right circumflex artery, which was responsible for the blood supply of the atria in the majority of patients, was significantly associated with LA enlargement compared to other coronary arteries.

Atrial remodeling can have an impact not only on the LA but also on the right atrium (RA). However, there is limited information about the pathophysiology of the RA and its prognostic implications for AF.[25-27] O'Neill *et al.* reported that increased RA size in patients who underwent ablation for AF showed a strong correlation with LA enlargement.[28] Our previously published data also supports this hypothesis.[29] In the present study, we found that among the examined parameters, an increase in the size of the RA had the most significant correlation with LA enlargement. In addition to the well-known pathophysiology that micro-reentry circuits in the PVs are responsible for the occurrence of AF, other triggering factors may also be responsible for the development of arrhythmia.

Making efforts to lower the number of hospital admissions is crucial for public health, and not just for economic reasons. AF patients who are hospitalized have a higher risk of stroke and mortality compared to those who receive ambulatory care.[30,31] It has been shown that enlargement of the LA is a predictor of cardiovascular consequences such as AF, heart failure, and mortality.[32] It is well-established that heart failure is a main comorbidity associated with AF, and both entities often coexist.[33] Furthermore, LA remodeling has an important impact both in preserved and reduced LVEF heart failure.

Evaluating the frequency of previous hospitalizations in our patients, we found that the number of emergency admissions, mainly due to acute heart failure, significantly increased as a function of atrial enlargement. The rate of emergency admissions was 30% for moderate enlargement, but reached 76% for large LA volumes. Another important observation of the study is that in the case of moderately enlarged LA, rhythm control was obtained mainly with pharmacologic cardioversion, while patients with highly enlarged LA required electric cardioversion, which can significantly prolong hospitalization and increase costs.

The goal of catheter ablation is to eliminate symptoms related to AF and improve quality of life. Numerous studies have shown that catheter ablation for AF is a safer and more effective approach than antiarrhythmic drugs to maintain sinus rhythm and prevent the recurrence of AF.[34-36] Similarly, several studies have demonstrated that following catheter ablation, there was improvement in LVEF, patient quality of life, and hospitalization compared to medical therapy.[37-39]

The present study demonstrated a low recurrence rate among patients following catheter ablation, in accordance with the largest study on this subject in the literature, which reported a recurrence rate of 34% after 1 year of follow-up.[40] The recurrence rate was significantly correlated with LAV, no recurrence being observed in cases with moderate enlargement. In cases with larger volumes, it increased to 53.84%, indicating that LA enlargement significantly influences the recurrence of AF following ablation therapy.

CONCLUSIONS

In addition to evaluating the size and function of the LA, it is important to pay attention to predictive factors, such as cardiovascular risk factors, CCS, and RAV, which may have an impact on the prognosis of the disease. The LAV determined by MSCT has an important role in the long-term outcome of AF and the frequency of emergency hospitalizations. Ablation treatment improves the patients' quality of life and has an important effect in reducing the frequency of hospitalizations, thereby having a favorable economic impact on the long-term treatment of patients.

CONFLICT OF INTEREST

Nothing to declare.

ACKNOWLEDGEMENT

This research has been funded by the research grant Intel-FAT, proposal registration code PN-III-P4-ID-PCE-2020-2861, contract number PCE 206/2021, Project funded by the European Union and the Government of Romania through the Ministry of European Funds, and the Doctoral School of the "George Emil Palade" University of Medicine, Pharmacy, Science and Technology of Târgu Mureș, Romania.

REFERENCES

1. Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of AF: the Task Force for the Management of AF of the European Society of Cardiology (ESC). Eur Heart J. 2010;31:2369–2429. doi: 10.1093/eurheartj/ehq278.
2. de Vos CB, Pisters R, Nieuwlaat R, et al. Progression from paroxysmal to persistent AF clinical correlates and prognosis. J Am Coll Cardiol. 2010;55:725–731. doi: 10.1016/j.jacc.2009.11.040.
3. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of AF developed in collaboration with EACTS. Eur Heart J. 2016;50:5:e1–e88. doi: 10.1093/ejcts/ezw313.
4. Vaziri SM, Larson MG, Benjamin EJ, Levy D. Echocardiographic predictors of nonrheumatic AF: the Framingham Heart Study. Circulation. 1994;89:724–730. doi: 10.1161/01.cir.89.2.724.
5. Takemoto Y, Barnes ME, Seward JB, et al. Usefulness of left atrial volume in predicting first congestive heart failure in patients ≥65 years of age with well-preserved left ventricular systolic function. Am J Cardiol. 2005;96:832–836. doi: 10.1016/j.amjcard.2005.05.031.
6. Benjamin EJ, D'Agostino RB, Belanger AJ, Wolf PA, Levy D. Left atrial size and the risk of stroke and death: the Framingham Heart Study. Circulation. 1995;92:835–841.
7. Su G, Cao H, Xu S, et al. Left Atrial Enlargement in the Early Stage of Hypertensive Heart Disease: A Common But Ignored Condition. The Journal of Clinical Hypertension. 2014;16:3:192-197. doi: 10.1111/jch.12282.
8. Guglielmo M, Baggiano A, Muscogiuri G, et al. Multimodality imaging of left atrium in patients with AF. Journal of Cardiovascular Computed Tomography. 2019;6:340-346. doi: 10.1016/j.jcct.2019.03.005.
9. Mahabadi AA, Samy B, Seneviratne SK, et al. Quantitative assessment of left atrial volume by electrocardiographic-gated contrast-enhanced multidetector computed tomography. J Cardiovasc Comput Tomogr. 2009;3:80–87. doi: 10.1016/j.jcct.2009.02.002.
10. Christiaens L, Lequeux B, Ardilouze P, et al. A new method for measurement of left atrial volumes using 64-slice spiral computed tomography: comparison with two-dimensional echocardiographic techniques. Int J Cardiol. 2009;131:217–224. doi: 10.1016/j.ijcard.2007.10.020.
11. Avelar E, Durst R, Rosito GA, et al. Comparison of the accuracy of multidetector computed tomography versus two-dimensional echocardiography to measure left atrial volume. Am J Cardiol. 2010;106:104–109. doi: 10.1016/j.amjcard.2010.02.021.
12. Blum S, Meyre P, Aeschbacher S, Berger S, et al. Incidence and Predictors of AF Progression: A Systematic Review and Meta-Analysis. Heart Rhythm. 2018;16:4:502–510. doi: 10.1016/j.hrthm.2018.10.022.
13. Nicolaou VN, Papadakis JE, Karatzis EN, et al. Impact of the metabolic syndrome on atrial size in patients with new-onset AF. Angiology. 2007;58:21–25. doi: 10.1177/0003319706297913.
14. Ayer JG, Almafragy HS, Patel AA, et al. Body mass index is an independent determinant of left atrial size. Heart Lung Circ. 2008;17:19–24. doi: 10.1016/j.hlc.2007.04.006.
15. Di Tullio MR, Sacco RL, Sciacca RR, Homma S. Left atrial size and the risk of ischemic stroke in an ethnically mixed population. Stroke. 1999;30:2019–2024. doi: 10.1161/01.str.30.10.2019.
16. Lemire F, Tajik AJ, Hagler DJ. Asymmetric left atrial enlargement; an echocardiographic observation. Chest. 1976;69:779–781. doi: 10.1378/chest.69.6.779.
17. Lester SJ, Ryan EW, Schiller NB, Foster E. Best method in clinical practice and in research studies to determine left atrial size. Am J Cardiol. 1999;84:829–832. doi: 10.1016/s0002-9149(99)00446-4.
18. Russo C, Jin Z, Homma S, et al. Left atrial minimum volume and reservoir function as correlates of left ventricular diastolic function: impact of left ventricular systolic function. Heart. 2012;98:813–820. doi: 10.1136/heartjnl-2011-301388.
19. Lee JS, Shim CY, Wi J, et al. Left ventricular diastolic function is closely associated with mechanical function of the left atrium in patients with paroxysmal AF. Circ J. 2013;77:697–704. doi: 10.1253/circj.cj-12-1009.

20. Park SM, Park SW, Casaclang-Verzosa G, et al. Diastolic dysfunction and left atrial enlargement as contributing factors to functional mitral regurgitation in dilated cardiomyopathy data from the Acorn trial. Am Heart J. 2009;157:762–710. doi: 10.1016/j.ahj.2008.12.018.
21. Cheng YJ, Church TS, Kimball TE, et al. Comparison of coronary artery calcium detected by electron beam tomography in patients with to those without symptomatic coronary heart disease. Am J Cardiol. 2003;92:498–503. doi: 10.1016/s0002-9149(03)00714-8.
22. Dzeshka MS, Lip GY, Snezhitskiy V, Shantsila E. Cardiac fibrosis in patients with AF: mechanisms and clinical implications. J Am Coll Cardiol. 2015;66:943–959. doi: 10.1016/j.jacc.2015.06.1313.
23. O'Neal WT, Efird JT, Qureshi WT, et al. Coronary artery calcium progression and AF: the multi-ethnic study of atherosclerosis. Circ Cardiovasc Imaging. 2015;8:e003786. doi: 10.1161/CIRCIMAGING.115.003786.
24. Pan NH, Tsao HM, Chang NC, Lee CM, Chen YJ, Chen SA. Dilated left atrium and pulmonary veins in patients with calcified coronary artery: a potential contributor to the genesis of AF. J Cardiovasc Electrophysiol. 2009;20:153–158. doi: 10.1111/j.1540-8167.2008.01290.x.
25. Allessie M, Ausma J, Schotten U. Electrical, contractile and structural remodeling during AF. Cardiovasc Res. 2002;54:230–246. doi: 10.1016/s0008-6363(02)00258-4.
26. Avitall B, Bi J, Mykytsey A, Chicos A. Atrial and ventricular fibrosis induced by AF: evidence to support early rhythm control. Heart Rhythm. 2008;5:839–845. doi: 10.1016/j.hrthm.2008.02.042.
27. Hu YF, Chen YJ, Lin YJ, Chen SA. Inflammation and the pathogenesis of AF. Nat Rev Cardiol. 2015;12:230–243. doi: 10.1038/nrcardio.2015.2.
28. O'Neill MD, Jaïs P, Takahashi Y, et al. The stepwise ablation approach for chronic AF--evidence for a cumulative effect. J Interv Card Electrophysiol. 2006;16:153–167. doi: 10.1007/s10840-006-9045-1.
29. Blîndu E, Korodi S, Bordi L, Kovács I, Benedek I. Epicardial Fat Volume as a New Imaging-Based Feature Associated with Risk of Recurrence after Pulmonary Veins Ablation in AF. Journal of Interdisciplinary Medicine. 2020;5:2:64–70. doi: 10.2478/jim-2020-0012.
30. Waldo AL, Becker RC, Tapson VF, Colgan KJ. Hospitalized patients with AF and a high risk of stroke are not being provided with adequate anticoagulation. J Am Coll Cardiol. 2005;46:1729–1736. doi: 10.1016/j.jacc.2005.06.077.
31. Andersson T, Magnuson A, Bryngelsson IL, et al. All-cause mortality in 272,186 patients hospitalized with incident AF 1995-2008: a Swedish nationwide long-term case-control study. Eur Heart J. 2013;34:1061–1067. doi: 10.1093/eurheartj/ehs469.
32. Chen SC, Chang JM, Tsai YC, et al. Left atrial diameter and albumin with renal outcomes in chronic kidney disease. Int J Med Sci. 2013;10:575–584. doi: 10.7150/ijms.5845.
33. Santhanakrishnan R, Wang N, Larson MG, et al. AF begets heart failure and vice versa: temporal associations and differences in preserved versus reduced ejection fraction. Circulation. 2016;133:484–492. doi: 10.1161/CIRCULATIONAHA.115.018614.
34. Pappone C, Augello G, Sala S, et al. A randomized trial of circumferential pulmonary vein ablation versus antiarrhythmic drug therapy in paroxysmal AF: the APAF study. J Am Coll Cardiol. 2006;48:2340–2347. doi: 10.1016/j.jacc.2006.08.037.
35. Jaïs P, Cauchemez B, Macle L, et al. Catheter ablation versus antiarrhythmic drugs for AF: the A4 study. Circulation. 2008;118:2498–2505. doi: 10.1161/CIRCULATIONAHA.108.772582.
36. Wilber DJ, Pappone C, Neuzil P, et al. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal AF: a randomized controlled trial. JAMA. 2010;303:333–340. doi: 10.1001/jama.2009.2029.
37. Marrouche NF, Brachmann J, Andresen D, Siebels et al. CASTLE-AF Investigators. Catheter ablation for AF with heart failure. N Engl J Med. 2018;378:417–427. doi: 10.1056/NEJMoa1707855.
38. Jones DG, Haldar SK, Hussain W, et al. A randomized trial to assess catheter ablation versus rate control in the management of persistent AF in heart failure. J Am Coll Cardiol. 2013;61:1894–1903. doi: 10.1016/j.jacc.2013.01.069.
39. Hunter RJ, Berriman TJ, Diab I, et al. A randomized controlled trial of catheter ablation versus medical treatment of AF in heart failure (the CAMTAF trial). Circ Arrhythm Electrophysiol. 2014;7:31–38. doi: 10.1161/CIRCEP.113.000806.
40. Siontis KC, Noseworthy PA. FIRE or ICE for paroxysmal AF?—perspectives from the largest randomized evaluation of cryoballoon and radiofrequency ablation to date. J Thorac Dis. 2017;9:3:419-422. doi: 10.21037/jtd.2017.02.93.