

# Transesophageal Echocardiographic Predictors of Stroke in Patients with Paroxysmal Atrial Fibrillation

## Paroksizmal Atrial Fibrilasyonlu Hastalarda Strokun Transözefagial Ekokardiyografik Prediktörleri

Tarık Yıldırım<sup>1</sup>, Eyüp Avcı<sup>1</sup>, Fatih Akın<sup>2</sup>, Seda Elçim Yıldırım<sup>2</sup>,  
İbrahim Altun<sup>2</sup>, Mustafa Özcan Soylu<sup>2</sup>

<sup>1</sup> Balıkesir Üniversitesi Tıp Fakültesi Kardiyoloji ABD, Balıkesir

<sup>2</sup> Muğla Sıtkı Koçman Üniversitesi Tıp Fakültesi Kardiyoloji ABD, Muğla

Yazışma Adresi / Correspondence:

**Tarık Yıldırım**

Balıkesir Üniversitesi Tıp Fakültesi Kardiyoloji ABD, Balıkesir

T: +90 532 250 51 02 E-mail: [kdrtarik@mail.com](mailto:kdrtarik@mail.com)

Geliş Tarihi / Received : 06.07.2019 Kabul Tarihi / Accepted : 09.10.2019

Orcid :

Tarık Yıldırım <https://orcid.org/0000-0002-6314-7371>

Eyüp Avcı <https://orcid.org/0000-0002-7790-8450>

Fatih Akın <https://orcid.org/0000-0003-4865-8947>

Seda Elçim Yıldırım <https://orcid.org/0000-0001-5175-0491>

İbrahim Altun <https://orcid.org/0000-0002-5916-614X>

Mustafa Özcan Soylu <https://orcid.org/0000-0002-1145-5591>

( Sakarya Tıp Dergisi / Sakarya Med J 2019, 9(4):597-601 ) DOI: 10.31832/smj.587975

### Abstract

Objective	The left atrial appendage is the most source of thrombus formation in atrial fibrillation. The aim of this study was to find out left atrial appendage functions in paroxysmal atrial fibrillation patients with or without stroke.
Materials and Methods	This retrospective study included 74 paroxysmal atrial fibrillation patients who were performed transesophageal echocardiography for evaluation of stroke or who had suspicion of atrial septal defect and patent foramen ovale. All patients had undergone 24 hours electrocardiography Holter recorder, 2-dimensional echocardiography, transesophageal echocardiography.
Results	There are no differences between the groups for diabetes, hypertension, smoking, hyperlipidemia and creatinine levels. Patients with stroke group had lower left atrial appendage filling velocity (26.81±5.03, 38.92±5.14) (p<0.001), had lower left atrial appendage contraction velocity (30.82±6.07, 46.61±7.03) (p<0.001) and had bigger left atrial appendage area (2.72±0.61, 2.43±0.45) (p=0.032) than without stroke group. Left atrial appendage contraction velocity (p=0.013) and filling velocity (p=0.045) are the independent predictors of stroke.
Conclusion	Our findings showed that stroke is associated with low filling velocity and low contraction velocity of left atrial appendage. Our findings suggest that these indices are independent predictors of stroke. If these results are confirmed in future studies, patients with paroxysmal atrial fibrillation without stroke and with low filling velocity and low contraction velocity of left atrial appendage should receive more medical attention, to reduce unfavorable outcomes.
Keywords	atrial fibrillation; stroke; transesophageal echocardiography

### Öz

Amaç	Atrial fibrilasyonda trombüs oluşumunun en sık olduğu yer sol atrial apendiksdir (SAA). Bu çalışmada amacımız paroksizmal atrial fibrilasyonu (PAF) olup strok geçiren ve geçirmeyen hastalarda SAA fonksiyonlarını ortaya çıkarmaktır.
Gereç ve Yöntemler	Strok nedeni ile veya atrial septal defekt, patent foramen ovale şüphesi ile transözefagial ekokardiyografi yapılan 74 hasta retrospektif olarak çalışmaya alındı. Tüm hastalara 24 saatlik EKG holter, 2 boyutlu ekokardiyografi ve transözefagial ekokardiyografi uygulandı.
Bulgular	İki grup arasında diyabet, hipertansiyon, sigara içimi ve kreatinin seviyesi açısından fark saptanmadı. Strok grubunda strok olmayan gruba göre daha düşük SAA dolum hızı (26.81±5.03, 38.92±5.14) (p<0.001), daha düşük kontraksiyon hızı (30.82±6.07, 46.61±7.03) (p<0.001) ve daha büyük SAA alanı (2.72±0.61, 2.43±0.45) (p=0.032) saptandı. SAA kontraksiyon hızı (p=0.013) ve dolum hızı (p=0.045) strok için bağımsız prediktörler olarak tespit edildi.
Sonuç	Bulgularımız düşük SAA kontraksiyon hızı ve düşük dolum hızının strok ile ilişkili olduğunu gösterdi. Bu indeksler strok oluşumunun bağımsız prediktörleri idi. Bu sonuçlar gelecekte yapılacak çalışmalarla desteklenirse, PAF'li olup strok geçirmemiş hastalarda düşük SAA kontraksiyon ve dolum hızı mevcut olumsuz sonuçları azaltmak için daha fazla medikal tedavi düşünülmelidir.
Anahtar Kelimeler	atrial fibrilasyon; strok; transözefagial ekokardiyografi

## INTRODUCTION

Atrial fibrillation (AF) is the most common type of the heart arrhythmia and characterized by rapid and irregular beating of the atria.<sup>1,2</sup> Atrial fibrillation has become one of the most important public health problems and patients have increased risk of death, heart failure, rehospitalization and thromboembolic events.<sup>3</sup> The risk of stroke is 5 times higher in AF patients than without AF. In patients with paroxysmal AF (PAF) have same risk for stroke as chronic AF.<sup>4,5</sup> Atrial fibrillation diminishes the left atrial functions therefore thrombus may occur in this area. The left atrial appendage (LAA) is the most source of thrombus formation in AF.<sup>6</sup> Left atrial appendage assessment with 2-dimensional echocardiography is not very useful. Transesophageal echocardiography is more suitable than 2 D echocardiography for the assessment of LAA functions. Reduced LAA flow velocity was defined as a risk factor for thromboembolism.

There are some studies comparing the LAA functions between in patients with PAF and with sinus rhythm. There isn't any investigation about determining stroke predictors in PAF patients. The aim of this study was to find out LAA functions in PAF patients with or without stroke.

## MATERIALS and METHODS

**Patients:** This retrospective descriptive cross-sectional study initiated after Balıkesir University Ethics Committee approve (4.10.2017-2017/83) between 2017-2018. This study included 106 patients who were performed transesophageal echocardiography for evaluation of stroke or who have doubt of atrial septal defect and patent foramen ovale at Muğla Sıtkı Koçman University and Balıkesir University Hospital. 32 patients with severe valvular heart disease, prosthetic valve disease, reduced ejection fraction and inadequate echocardiographic studies were excluded. In patients with stroke were determined with computed tomography, magnetic resonance imaging and neurological examinations. All patients had undergone 24 hours electrocardiography Holter recorder, 2-dimensional echocar-

diography and transesophageal echocardiography. 74 PAF patients were evaluated.

## ECG Holter Monitoring

3 lead Holter monitor device DMS Cardioscan 11 (serial number: 3A-1554, 3A-1650, 3A-1668) were used for the evaluation of PAF. Paroxysmal AF was defined one period >30 second atrial fibrillation or atrial flutter rhythm.

## Echocardiographic data analyse

Patients with sinus rhythm had evaluated in echocardiographic examination. Transthoracic echocardiography was performed using A Philips Epiq 7, equipped with a S5-1broadband transducer (5-1 MHz) (Philips Healthcare, Bothell, WA, USA) and a S7-3t TEE transducer. All patients were monitored ECG before echocardiographic examination. All echocardiographic measurements by TTE and TEE done according to the guidelines of American Society of Echocardiography.

## TTE

The patients underwent M-mode, two dimensional echocardiography, pulse wave (PW) and continuous wave (CW) Doppler and colored tissue Doppler echocardiographic evaluation. All Doppler measurements were recorded at the end of the expirium while patients were holding their breath. An average of 3 consecutive measurements were calculated. An echocardiographic evaluation was performed using the parasternal long axis, short axis, and apical 4 and 2 chamber images to analyze the left ventricular functions. Following the evaluation of aortic and left ventricular wall thickness, the left ventricular ejection fraction was calculated by the Teicholz method. Wall motion was evaluated from the parasternal short axis view. Biplane ejection fraction was determined from the apical 4 chamber and 2 chamber views using the Simpson method.

## TEE

Three cardiac cycles were recorded for further analysis. LAA was shown in long axis views between 50-110°. The

spontaneous echo contrast (SEC) was defined swirling in a circular pattern into the LAA or LA cavity. LAA was inspected for the spontaneous thrombus. Sample volume was positioned 1cm from the LAA orifice and LAA flow velocities by pulsed-Doppler were measured as LAA contracting and filling velocities. The neck of LAA was calculated between the ostium of LAA and left lateral atrial wall. The LAA orifice was obtained from the short axis views.

### Statistical analysis

All analyses were performed using SPSS V 16.0 for Windows (version 16.0, SPSS, Chicago, Illinois). All data are presented as mean±standard deviation unless otherwise stated. Comparison of parametric values between the 2 groups was performed by means of independent samples t test. Categorical variables were compared by the chi-square test. Univariate logistic regression models were first performed to evaluate the crude association between stroke and each of the factors. Those factors that were significant at the  $p \leq 0.10$  level in the univariate models were put into the multiple logistic regression models to identify the factors that were independently associated with stroke. A receiver-operating characteristic (ROC) curve was constructed. All statistical tests were two-sided, and statistical significance was determined at a p value  $< 0.05$ .

### RESULTS

The baseline characteristics are shown in table 1. All patients had PAF and in strokes groups mean age was  $69.12 \pm 7.03$  and without strokes groups mean age was  $70.01 \pm 6.14$  respectively ( $p=0.602$ ). There are no differences between the groups for diabetes, hypertension, smoking, hyperlipidemia and creatinine levels.

The results of 2D echocardiographic parameters and TEE parameters demonstrate in table 2. Assessment of left ventricular ejection fraction no difference was found between the groups ( $61.92 \pm 5.04$ ,  $59.40 \pm 7.02$ ) ( $p=0.097$ ). Patients with stroke group had lower LAA filling velocity ( $26.81 \pm 5.03$ ,  $38.92 \pm 5.14$ ) ( $p < 0.001$ ), had lower LAA contraction velocity ( $30.82 \pm 6.07$ ,  $46.61 \pm 7.03$ ) ( $p < 0.001$ ) and had greater LAA area ( $2.72 \pm 0.61$ ,  $2.43 \pm 0.45$ ) ( $p=0.032$ ) than without stroke group (figure 2). There was no difference between the groups for the LAA SEC and thrombus. Contraction velocity ( $p=0.000$ ) and LAA filling velocity ( $p=0.021$ ) were the predictors of thrombus LAA.

reaction velocity ( $30.82 \pm 6.07$ ,  $46.61 \pm 7.03$ ) ( $p < 0.001$ ) and had greater LAA area ( $2.72 \pm 0.61$ ,  $2.43 \pm 0.45$ ) ( $p=0.032$ ) than without stroke group (figure 2). There was no difference between the groups for the LAA SEC and thrombus. Contraction velocity ( $p=0.000$ ) and LAA filling velocity ( $p=0.021$ ) were the predictors of thrombus LAA.

Figure 2. Receiver operating characteristic curve for LAA apical contraction and LAA apical filling as a predictors of CVD

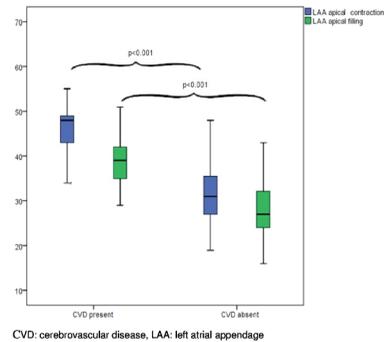


Table 1. Baseline clinical and laboratory characteristics of CVD and non-CVD groups.

	Non-CVD (n=34)	CVD (n=40)	p
Age	70.01±6.14	69.12±7.03	0.602
Male	16 (47%)	22 (55%)	0.496
Hypertension	23(67%)	28(70%)	0.827
Diabetes	15(44%)	18(45%)	0.939
Hyperlipidemia	30(41.7%)	105(47.5%)	0.262
Carotid stenosis	0	2(5%)	0.186
Hemoglobin (g/dl)	13.00±1.12	13.30±1.41	0.353
Creatinine (mg/dl)	1.01±0.21	0.92±0.23	0.504

CVD: Cerebrovascular Disease

Table 2. Echocardiographic and transesophageal echocardiographic characteristics of CVD and non-CVD groups

	Non-CVD (n=34)	CVD (n=40)	p
Thrombus	0	2(5%)	0.186
SEC	3(9%)	7(17.5%)	0.277
EF	61.9±5	59.4±7	0.097
LAA orifice	1.71±0.21	1.85±0.50	0.364
LAA contraction	46.63±7.03	30.82±6.04	<0.001
LAA apical filling	38.94±5.02	26.83±5.06	<0.001
LAA area	2.48±0.45	2.72±0.61	0.035

CVD: Cerebrovascular Disease, EF: Ejection Fraction, LAA: Left Atrial Appendage; SEC: Spontaneous Echo Contrast

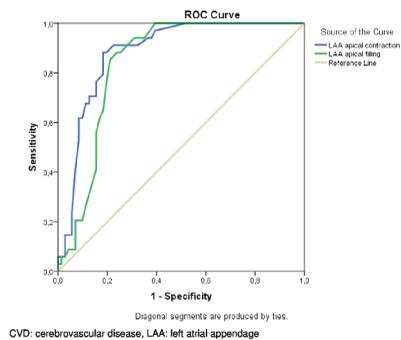
Multivariate logistic regression analysis showed that LAA contraction velocity ( $p=0.013$ ) and filling velocity ( $p=0,045$ ) are the independent predictors of stroke (table 3).

	Odds ratio	95% CI	P
EF	0.999	0.879-1.139	0.983
LAA contraction	0.824	0.707-0.960	0.013
LAA apical filling	0.800	0.643-0.995	0.045
LAA area	4.824	0.937-24.163	0.060

CI : Confidence Interval, EF: Ejection Fraction, LAA: Left Atrial Appendage

Receiver operating characteristic curve (ROC) analysis showed that LAA contraction velocity  $<38.5\text{cm/s}$  was 88% sensitive and 90% specific predictor of stroke (Area Under Curve (AUC) 0.883,  $p<0.001$ ). And LAA filling velocity  $<32\text{ cm/s}$  was 88% sensitive and 77% specific predictor of stroke (AUC 0.841,  $p<0.001$ ). These parameters are shown in figure 1.

**Figure 1.** Comparison of LAA apical contraction and LAA apical filling velocities in patients with CVD and control group



## DISCUSSION

This study examined LAA functions in PAF patients with and without stroke. We found that stroke is associated with low filling velocity and low contraction velocity of LAA, and LAA area was greater in patients with stroke. In addition, multivariate logistic regression analysis showed that the filling flow velocity and contraction velocity were the

independent predictors of stroke. ROC analysis demonstrated that the filling flow velocity less than 32.6 cm/s, and contraction velocity less than 38.5 cm/s were associated with stroke.

Scherr et al. showed that even though in patients who received one-month effective anticoagulant treatment, had 1.6 % LAA thrombus.<sup>7</sup> Therefore noninvasive evaluation of LAA is very important, but TEE has limited sensitivity to find out of small thrombi within a side lobe of LAA. Thus if LAA is shown clear, it doesn't mean there isn't any thrombus here. Decreased LAA emptying velocity measurement with TEE is related with the presence of SEC and thrombus and thromboembolism in AF patients.<sup>8</sup> For these reasons Doppler measurements must be performed for better evaluation.<sup>9</sup> Zhu et al. found that the incidence of persistent AF in patients with thrombus was higher than in patients without PAF.<sup>10</sup> Similarly we found in patients with PAF with stroke had 5 % LAA thrombus and 17.5% SEC.

Decreased LAA functions and contractile functions, elevated filling pressures may lead thrombus formation.<sup>11</sup> Similarly our study demonstrates that decreasing filling velocity and contraction velocity associate with LAA thrombus.

Normally LAA filling velocity is between  $(50\pm6,83\pm25)$  cm/s. Flow velocity less than 40 cm/s is associated with spontaneous echo contrast and thrombus.<sup>12,13</sup> In patients with PAF, LAA flow velocity decreased even if the electrocardiogram showed sinus rhythm during transesophageal echocardiographic examination.<sup>14</sup> We found that same findings about filling and contraction flow velocities. We also found that these velocities are associated with stroke.

It is known that atrial fibrillation is the most common cause of ischemic stroke but imaging modalities may contribute to evaluation and further treatment to these patients.<sup>15</sup> Our study demonstrated that in PAF patients with stroke have lower velocities than PAF patients without stroke.

#### Kaynaklar

1. Naccarelli GV, Varker H, Lin J, Schulman KL. Increasing prevalence of atrial fibrillation and flutter in the United States. *Am J Cardiol* 2009;104:1534-9.
2. Anderson JL, Halperin JL, Albert NM, Bozkurt B, Brindis RG, Curtis LH et al. Management of patients with atrial fibrillation (compilation of 2006 ACCF/AHA/ESC and 2011 ACCF/AHA/HRS recommendations): a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013;61:1935-44.
3. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J* 2016;37(38):2893-962.
4. Marini C, De Santis F, Sacco S, Russo T, Olivieri L, Totaro R et al. Contribution of atrial fibrillation to incidence and outcome of ischemic stroke : results from a population-based study. *Stroke* 2005;36:1115-9.
5. Roy D, Marchand E, Gagné P, Chabot M, Cartier R. Usefulness of anticoagulant therapy in the prevention of embolic complications of atrial fibrillation. *Am Heart J* 1986;112:1039-43.
6. Blackshear JL, Odell JA. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. *Ann Thorac Surg* 1996;61:755-9.
7. Scherr D, Dalal D, Chilukuri K, Dong J, Spragg D, Henrikson CA et al. Incidence and predictor of left atrial thrombus prior to catheter ablation of atrial fibrillation. *J Cardiovasc Electrophysiol*. 2009;20:379-84.
8. No authors listed. The Stroke Prevention in Atrial Fibrillation Investigators Committee on Echocardiography. Transesophageal echocardiographic correlates of thromboembolism in high risk patients with nonvalvular atrial fibrillation. *Ann Intern Med*, 1998;128:639-47.
9. Agmon Y, Khandheria BK, Gentile F, Seward JB. Echocardiographic assesment of the left atrial appendage. *J Am Coll Cardiol* 1999;34:1867-77.
10. Zhu MR, Wang M, Ma XX, Zheng Dy Zhang YL. The value of left atrial strain and strain rate in predicting left atrial appendage stasis in patientswith nonvalvular atrial fibrillation. *Cardiol J*. 2018;25(1):87-96.
11. Beigel R, Wunderlich NC, Ho SY, Arsanjani R, Siegel RJ. The left atrial Appendage: Anatomy, function, and noninvasive evaluation. *JACC* 2014;7:1251-65.
12. Mügge A, Kühn H, Nikutta P, Grote J, Lopez JA, Daniel WG. Assessment of left atrial appendage function by biplane transesophageal echocardiography in patients with nonrheumatic atrial fibrillation: identification of patients at increased embolic risc. *J Am Coll Cardiol*. 1994;23:599-607.
13. Agmon Y, Khandheria BK, Meissner I, Schwartz GL, Petterson TM, O'Fallon WM et al. Left atrial appendage flow velocities in subjects with normal left ventricular function. *Am J Cardiol* 2000;86:769-73.
14. Taguchi Y, Takashima S, Hirai T, FukudaN, Ohara K, Nakagawa K et al. Significant impairment of left atrial function in patients with cardioembolic stroke caused by paroxysmal atrial fibrillation. *Intern Med* 2010;49:1727-32.
15. Matsumoto Y, Morino Y, Kumagai A, Hozawa M, Nakamura M, Terayama Y et al. Characteristics of anatomy and function of the left atrial appendage and their relationships in patients with cardioembolic stroke: A 3-D dimensional transesophageal echocardiographic study. *J Stroke Cerebrovasc Dis* 2017;26:470-9.