Galectin-3 in Middle-Aged Patients with First Episode of Non-valvular Atrial Fibrillation: a Speckle-tracking Study

Alev Kılıçgedik, Süleyman Çağan Efe, Ahmet Seyfettin Gürbüz, Emrah Acar, Mehmet Fatih Yılmaz, Fatih Yılmaz, Ali Yaman, Gökhan Kahveci, İbrahim Akın İzgi, Cevat Kırma

University of Health Sciences, Kartal Koşuyolu High Specialization Health Application and Research Center, Clinic of Cardiology, İstanbul, Turkey

ABSTRACT

Introduction: Recent studies have shown a significant association between left atrial (LA) global longitudinal strain (GLS) and the progression of atrial fibrillation (AF) with significantly decreased LA GLS in patients with paroxysmal AF. Significantly higher levels of serum galectin-3 have also been found in patients with non-valvular AF. This study aimed to examine the relationship of the early stage of atrial fibrosis and reduced atrial deformation with serum galectin-3 concentration in middle-aged patients with a first episode of non-valvular AF.

Patients and Methods: This study prospectively enrolled 34 patients who were admitted to our emergency department and required either a medical or electrical cardioversion due to the first episode of AF, without any structural or coronary heart disease and with normal LA size. Additionally, 31 control subjects were also enrolled. The diameter, volume, and mechanical function of LA, including strain (S) and strain rate (SR), and serum galectin-3 levels were measured.

Results: The average age was 48.5 ± 10.4 years. Galectin-3 values were not significantly different between the AF and control groups (r= 0.42; p= 0.51) and were found to correlate inversely with peak negative SR on apical four chamber (r= –0.31, p= 0.02) and two chamber (r= –0.25, p= 0.04) views. In comparison to the control group, the AF group had significantly lower values of peak systolic S on four chamber view (p= 0.037), peak late diastolic S (p= 0.04), peak positive SR on apical four-chamber view (p= 0.04), and peak late negative SR on apical four chamber (p= 0.03) and two-chamber (p= 0.02) views.

Conclusion: Middle-aged patients with the first episode of AF and normal LA sizes had reduced LA reservoir and active atrial functions. Although beginning signs of LA functional remodeling were shown on S and SR imaging, these were not completely reflected by serum galectin-3 levels.

Key Words: Atrial fibrillation; strain; strain rate; galectin-3

İlk Atak Non-valvular Atrial Fibrilasyonlu Orta Yaşlı Hastalarda Galectin-3

ÖZET

Giriş: Biz bu çalışmada ilk atak non-valvular atriyal fibrilasyon (AF)'lu orta yaşlı hasta grubunda serum galectin konsantrasyonu ile AF erken evresi arasındaki ilişkiyi araştırdık.

Hastalar ve Yöntem: Bu çalışmaya acil servisimize ilk atak AF ile başvuran, medikal ya da elektriki kardiyoversiyon yapılmış, yapısal ya da koroner kalp hastalığı olmayan normal LA boyuta sahip 34 hasta ve 31 kontrol hastası prospektif olarak dahil edildi. Ekokardiyografik bulgular kayıt altına alındı ve serum galectin düzeyleri ekokardiyografi öncesi alınan kan örneklerinden ölçüldü.

Bulgular: Hastaların ortalama yaşı 48.5 ± 10.4 yıldı. Galectin değerleri arasında AF ve kontrol grubu arasında anlamlı fark saptanmadı (r= 0.42 ; p= 0.51) ve apikal dört boşluk (r= -0.31, p= 0.02) ve iki boşluk görüntüden (r= -0.25 , p= 0.04) pik negatif SR ile negatif korele bulundu. Kontrol grubu ile karşılaştırıldığında, AF grubunda dört boşluk görüntüden pik sistolik strain (p= 0.037), pik geç diastolik strain (p= 0.04), pik positif SR (p= 0.04) ve pik geç negatif SR apikal dört (p= 0.03) ve iki boşluk (p= 0.02) görüntüden değerleri anlamlı olarak daha düşük olarak bulunmuştur.

Sonuç: İlk atak AF'li orta yaşlı ve normal LA boyutuna sahip hastalarda LA rezervuar ve aktif atriyal fonksiyonlar azalmıştır. Strain ve SR görüntüleme ile gösterilmiş LA fonksiyonel remodeling belirtileri başlamış olmasına rağmen bu durum serum galectin düzeyleri ile tam olarak gösterilememiştir.

Anahtar Kelimeler: Atriyal fibrilasyon; strain; strain rate; galectin

Correspondence

Alev Kılıçgedik

E-mail: akilicgedik@yahoo.com
Submitted: 17.01.2017
Accepted: 26.02.2017

INTRODUCTION

Atrial fibrillation (AF) is a common rhythm disturbance associated with increased morbidity and mortality in the general population[1]. Apart from cardiac conditions, multiple risk factors, including hypertension (HTN), diabetes mellitus (DM), obesity, and old age may predispose an individual to develop AF. Atrial fibrosis is a hallmark of structural remodeling and serves as a substrate for AF[2]. Moreover, atrial remodeling and fibrosis play important roles in persistent AF[3,4]. Recent studies have shown a significant association between left atrial (LA) global longitudinal strain (GLS) and AF progression, with significantly decreased LA GLS in patients with paroxysmal AF[4,5]. In long-term AF, fibrosis is an important factor causing mechanical dysfunction[2].

Galectin-3 is a β-galactosidase-binding lectin that is mostly expressed in fibrotic tissue. It has been shown to be related to cardiac fibrosis and is accepted as a novel blood biomarker in cardiac diseases[3]. Significantly higher levels of serum galectin-3 have also been found in patients with non-valvular AF[6]. This study was designed to examine the relationship of the early stage of atrial strain and fibrosis, as measured by speckle-tracking echocardiography, with serum galectin-3 levels in middle-aged patients with a first episode of non-valvular AF.

PATIENTS and METHODS

The study prospectively included 34 consecutive patients who were admitted to our emergency department and required either medical or electrical cardioversion due to the first episode of AF. Patients who had any of the following conditions were excluded from the study: structural or valvular heart disease, coronary artery disease, chronic kidney disease, chronic obstructive lung disease, abnormal thyroid or hepatic function, previous history of attempted AF ablation, LA diameter > 40 mm, and systolic left ventricular (LV) dysfunction. At least 1 month after the initial admission, each patient underwent echocardiographic examinations, and their blood samples were obtained. Exercise stress test was normal in each patient. Weight, height, and blood pressure were measured and recorded appropriately. As a control group, 31 age- and gender-matched healthy subjects were enrolled. Local ethics committee approved the study.

Blood Samples

Blood samples were obtained on the same day of echocardiographic examination to determine serum galectin-3 levels. These were collected using pyrogen-free tubes containing ethylenediaminetetraacetic acid and centrifuged at 5000 r.p.m. for 10 minutes. Serum samples were stored at -20ºC and analyzed using human lectin-galactose binding-soluble 3 enzyme-linked immunosorbent assay kit (Shanghai YehuaBiological Technology Co., Ltd., Shanghai, China,) with an assay range of 1-380 pg/ml and a sensitivity of 0.51 pg/mL.

Echocardiographic Examination

Standard echocardiographic evaluations were performed using a 1-5 MHz X5-1 transducer (iE33, Philips Healthcare, Inc., Andover, MA). Patients were examined in the left lateral position. All measurements were averaged over three consecutive heart cycles. All standard two-dimensional (2D) transthoracic echocardographic images (i.e., parasternal long axis and short axis, and apical four-, three- and two- chamber views), color Doppler and tissue Doppler images were triggered to the QRS complex and were stored in cine loop format. The LV diastolic and systolic diameters were measured using M-mode or 2D echocardiography. LV ejection fraction (LVEF) was calculated by using the Simpson's formula and by employing a 2D image of the LV chamber during systole and diastole in the four- and two-chamber apical views.

Mitral inflow velocities were measured by pulsed wave (PW) Doppler, with the sample volume placed at the tip of the mitral valve in the LV. E and A waves were recorded. Mitral annular velocities were measured by PW tissue Doppler imaging (PW-TDI), with the sample volume placed at the level of the lateral and septal mitral annulus. Septal and lateral E' and A' waves were recorded and E/E' for septal and lateral mitral annulus and E/A were calculated.

Pulmonary artery pressure was estimated from tricuspid regurgitation jet. Tricuspid annular plane systolic excursion in the apical four-chamber view and tricuspid annulus peak systolic velocity with TDI were used to evaluate right ventricular function.

Circumferential and longitudinal LV strains were evaluated using 2D speckle-tracking imaging. Global circumferential strain (GCS) was assessed by applying 2D speckle-tracking imaging to the parasternal short axis views of LV. The longitudinal peak systolic strain was assessed by applying 2D speckle-tracking imaging to the apical four-, three-, and two chamber views.

LA diameter was measured at the end-systole along the parasternal long-axis view. LA volume was calculated from the apical four- and two- chamber views of the LA using the biplane area length method. LA volume index (LAVI) was calculated on the basis of the patient's body surface area. LA strain (S) and strain rate (SR) values were obtained from apical four- and two-chamber views by speckle-tracking method (Figure 1). The first positive peak of strain (LAS), plateau (COND.), and return to zero line (ATRIAL) were considered to represent LA reservoir, conduit, and contractile phase, respectively. Accordingly, three SR parameters were evaluated: 1) peak positive strain rate (SRs, which corresponded to atrial reservoir function); 2) peak early negative strain rate (SRe, which corresponded to atrial conduit function), and 3) peak late negative strain rate (SRa, which corresponded to atrial contraction).

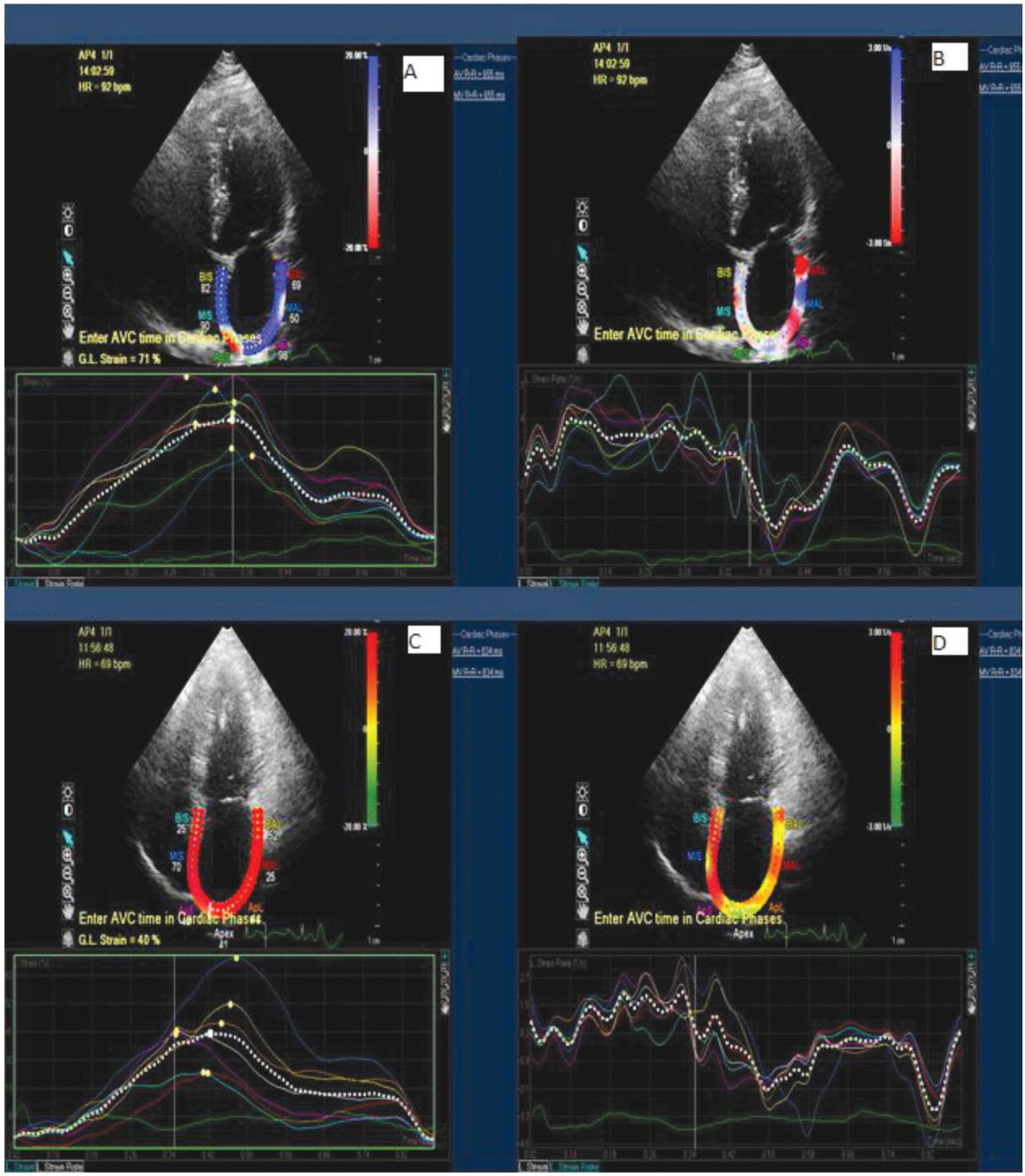

Figure 1. Atrial strain and strain rate imaging; in the control group **(A,B)**. In the atrial fibrillation group **(C,D).**

Statistical Analysis

Data were analyzed using IBM SPSS Statistics 17.0 software (SPSS, Chicago, IL) and presented as mean ± standard deviation for interval scale variables and as percentage for categorical variables. Categorical variables were compared using the chi square test or Fisher's exact test, as appropriate. One-way MANOVA was applied to interval scale variables. Each variable of atrial strain was considered as a dependent variable for galectin-3 values. In this multivariate analysis, Box's test was used to determine whether the covariance matrices were equivalent. Levene's test showed homogeneity of the variances. Correlations were determined by Pearson's test or Spearman's correlation test, as appropriate. A p value of less than 0.05 was considered statistically significant.

RESULT

The baseline clinical features and echocardiographic findings of the patients are summarized in Tables 1 and 2, respectively. The AF and control groups were similar in terms of age (p= 0.39), gender (p= 0.66), body mass index (p= 0.45), heart rate (p= 0.33), and systolic (p= 0.25) and diastolic (p= 0.63) blood pressure values. The rate of cigarette smoking was higher in the AF group than in the control group (15% vs. 9%). Speckle-tracking echocardiographic features are presented in Table 3. Galectin-3 levels did not differ significantly in the AF and the control groups (p= 0.51) and correlated inversely with SRa values obtained from both the apical two-chamber (SRa2; r= -0.25, p= 0.04) and four-chamber views (SRa4; r= -0.31, p= 0.02). In addition, heart rate correlated significantly with SRs4 (r= 0.3, p= 0.04), SRe2 (r= -0.36, p= 0.01), and SRa2 (r= -0.33, p= 0.02).

In comparison to the control group, the AF group showed significantly lower LAS in the apical four-chamber view (LAS4) (p= 0.037), ATRIAL4 (p= 0.04), SRs4 (p= 0.04), SRa4 (p= 0.03), and SRa2 (p= 0.02) (Table 3). LAS4 correlated inversely with age (r= -0.35, p= 0.007) but correlated positively with the E/A ratio (r= 0.40, p= 0.002). The E/A ratio correlated significantly with SRe4 (r= -0.37, p= 0.007), SRe2 (r= -0.39, p= 0.006), and SRa2 (r= -0.40, p= 0.005).

Galectin-3 levels did not correlate with LA volume (r= -0.06, p= 0.67), LA volume index (r= -0.05, p= 0.70) and the S and SR values of both two- and four-chamber views. LA diameter correlated with SRs2 (r= 0.46, p= 0.001) and SRe2 (r= 0.36, p= 0.01). In the AF group, galectin-3 correlated only with SRe2 (r= -0.62, p= 0.001) and SRa2 (r= –0.51, p= 0.01).

Although these values were in the normal range, in comparison to the control group, the AF group had significantly lower LVEF (p= 0.000) and LV GLS (p= 0.002) values. LV GCS value (p= 0.79) was not significantly different between the groups.

DISCUSSION

Our study demonstrated that with age- and gender-matched healthy individuals, middle-aged patients with the first episode of AF had lower LA function, reservoir function, and active atrial function, regardless of the LA size. Although reduced atrial deformation during the reservoir phase of the cardiac cycle is considered to be an early and non-invasive marker of the amount of atrial wall fibrosis, serum galectin-3 concentrations did not seem to validate this assumption in the current patient group.

During the cardiac cycle, LA undergoes three phases: 1) the reservoir phase, in which pulmonary venous return is stored during LV systole; 2) the conduit phase, which represents the passive transfer of blood to the LV during early diastole, and 3) the contractile phase, which involves active priming of the

Table 1. Clinical characteristics of the study population

	New-onset AF	Control	p
Age (years)	48.5 ± 10.4	46.5 ± 8.7	0.39
Gender (male/female)	19/15	19/12	0.66
Risk factors			
DM, n (%)	2 (5.8%)	1 (3.2%)	0.61
HTN, n (%)	10 (39.4%)	4 (12.9)	0.10
Smoking, n (%)	5 (14.7%)	3 (9.6%)	0.02
HL, n (%)	4 (11.7%)	7 (22.5%)	0.25
BMI (kg/m²)	29.0 ± 3.5	26.8 ± 4.41	0.45
HR (bpm)	69.2 ± 10.1	71.9 ± 11.4	0.33
SBP (mmHg)	125.5 ± 19.4	130.3 ± 11.6	0.25
DBP (mmHg)	72.7 ± 10.5	74 ± 10.1	0.63
CRP (mIU/mL)	0.6 ± 1	1.6 ± 2.2	0.19
TSH (mg/dL)	1.9 ± 1.34	1.7 ± 0.98	0.66
Galectin-3 (pg/mL)	208 ± 248	212.5 ± 116	0.94

AF: Atrial fibrillation, DM: Diabetes mellitus, HTN: Hypertension, HL: Hyperlipidemia, BMI: Body mass index, HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CRP: C- Reactive protein, TSH: Thyroid-stimulating hormone.

Table 2. Standard echocardiographic features of the study population

	New-onset AF	Control	p
LVEDD (cm)	4.8 ± 0.49	4.7 ± 0.47	0.41
LVESD (cm)	3.0 ± 0.43	2.8 ± 0.44	0.17
LVEF (%)	62.6 ± 4.5	65.7 ± 0.97	0.000
LA (cm)	3.4 ± 0.45	3.2 ± 0.47	0.77
LAV (mL)	52.1 ± 14.5	47.9 ± 12.2	0.23
LAVI (mL/m²)	1.8 ± 0.5	1.7 ± 0.58	0.63
E (cm/sec)	70.6 ± 14.6	74.6 ± 19.1	0.33
A (cm/sec)	64.1 ± 14.2	66.2 ± 18	0.59
E/A ratio	1.14 ± 0.29	1.19 ± 0.39	0.57
DECT (msec)	227.6 ± 62.1	198.8 ± 49.7	0.048
LATE/e'	7.36 ± 2.4	6.19 ± 1.6	0.03
SEPTE/e'	8.99 ± 3.2	7.89 ± 2.3	0.13
TAPSE (mm)	25.3 ± 4.6	24.5 ± 3.9	0.42
ST (cm/sec)	14.5 ± 2.5	15.0 ± 2.27	0.40

AF: Atrial fibrillation, LVESD: Left ventricular end-systolic diameter, LVEDD: Left ventricular end-diastolic diameter, LVEF: Left ventricular ejection fraction, LA: Left atrium, LAV: Eft atrial volume, LAVI: Left atrial volume index, E: Mitral inflow E Wave, A: Mitral inflow A wave, DECT: Deceleration time, LATE/e': Lateral annular E/e', SEPTE/e': Septal annular E/e', TAPSE: Tricuspid annular plane systolic excursion, ST: Tricuspid annular peak systolic velocity.

Table 3. Speckle-tracking echocardiographic values of study population

	New-onset AF	Control	p
LV GCS (%)	22.5 ± 5.2	22.8 ± 4.57	0.79
LV GLS (%)	18.5 ± 3.6	21 ± 2.25	0.002
LASTR4 (%)	40.0 ± 20.2	50.5 ± 19.4	0.03
COND4 (%)	15.4 ± 9	19.6 ± 10.4	0.109
ATRIAL4 (%)	19.8 ± 9.2	25.1 ± 11	0.049
SRs4 (s^{-1})	1.38 ± 1.23	0.85 ± 0.68	0.049
SRe4 (s^{-1})	-1.73 ± 1.14	-2.29 ± 1.3	0.09
SRa4 (s^{-1})	-2.49 ± 1.41	-3.32 ± 1.5	0.03
LASTR2 (%)	36.9 ± 17.1	41.7 ± 16.7	0.26
COND2 (%)	13.0 ± 10.1	15.73 ± 10.1	0.31
ATRIAL2 (%)	17.8 ± 9.5	23.5 ± 12.2	0.05
SRs2 (s^{-1})	0.80 ± 0.2	0.83 ± 0.4	0.73
SRe2 (s^{-1})	-1.66 ± 0.95	-1.90 ± 1.6	0.5
SRa2 (s^{-1})	-2.36 ± 1.35	-3.24 ± 1.44	0.02

AF: Atrial fibrillation, LV: left ventricular, GCS: Global circumferential strain, GLS: Global longitudinal strain, LASTR4/2: Left atrial first positive peak of strain, COND4/2: Plateau and return to the zero line, ATRIAL4/2: The contractile phase, SRs4/2: Peak positive strain rate (SRs corresponds to the atrial reservoir function), SRe4/2: Peak early negative strain rate (SRe corresponds to the atrial conduit function), SRa4/2: Peak late negative strain rate (SRa corresponds to the atrial contraction) values were derived from four- and two- chamber views.

LV in late diastole[7]. A 2D strain analysis enables identification of these phases. Various studies have demonstrated impaired LA global and regional function in patients with paroxysmal AF despite a normal or mildly enlarged LA[8-10]. As demonstrated by the present study, impairment in the reservoir function was detected even before atrial dilatation occurred. This was due to atrial fibrosis and reduced atrial compliance[11]. LA size has an important role in the onset and recurrence of AF. Therefore, the use of atrial strain analysis for early detection of functional remodeling, even before anatomical alterations have taken place, may allow us to predict the risk for AF recurrence. Increased interstitial fibrosis and a high likelihood of local intra-atrial conduction block were considered the cause of susceptibility to AF[11]. Compared with traditional parameters, LA strain was shown to be a better predictor of the degree of fibrosis and to have a close correlation with histological findings on the atrial wall in patients undergoing surgical correction for severe primary mitral regurgitation[12]. Kuppahally et al. found that larger extension of LA enhancement on delayed contrast enhanced cardiac magnetic resonance imaging was associated with lower performance of the atrial reservoir and the amount of fibrosis. Furthermore, the corresponding reduction in atrial strain was significantly greater in patients with chronic AF than in those with paroxysmal AF[3]. Reduced atrial deformation during the reservoir phase of the cardiac cycle may be an early and non-invasive marker of the amount of atrial wall fibrosis[11].

Galectin-3 is a β-galactosidase-binding lectin that is highly expressed in fibrotic tissues. It has been shown to be related to cardiac fibrosis and heart failure, age, diabetic nephropathy, and fibrotic conditions of the kidneys, liver, and lungs[13]. Galectin-3 induces cardiac fibrosis by promoting cardiac fibroblast proliferation, collagen deposition, and ventricular dysfunction[13]. It was also found to be elevated in AF patients with preserved LV function, being more pronounced in persistent AF than in paroxysmal AF[14]. In an age- and gender-adjusted analysis, HO et al. showed that higher serum galectin-3 concentrations were associated with increased risk of developing AF over the subsequent 10 years, whereas no significant associations were found for the traditional clinical risk factors of AF even after adjustment[15]. In our study, serum galectin-3 concentrations failed to show an upward trend. This probably resulted from the fact that progressive atrial fibrosis is commonly accompanied by older age, HTN, DM, and obesity. Our study population was younger than the patient groups reported by other studies (Table 1). The number of women and patients with DM and HTN, which are known to be associated with high serum galectin-3 concentrations, were relatively lower in our study group. The amount of fibrosis increases with the persistence and recurrence of AF. Our patients experienced their first episode of AF and may have relatively less atrial fibrosis. However, atrial fibrosis involves multifactorial processes that result from complex interactions among neurohormonal and cellular mediators; therefore, the presence of atrial fibrosis in patients with AF remains a challenging issue[11]. Although serum galectin-3 levels did not differ significantly between the two groups, they correlated inversely with LA SRa4 and SRa2. This may imply LA functional remodeling caused by atrial fibrosis was still in the beginning stages and has yet to reach an extent that is sufficient to increase the galectin-3 concentrations.

E/A ratio was associated with LAS4 and SR, suggesting a direct relationship between the extent of increase in LA pressure and the degree of cavity dysfunction[10].

CONCLUSION

Middle-aged patients with the first episode of AF showed reduced LA reservoir and active atrial functions, despite having normal LA sizes. In this patient group, LA functional remodeling may still be at the initial stage, as shown by S and SR imaging, such that the increase in serum galectin-3 levels was not yet involved.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: AK, CK, SE

Analysis/Interpretation: AK, CK, AY

Data Acquisition: SE, AG, EA, MY

Writting: AK, CK

Critical Revision: CK, FY, İİ, GK

Final Approval: All of authors

REFERENCES

1. Kannel WB, Benjamin EJ. Current perceptions of the epidemiology of atrial fibrillation. Cardiol Clin 2009;27:13-24.
2. Kuppahally SS, Akoum N, Burgon NS, Badger TJ, Kholmovski EG, Vijayakumar S, et al. Left atrial strain and strain rate in patients with paroxysmal and persistent atrial fibrillation: relationship to left atrial structural remodeling detected by delayed-enhancement MRI. Circ Cardiovasc Imaging 2010;3:231-9.
3. He B, Huang B, Lu Z, He W, Jiang H. Galectin-3: A potential new target for upstream therapy of atrial fibrillation. Int J Cardiol 2016;203:1131-2.
4. Yoon YE, Oh IY, Kim SA Park KH, Kim SH, Park JH, et al. Echocardiographic predictors of progression to persistent or permanent atrial fibrillation in patients with paroxysmal atrial fibrillation (E6P study). J Am Soc Echocardiogr 2015;28:709-17.
5. Clementy N, Piver E, Benhenda N, Bernard A, Pierre B, Simeon E, et al. Galectin-3 in patients undergoing ablation of atrial fibrillation. IJC Metabolic &Endocrine 2014;5:56-60.
6. Sonmez O, Ertem FU, Vatankulu MA, et al. Novel fibro-inflammation markers in assessing leftatrial remodeling in non-valvular atrial fibrillation. Med Sci Monit 2014;20:463-70.
7. Todaro MC, Choudhuri I, Belohlavek M, Jahangir A, Carerj S, Oreto L, et al. New echocardiographic techniques for evaluation of left atrial mechanics. Eur Heart J Cardiovasc Imaging 2012;13:973-84.
8. Sarvari SI, Haugaa KH, Stokke TM, Ansari HZ, Leren IS, Hegbom F, et al. Strain echocardiographic assessment of left atrial function predicts recurrence of atrial fibrillation. Eur Heart J Cardiovasc Imaging 2016;17:660-7.
9. Kojima T, Kawasaki M, Tanaka R, Ono K, Hirose T, Iwama M, et al. Left atrial global and regional function in patients with paroxysmal atrial fibrillation has already been impaired before enlargement of left atrium: velocity vector imaging echocardiography study. Eur Heart J Cardiovasc Imaging 2012;13:227-34.
10. Henein M, Zhao Y, Henein MY, Lindqvist P. Disturbed left atrial mechanical function in paroxysmal atrial fibrillation: a speckle tracking study. Int J Cardiol 2012;155:437-41.
11. Longobardo L, Todaro MC, Zito C, Piccione MC, Di Bella G, Oreto L, et al. Role of imaging in assessment of atrial fibrosis in patients with atrial fibrillation: state-of-the-art review. Eur Heart J Cardiovasc Imaging 2014;15:1-5.
12. Cameli M, Lisi M, Righini FM, Massoni A, Natali BM, Focardi M, et al. Usefulness of atrialdeformation analysis to predict left atrial fibrosis and endocardial thickness in patients undergoing mitral valve operations for severe mitral regurgitation secondary to mitral valve prolapse. Am J Cardiol 2013;111:595-601.
13. Suarez G, Meyerrose G. Heart failure and galectin 3. Ann Transl Med 2014;2:86.
14. 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;115:647-51.
15. 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;167:729-34.