Predictors of the paroxysmal atrial fibrillation recurrence following cryoballoon-based pulmonary vein isolation: Assessment of left atrial volume, left atrial volume index, galectin-3 level and neutrophil-to-lymphocyte ratio

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ABSTRACT

Background: Cryoballoon-based pulmonary vein isolation (PVI) is a treatment option for atrial fibrillation (AF). Left atrial volume (LAV) and left atrial volume index (LAVi) are important parameters for long term success of PVI. Galectin-3 (Gal-3) and neutrophil to lymphocyte ratio (N/L ratio) are biomarkers to demonstrate the cardiac fibrosis and remodelling.

Methods: 50 patients with symptomatic PAF despite ≥ 1 antiarrhythmic drug(s), who underwent PVI were enrolled. LAV, LAVi, Gal-3 and N/L ratio were calculated before ablation and after ablation at 6 and 12 months. According to AF recurrence patients were divided into two groups, recurrent AF (n = 14) and non-recurrent AF (n = 36).

Results: In both groups (recurrent and non-recurrent), initial and 12 months follow-up LAV values were 41.39 ± 18.13 ml and 53.24 ± 22.11 ml vs 48.85 ± 12.89 ml and 42.08 ± 13.85 (p = 0.037). LAVi were 20.9 ± 8.91 ml/m2 and 26.85 ± 11.28 ml/m2 vs 25.36 ± 6.21 and 21.87 ± 6.66 (p = 0.05) for recurrent and non-recurrent AF groups, respectively. In both groups PVI had no significant effect on serum Gal-3 levels and N/L ratio during 12 months follow-up. The comparison between two groups at the end of 12th month showed Gal-3 values of 6.66 ± 4.09 ng/ml and 6.02 ± 2.95 ng/ml (p = 0.516), N/L ratio values of $2.28 \pm 1.07 \ 10^3/\mu l$ and $1.98 \pm 0.66 \ 10^3/\mu l$ (p = 0.674).

Conclusion: LAV and LAVi are useful to predict the remodelling of the left atrium and AF recurrence after cryoballoon-based PVI. However, biomarkers such as Gal-3 and N/L ratio are not associated with AF recurrence.

1. Introduction

Catheter ablation which has been widely adopted in cardiology clinics is an effective treatment modality for atrial fibrillation (AF). Some studies revealed the success rate of catheter ablation was 70–80% at six month after the procedure. Even though the results were favourable, the recurrence rate of AF was up to 30–50% at the end of 12th month [1,2]. Recently, besides clinical parameters such as persistent form of AF, diabetes mellitus, heart failure; left atrial structural changes and inflammatory markers were used in many studies to predict the AF recurrence after ablation.

Structural remodelling secondary to fibrosis is important for AF [3–5]. This intersitisyel fibrosis separates the cardiac muscle fibers and causes AF by the mechanism of reentry and focal triggers [3]. Galectin-3 (Gal-3) is an alpha-galactose-binding lectin and Gal-3 is in epithelial, fibroblastic, dendritic and inflammatory cells. The concentration of Gal-3 increases in fibrosis which develops due to tissue inflammation and this is an accurate indicator of fibrosis. Fibrosis of atrial tissue causes recurrence and permanence of AF by triggering structural remodelling. Several studies has shown the elevated levels of Gal-3 in the patients with AF [6,7]. Neutrophil to lymphocyte ratio (N/L ratio) is another bioindicator of inflammation. N/L ratio increases in AF, left atrial (LA) thrombus, ischemic heart disease and stroke [8]. The studies conducted in the recent years have shown that development and recurrence of AF is correlated with N/L ratio [9].

This study has investigated the changes in left atrial volume (LAV), left atrial volume index (LAVi), Gal-3 and N/L ratio during 12-month follow-up period after cryoballoon pulmonary vein isolation (PVI) in the patients with PAF and analyzed the relationship between these changes and recurrence of AF.

2. Methods

2.1. Study population

The study has included 50 patients who had symptomatic PAF despite use of at least one antiarrhythmic drug and consequently underwent pulmonary vein isolation (PVI). An electrocardiogram (ECG) with AF, 24-h holter ECG or event recorder which were documented in the recent three months were used for detection of paroxysmal AF. PAF is described as spontaneous improvement of AF episode within the first 48 h or correction with cardioversion within the first 7 days. Prior to procedure, the patients were performed transthoracic echocardiography (TTE) and transesophageal echcardiography (TEE), complete blood count, fasting blood glucose, kidney function tests, liver function tests, lipid profile and thyroid function tests. Venous blood samples for measurement of Gal-3 levels were obtained from all the patients prior to PVI. Baseline demographic and clinical characteristics, including age, sex, body surface area (BSA), history of smoking cigarette, use of alcohol ($\leq$1 drinks/day for women and $\leq$2 drinks/day for men), history of stroke/TIA and symptomatic severity of the patients according to the European Heart Rhythm Association (EHRA) scoring, CHA_2DS_2-VASc scores and all medication regimes were recorded. The patients aged below 18 years old and with history of acute coronary syndrome, mild or severe cardiac valvular disease, left ventricular ejection fraction <50%, size of LA >50 mm, advanced renal failure (cockcroft GFR < 30 ml/min/1.73 m^2), advanced liver failure (ALT and AST levels higher than 3-folds of normal levels), malignancy, active infection, collagen tissue disease, pregnancy and chronic obstructive pulmonary disease with medication history of β-sympathomimetic drugs were excluded from the study.

Informed consents were obtained from the patients. The study was conducted in compliance with the principles outlined in the Declaration of Helsinki and approved by the Institutional Ethics Committee.

2.2. The evaluation of the left atrium

All patients were performed TTE before and at the 6th and 12th months after PVI. Prior to the procedure, TEE was performed to eliminate left atrial thrombus and left atrial appendage thrombus. TTE examinations were performed using Vivid S5® cardiovascular ultrasound system (3 S 1.5−3.6 MHz probe Transthoracic GE Medical System, Buckinghamshire, UK) while TEE examinations were performed using Vivid S5® cardiovascular ultrasound system (6 T-RS, 5.0 MHz probe TEE GE Medical System, Norway). LAV was calculated using the prolate ellipse method by the measurements obtained from the standard views in accordance with the recommendations of the American Society of Echocardiography. LAV was calculated using the formula LAV= (D1xD2xD3) x 0.523 while D1: anteroposterior diameter in parasternal long-axis, D2: superoinferior diameter measured from apical 4-chamber view, D3:mediolateral diameter measured from apical 4-chamber view. LAVi was calculated by dividing left atrial volume to the body surface area.

2.3. The calculation of serum Gal-3 count ve N/L ratio

Venous blood samples of all the patients were collected for testing serum Gal-3 before and at the 6th and 12th months after PVI. The samples were centrifuged and stored at $-80\,^{\circ}C$ until time of analysis. At time of analysis, samples reached to room temperature and measured by applying ELISA (Enzyme Linked Immunosorbent Assay) using DSX Four-Plate Automated ELISA Processing System (DynexTecnologies, Virginia, USA) microELISA device. Elabscience Human Gal-3 Elisa Kit was used. Complete blood samples of all the patients included in the study were obtained before and at the 6th and 12th months after PVI. The samples were stored in the Greiner Bio-One 4.5 ml K3E K3EDTA tubes. N/L ratio was calculated in terms of $10^3/\mu l$.

2.4. Ablation procedure

All the patients included in the study were sedated with midazolam before cryoablation procedure. Invasive arterial blood pressure, oxygen saturation and electrocardiogram were monitored along the whole procedure. Right femoral vein, left femoral vein and artery were entered using Seldinger technique. Medtronic ArcticFront Advance 2AF283 balloon in diameter of 28 mm and Medtronic Flexcath Advance 4FC12 12 Fr sheath were used in the patients for PVI procedure. Medtronic Achieve 15 mm or 20 mm mapping catheter was used for mapping of the pulmonary veins. When LA was passed following transseptal puncture, administration of heparin boluses was initiated and activated clotting time was maintained between 300-350 s. When the balloon closed the gap of the pulmonary vein completely in LA, cryothermal energy was delivered. Each pulmonary vein was ablated for at least 2 cycles as each cycle was adjusted to last averagely 240 s. The ablation procedure was initiated at left upper pulmonary vein and continued by left lower, right upper and right lower pulmonary veins. During ablation, pulmonary veins and their action potentials were displayed and also disappearance patterns of the pulmonary veins were recorded. The success of the procedure was defined as completely disappearance of the pulmonary vein potentials.

2.5. Follow-up period

The first 3 months following discharge was accepted as the blanking period. The patients were called for visit at the 6th and 12th months after PVI. Event recorders (Novacor® R.Test Evolution 4) were connected 7 days on all the patients to detect the recurrence of AF at their every visits. A symptomatic or asymptomatic occurrence of paroxysmal atrial fibrillation for 30 s or longer was accepted as the criteria of recurrence. LAV and LAVi were calculated by TTE in all the patients who underwent PVI at their visits at the 6th and 12th months, their venous blood samples were obtained for measurement of Gal-3 and N/L ratio. The patients were anticoagulated in the first 3 months and then subsequently evaluated according to CHA_2DS_2-VASc score. All of the antiarrhythmic

medications were interrupted following ablation procedure.

2.6. Statistical analysis

IBM SPSS Statistics Version 20.0 packaged software was used for analysis of the obtained data. The categorical measurements were expressed as numbers and percentage while numerical measurements were summarized as mean and standard deviation (as median and minimum-maximum when needed). Chi-Square test was used in comparison of the categorical measurements between the groups. Kolmogorov Smirnov test was used to control whether the numerical measurements showed normal distribution. T-test was used in the comparison of the independent groups when intergroup comparison of the numerical measurements confirmed the hypothesis whereas Mann-Whitney U test was used when the hypothesis was not confirmed. The analysis of repeated measurements was used in comparison of the numerical measurements obtained during the one-year follow-up period of the patients. Statistical significance level was accepted as 0.05.

3. Results

Mean age of the patients in the study was found out 49.84 ± 12.45 years. The patients were composed of 56% male and 44% female patients. Hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease and cerebrovascular event or transient ischemic attack were present in 52%, 10%, 28%, 20%, and 6% of the patients, respectively. Mean CHA_2DS_2-VASc score of the patients was calculated 1.34. The analysis regarding use of the anticoagulants/antiaggregants showed that 30% of the patients were not using any anticoagulant or antiaggregant. Of the patients; 32%, 16%, 18% and 4% were using Vitamin K-antagonist, one of NOACs, acetylsalicylic acid and clopidogrel, respectively. Totally 42% and 20% of the patients were taking ACEi/ARB and statins, respectively. Mean LAV and LAVi values of the patients were calculated respectively 46.76 ± 14.74 ml and 24.11 ± 7.26 ml/m2 by echocardiography prior to the cryoablation. Mean Gal-3 and N/L ratio values of the patients were measured 6.76 ± 3.03 ng/ml and $2.52 \pm 1.3103/\mu l$ prior to cryoablation, respectively. (Table 1).

Primary endpoint was determined according to presence of recurrence during the follow-up visits at the 6th and 12th months after PVI. Recurrence developed in 28% of the patients at the end of the 12th month. Recurrence developed in none of the patients who were using statins before PVI ($p = 0.045$) (Table 2).

LAV and LAVi values before and at the 6th and 12th months after PVI were compared. Prior to ablation, LAV values of the recurrence and non-recurrence groups were 41.39 ± 18.13 ml and 48.85 ± 12.89 ml ($p = 0.109$), respectively. The comparison between these two groups at the end of 12th month showed LAV values of 53.24 ± 22.11 ml and 42.08 ± 13.85 ml in the recurrence and non-recurrence groups ($p = 0.037$), respectively. LAVi values were encountered 20.9 ± 8.91 ml/m^2 and 25.36 ± 6.21 ml/m^2 in the recurrence group prior to ablation and non-recurrence groups ($p = 0.05$), respectively. The comparison between these two groups at the end of 12th month showed LAVi values of 26.85 ± 11.28 ml/m^2 and 21.87 ± 6.66 ml/m^2 in the recurrence and non-recurrence groups ($p = 0.05$) (Table 3), respectively. The comparison between the groups showed a statistically significant difference between the LAV and LAVi values at the end of 12th month. In the ROC analysis (Fig. 1) LAV 12th months after PVI above 48.3 ml predicted AF recurrence with a sensitivity of 64.2% and a specifity of 80.5%.

Gal-3 and N/L ratio values before and at the 6th and 12th months after PVI were evaluated. Prior to ablation, Gal-3 values of the recurrence and non-recurrence groups were 6.34 ± 4.13 and 6.92 ± 2.53 ng/ml ($p = 0.627$), respectively. The comparison

Table 1
Demographical, clinical, laboratory and echocardiographic parameters.

Sex	
• Female (%)	22 (44%)
• Male (%)	28 (56%)
Age (years)	49.84 ($\pm$12.45)
Body surface area (BSA) (m^2)	1.92 ($\pm$0.16)
Hypertension, n (%)	26 (52%)
Diabetes mellitus, n (%)	5 (10%)
Hyperlipidemia, n (%)	14 (28%)
Coronary artery disease, n (%)	10 (20%)
CVD/TIA, n (%)	3 (6%)
Smoking, n (%)	
• Never used	26 (52%)
• Stopped smoking	18 (36%)
• Currently smoking	6 (12%)
Use of alcoholic beverage;	10 (20%)
EHRA score (1,2,3,4)	
• 1	10 (20%)
• 2	23 (46%)
• 3	17 (34%)
• 4	0 (0%)
CHA_2DS_2-VASC score	1.34
Use of Anticoagulant/antiaggregant medications, n (%)	
• None	15 (30%)
• Vitamin K-antagonist	16 (32%)
• NOAC	8 (16%)
• Acetylsalicylic acid	9 (18%)
• Clopidogrel	2 (4%)
Use of ACEi/ARB, n (%)	21 (42%)
Use of Statins, n (%)	10 (20%)
LAV (ml)	46.76 ($\pm$14.74)
LAVi (ml/m^2)	24.11 ($\pm$7.26)
Galectin-3 (ng/ml)	6.76 ($\pm$3.03)
N/L ratio (10^3/μl)	2.52 ($\pm$1.3)

CVD/TIA: Cerebrovascular disease/Transient ischemic attack, EHRA: European Heart Rhythm Association, NOAC: Novel oral anticoagulants, ACEi: Angiotensin converting enzyme inhibitor, ARB: Angiotensin receptor blocker, LAV: Left atrial volume, LAVi: Left atrial volume index, N/L: Neutrophil/lymphocyte ratio.

between two groups at the end of 12th month showed Gal-3 values of 6.66 ± 4.09 ng/ml and 6.02 ± 2.95 ng/ml in the recurrence and non-recurrence groups ($p = 0.516$), respectively. N/L ratio values were 3.15 ± 1.59 $10^3/\mu l$ and 2.27 ± 1.09 $10^3/\mu l$ in the recurrence group prior to ablation and non-recurrence groups ($p = 0.05$), respectively. The comparison between these two groups at the end of 12th month showed N/L ratio values of 2.28 ± 1.07 $10^3/\mu l$ and 1.98 ± 0.66 $10^3/\mu l$ in the recurrence and non-recurrence groups ($p = 0.674$), respectively. The comparison between the groups showed no statistically significant difference in terms of either Gal-3 and N/L ratio values, however, Gal-3 levels showed an elevation and a reduction respectively in the recurrence group and non-recurrence groups (Table 4) even though these changes were not statistically significant.

4. Discussion

Many parameters were analyzed to predict recurrence of AF in the long-term follow-up period after ablation procedure for AF. LAV and LAVi play important roles among the factors which affect the long-term success of the ablation procedure [10]. A successful ablation prevents LA remodelling and consequently increased levels of LAV and LAVi [11]. Costa et al. have measured LAV using computed tomography prior to ablation in their study and observed that measurement of LAV is more important than the type of AF in predicting success of PVI in a 2-year follow-up period [12]. Erdei et al. encountered that size of LA was enlarged and functionality of LA was reduced in the patients with patients with recurrent paroxysmal AF who underwent ablation [13]. Nedios et al. have conducted a study on 103 patients, they have performed ablation in

Table 2
The distribution of the patients with recurrence and non-recurrence in terms of demographic and clinical data.

	Recurrent, n = 14 (28%)	Non-recurrent, n = 36 (72%)	P value
Sex;			
• Female (%)	3 (13.6%)	19 (86.4%)	0.061
• Male (%)	11 (39.3%)	17 (60.7%)	
Age (years)	43.71 (±17.02)	52.22 (±9.42)	0.096
Body surface area (BSA) (m^2)	1.97 (±0.17)	1.91 (±0.15)	0.236
Hypertension, n (%)	5 (19.2%)	21 (80.8%)	0.211
Diabetes mellitus, n (%)	2 (40%)	3 (60%)	0.611
Hyperlipidemia, n (%)	1 (7.1%)	13 (92.9%)	0.760
Coronary artery disease, n (%)	1 (10%)	9 (90%)	0.246
CVD/TIA, n (%)	0 (0%)	3 (100%)	0.550
Smoking cigarette, n (%)			
• Never used.	7 (26.9%)	19 (73.1%)	0.182
• Stopped smoking.	7 (38.9%)	11 (61.1%)	
• Currently smoking	0 (0%)	6 (100%)	
Use of alcoholic beverage;	5 (50%)	5 (50%)	0.416
EHRA score (1,2a, 2b,3,4)			
• 1	3 (30%)	7 (70%)	0.485
• 2	8 (34.8%)	15 (65.2%)	
• 3	3 (17.6%)	14 (82.4%)	
• 4	0 (0%)	0 (0%)	
CHA$_2$DS$_2$-VASC score	0.92	1.5	0.505
Use of Anticoagulant/antiaggregant medications, n (%)			
• None	7 (46.7%)	8 (53.3%)	0.271
• Vitamin K antagonist	2 (12.5%)	14 (87.5%)	
• NOAC	2 (25%)	6 (75%)	
• Acetylsalicylic acid	2 (22.2%)	7 (77.8%)	
• Clopidogrel	1 (50%)	1 (50%)	
Use of ACEi/ARB, n (%)	4 (19%)	17 (81%)	0.341
Use of Statins, n (%)	0 (0%)	10 (100%)	0.045

CVD/TIA: Cerebrovascular disease/Transient ischemic attack, EHRA: European Heart Rhythm Association, NOAC: Novel oral anticoagulants, ACEi: Angiotensin converting enzyme inhibitor, ARB: Angiotensin receptor blocker.

Table 3
Changes in the LAV and LAVi values of the recurrent and non-recurrent groups at the before and at the 6th and 12th months after the procedure.

	Recurrent, n = 14 (28%)	Non-recurrent, n = 36 (72%)	P value
LAV			
• Prior to the procedure	41.39 (±18.13)	48.85 (±12.89)	0.109
• 6th month	46.59 (±16.37)	47.85 (±14.45)	0.791
• 12th month	53.24 (±22.11)	42.08 (±13.85)	0.037
LAVi			
• Prior to the procedure	20.9 (±8.91)	25.36 (±6.21)	0.05
• 6th month	23.45 (±8.01)	24.80 (±6.58)	0.542
• 12th month	26.85 (±11.28)	21.87 (±6.66)	0.05

LAV: Left atrial volume, LAVi: Left atrial volume index.

the patients with paroxysmal and persistent AF and then followed-up these patients for approximately 2 years. The size of LA was evaluated by either echocardiography and computed tomography. No dilatation of LA was encountered in the patients who underwent successful ablation procedure at the end of the follow-up period [14]. The size of LA and LA ejection fraction were investigated prior to catheter ablation in a meta-analysis involving 25 studies and it was found out that particularly sizes and diameters of LA showed a significant reduction after a successful ablation. The same meta-analysis showed a significant improvement in the patients with paroxysmal AF whereas no significant change was encountered in LA ejection fraction of the patients with persistent AF [15]. In our study, LAV and LAVi were determined as the most precious parameters in predicting recurrence during the 6- and 12-month follow-up periods after PVI in the patients with PAF. A statistically significant difference was found out between either LAV and LAVi values in comparison of the recurrence and non-recurrence at the end of the 12th month (p = 0.037 and p = 0.05, respectively). LAV and LAVi may be a guide for success of AF ablation. Closer and long-term monitoring is recommended in patients

whose LAV and LAVi increased after AF ablation.

Gal-3, as another parameter investigated in the study, has been known as an indicator of particularly myocardial fibrosis since a long while. Most of the studies conducted with Gal-3 involved the cases with heart failure who applied due to complaints of impaired systolic function. It has been proposed in the recent years that Gal-3 is not only an indicator of ventricular fibrosis but also it is an indicator of atrial fibrosis, however, role of Gal-3 in atrial modelling is controversial. Ho et al. have analyzed a Framingham cohort study and followed-up 3306 subjects along 10 years. AF developed in 250 subjects. The analysis of the Gal-3 levels of the subjects regarding age and sex in whom AF developed showed statistically significant higher levels of Gal-3 in the cases with AF, however, no statistically significant relationship was found between Gal-3 values and AF in terms of the previously known traditional risk factors of AF [16]. In another study, Clementy et al. have followed-up the patients for one year period. A significant rate of AF recurrence was encountered in the patients with high levels of Gal-3 prior to ablation and large size of LA [17]. It may be noticed in many studies that high levels of Gal-3 prior to ablation were found associated with AF
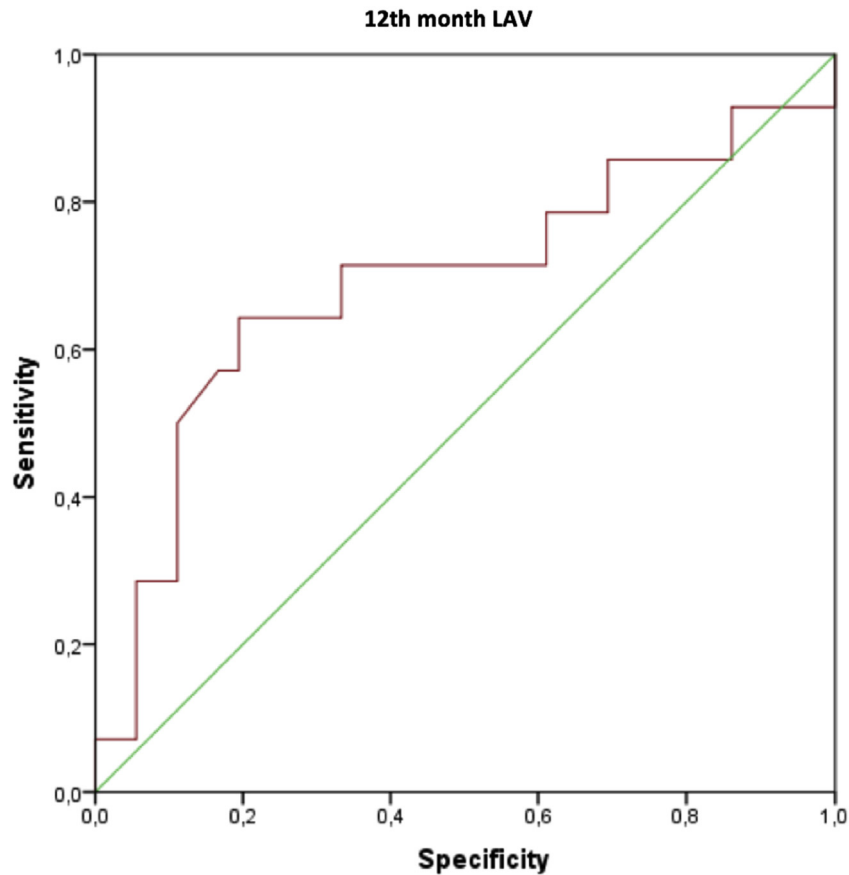
Fig. 1. ROC analysis demonstrating 12th LAV predicting AF recurrence (Area under curve: 0.690).

Table 4
Changes in the Galectin-3 and N/L ratio values of the recurrent and non-recurrent groups at the before and at the 6th and 12th months after the procedure.

	Recurrent, n = 14 (28%)	Non-recurrent, n = 36 (72%)	P value
Galectin-3			
• Prior to the procedure	6.34 (±4.13)	6.92 (±2.53)	0.627
• 6th month	6.82 (±4.00)	6.21 (±3.14)	0.703
• 12th month	6.66 (±4.09)	6.02 (±2.95)	0.516
N/L ratio			
• Prior to the procedure	3.15 (±1.59)	2.27 (±1.09)	0.106
• 6th month	2.79 (±0.97)	2.16 (±0.92)	0.031
• 12th month	2.28 (±1.07)	1.98 (±0.66)	0.674

N/L: Neutrophil/lymphocyte ratio.

recurrence during follow-up. However, Kornej et al. have analyzed the change in levels of Gal-3 after ablation in their study and have found that Gal-3 levels are significantly higher prior to catheter ablation than the control group in the patients with AF, however, no significant difference was encountered between the groups with respect to Gal-3 levels tested at the 6th month. It has been concluded according to the results of this study that Gal-3 levels may be due to other comorbid circumstances but they were not associated with rhythm, therefore, Gal-3 levels can not be used in predicting control rhythm after catheter ablation [18].

In our study, no statistically significant difference between the groups in terms of Gal-3 levels tested at the 6th and 12th after ablation (p = 0.516), however, Gal-3 levels showed an elevation and a reduction respectively in the recurrence group and non-recurrence groups even though these changes were not statistically significant.

Another indicator of fibrosis in the atrial tissue is N/L ratio. N/L ratio represents the balance between neuthrophils and lymphocytes and their counts may change according to inflammation or stress response. The studies have suggested a controversial relationship between N/L ratio and development of AF or recurrence after ablation. Canpolat et al. have followed-up the patients for 19-month period in their study and found a higher ratio of N/L prior to ablation in the patients who experienced recurrence. Sönmez et al. have tested many parameters such as Gal-3, matrix metalloproteinase-9, lipocalin-2, N-terminal propeptide type 3 procollagen, Hs-CRP and N/L ratio which indicate myocardial fibrosis in their study and in the patients with AF and all the parameters were determined significantly higher in the group with AF [19]. However, change in N/L ratio was not found significantly associated in development of AF in some studies. For example, Durukan et al. have monitored the patients who were undergone

coronary artery bypass grafting surgery. N/L ratios of the patients who experienced AF after surgery and the patients with normal sinus rhythm were analyzed and no significant difference was found [20]. In this study, no significant difference between the groups in terms of N/L ratios at the end of 12th month ($p = 0.674$).

5. Conclusion

LAV and LAVi may be used in monitoring atrial remodelling after PVI and predicting recurrence in the patients with PAF. The indicators of fibrosis such as Gal-3 and N/L ratio were not found significantly accurate in predicting recurrence of AF because of the limited number of the patients in the study, therefore, analyzing indicators of atrial fibrosis along longer durations of follow-up terms with a larger size of patient groups may provide significant outcomes.

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Conflicts of interest

None declared.

References

[1] Kuck KH, Brugada J, Fürnkranz A, Metzner A, Ouyang F, Chun KR, et al. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. N Engl J Med 2016 Jun 9;374(23):2235—45. https://doi.org/10.1056/NEJMoa1602014.

[2] Aytemir K, Oto A, Canpolat U, Sunman H, Yorgun H, Şahiner L, et al. Immediate and medium-term outcomes of cryoballoon-based pulmonary vein isolation in patients with paroxysmal and persistent atrial fibrillation: single-centre experience. J Intervent Card Electrophysiol 2013 Dec;38(3):187—95. https://doi.org/10.1007/s10840-013-9834-2.

[3] Yue L, Xie J, Nattel S. Molecular determinants of cardiac fibroblast electrical function and therapeutic implications for atrial fibrillation. Cardiovasc Res 2011;89:744—53.

[4] Burstein B, Comtois P, Michael G, Nishida K, Villeneuve L, Yeh YH, et al. Changes in connexin expression and the atrial fibrillation sub- strate in congestive heart failure. Circ Res 2009;105:1213—22.

[5] Burstein B, Nattel S. Atrial fibrosis: mechanisms and clinical relevance in atrial fibrillation. J Am Coll Cardiol 2008;51:802—9.

[6] Gurses KM, Yalcin MU, Kocyigit D, Canpinar H, Evranos B, Yorgun H, et al. Effects of persistent atrial fibrillation on serum Galectin-3 levels. Am J Cardiol 2015 Mar 1;115(5):647—51. https://doi.org/10.1016/j.amjcard.2014.12.021.

[7] Clementy Nicolas PE, Benhendaa N, Bernarda A, Pierrea B, Siméona E, Fauchiera L, et al. Galectin-3 in patients undergoing ablation of atrial fibrillation. IJC Metab. Endocr. 2014;5:5.

[8] Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, et al. Intermountain Heart Collaborative Study Group. Which white blood cell subtypes predict increased cardiovascular risk? J Am Coll Cardiol 2005;45(10):1638—43.

[9] Trivedi C, Di Biase L. Baseline neutrophil/lymphocyte ratio predicts recurrences after radiofrequency catheter ablation: results from prospective study on paroxysmal atrial fibrillation. Circulation 2013;128. A18588.

[10] Abecasis J, Dourado R, Ferreira A, Saraiva C, Cavaco D, Santos KR, et al. Left atrial volume calculated by multi-detector computed tomography may predict successful pulmonary vein isolation in catheter ablation of atrial fibrillation. Europace 2009 Oct;11(10):1289—94. https://doi.org/10.1093/europace/eup198.

[11] Reant P, Lafitte S, Jaïs P, Serri K, Weerasooriya R, Hocini M, et al. Reverse remodeling of the left cardiac chambers after catheter ablation after 1 year in a series of patients with isolated atrial fibrillation. Circulation 2005 Nov 8;112(19):2896—903.

[12] Jeevanantham V, Ntim W, Navaneethan SD, Shah S, Johnson AC, Hall B, et al. Meta-analysis of the effect of radiofrequency catheter ablation on left atrial size, volumes and function in patients with atrial fibrillation. Am J Cardiol 2010 May 1;105(9):1317—26. https://doi.org/10.1016/j.amjcard.2009.12.046.

[13] Erdei T, Dénes M, Kardos A, Mihálcz A, Földesi C, Temesvári A, et al. Could successful cryoballoon ablation of paroxysmal atrial fibrillation prevent progressive left atrial remodeling? Cardiovasc Ultrasound 2012 Mar 19;10:11. https://doi.org/10.1186/1476-7120-10-11.

[14] Nedios S, Kosiuk J, Koutalas E, Kornej J, Sommer P, Arya A, et al. Comparison of left atrial dimensions in CT and echocardiography as predictors of long-term success after catheter ablation of atrial fibrillation. J Intervent Card Electrophysiol 2015 Sep;43(3):237—44. https://doi.org/10.1007/s10840-015-0010-8.

[15] Xiong B, Li D, Wang J, Gyawali L, Jing J, Su L. The effect of catheter ablation on left atrial size and function for patients with atrial fibrillation: an updated meta-analysis. PLoS One 2015 Jul 6;10(7), e0129274. https://doi.org/10.1371/journal.pone.0129274.

[16] Ho JE, Yin X, Levy D, Vasan RS, Magnani JW, Ellinor PT, et al. Galectin 3 and incident atrial fibrillation in the community. Am Heart J 2014 May;167(5):729—34. https://doi.org/10.1016/j.ahj.2014.02.009. e1.

[17] Clementy N, Benhenda N, Piver E, Pierre B, Bernard A, Fauchier L, et al. Serum Galectin-3 levels predict recurrences after ablation of atrial fibrillation. Sci Rep 2016 Sep 28;6:34357. https://doi.org/10.1038/srep34357.

[18] Kornej J, Schmidl J, Ueberham L, John S, Daneschnejad S, Dinov B, et al. Galectin-3 in patients with atrial fibrillation undergoing radiofrequency catheter ablation. PLoS One 2015 Apr 15;10(4), e0123574. https://doi.org/10.1371/journal.pone.0123574.

[19] Sonmez O, Ertem FU, Vatankulu MA, Erdogan E, Tasal A, Kucukbuzcu S, et al. Novel fibro-inflammation markers in assessing left atrial remodeling in non-valvular atrial fibrillation. Med Sci Mon Int Med J Exp Clin Res 2014 Mar 21;20:463—70. https://doi.org/10.12659/MSM.890635.

[20] Durukan AB, Gurbuz HA, Unal EU, Tavlasoglu M, Durukan E, Salman N, et al. Role of neutrophil/lymphocyte ratio in assessing the risk of postoperative atrial fibrillation. J Cardiovasc Surg 2014 Apr;55(2):287—93.