# The role of the TAPSE/PASP ratio in the prediction of paroxysmal atrial fibrillation in patients with acute ischemic stroke

## <sup>™</sup>Tolga Çakmak¹, <sup>®</sup>Özgen Şafak

<sup>1</sup>Departman of Cardiology, Balıkesir Atatürk City Hospital, University of Health Sciences, Balıkesir, Turkey <sup>2</sup>Departman of Cardiology, Faculty of Medicine, Balıkesir University, Balıkesir, Turkey

**Cite this article as**: Çakmak T, Şafak Ö. The role of the TAPSE/PASP ratio in the prediction of paroxysmal atrial fibrillation in patients with acute ischemic stroke. *J Med Palliat Care*. 2023;4(4):355-361.

Received: 05.08.2023   Accepted: 29.08.2023   Published: 30.08   Published: 30.08   Published: 30.08   Image: Non-State State Stat	.2023
--	-------

#### ABSTRACT

**Aims**: Atrial fibrillation (AF) remains the most prevalent cause of cardioembolic stroke. Paroxysmal AF (PAF) is often difficult to be diagnosed and is sometimes first detected during embolic stroke. Yet, TAPSE and PASP can be easily revealed in routine transthoracic echocardiography (TTE). Then, the TAPSE/PASP ratio is often shown to have prognostic significance in many cardiac disorders. Nevertheless, the insufficient scholarly knowledge of the relationship between this ratio and the development of PAF became the primary motive of the present study.

**Methods**: We carried out this study with 114 patients experiencing acute ischemic stroke without a previous diagnosis of AF. We noted down the patients' blood parameters and prescribed drugs and calculated TAPSE/PASP ratio relying on their TTE findings. We also recorded the 24-hour heart rhythm findings of each patient through Holter monitoring. After categorizing PAF attacks (i.e., PAF attack was (not) observed), we explored any statistical relationship between the TAPSE/PASP ratio and the presence of PAF.

**Results**: The findings revealed a significant difference between the TAPSE/PASP ratios between the groups with PAF ( $0.62\pm0.07$ ) and without PAF ( $0.77\pm0.08$ ). Moreover, the receiver operating characteristic (ROC) curve analysis yielded the TAPSE/PASP ratio to demonstrate a diagnostic value in predicting PAF (area under the ROC curve [AUC]=0.89;82.7%; p<0.001). Besides, the TAPSE/PASP ratio measured <0.67 at admission was found to have 87.1% sensitivity and 82.7% specificity in predicting PAF. Finally, the multivariate analysis showed the TAPSE/PASP ratio to be a significant risk factor for PAF (odds ratio [OR]=2.971;95% confidence interval [CI]=1.073-8.959; p=0.000).

**Conclusion**: Overall, a low TAPSE/PASP ratio (<0.67) may be a precursor of the presence of PAF in patients.

**Keywords**: Acute ischemic stroke, tricuspid annular plane systolic excursion, mean pulmonary artery systolic pressure, paroxysmal atrial fibrillation

## **INTRODUCTION**

Stroke remains to be a major cause of neurological morbidity and mortality worldwide.<sup>1</sup> While it is known that cardiac embolism accounts for about 20% of all ischemic strokes,<sup>2-4</sup> atrial fibrillation (AF) continues to be the most prevalent cause of cardioembolic stroke.<sup>3-5</sup> Acute myocardial infarction (AMI), ventricular thrombus, structural heart defects, heart tumors, and heart valve disease can be shown as other causes of cardioembolic stroke.<sup>4</sup> According to the American College of Cardiology, the American Heart Association, and the European Society of Cardiology, AF is classified in different forms:6 1) Paroxysmal AF (PAF), a selfterminating or intermittent form, usually takes less than seven days and less than 24 hours; 2) Persistent AF is not self-limiting and lasts longer than seven days; 3) permanent AF lasts more than a year. PAF can also be particularly difficult to detect and is sometimes first detected during an embolic stroke.

Yet, tricuspid annular plane systolic excursion (TAPSE) and mean pulmonary artery systolic pressure (PASP) can be quickly revealed in routine transthoracic echocardiography (TTE). Then, the TAPSE/PASP ratio is often shown to have prognostic significance in many cardiac disorders. Despite being the subject of research on cardiac disorders, the TAPSE/PASP ratio has not appeared with the development of PAF so far. Therefore, the present study was intended to explore the role of the TAPSE/PASP ratio in predicting PAF.

Corresponding Author: Tolga Çakmak, tolgacakmak85@gmail.com



## **METHODS**

The study was carried out with the permission of theBalıkesir University Clinical Researches Ethics Committee (Date: 05.17.2023, Decision No: 2023-55). In all stages of the study, we strictly adhered to the rules and the principles set forth in the Declaration of Helsinki.

Our study was designed retrospectively. The subjects were enrolled randomly files. We carried out this single-center study with 114 patients hospitalized in the neurology department due to the diagnosis of acute ischemic stroke and for whom we consulted the cardiology clinic for cardioembolic etiology. Despite no age-related criterion, we set the exclusion criteria as follows: the presence of permanent or persistent AF, chronic obstructive pulmonary disease (COPD), severe heart valve disease, moderate to severe renal failure (Glomerular Filtration Rate (GFR) below 60 mL/min), severe anemia, antiarrhythmic drug use, congenital heart disease, mild to advanced pulmonary hypertension, history of malignancy, hepatic dysfunction (the presence of cirrhosis or alanine aminotransferase [ALT] and/or aspartate aminotransferase [AST] > 3×Upper limit of the normal range (ULN) and total bilirubin  $> 2 \times ULN$ ), alcohol/substance abuse, and active infection. TTE was performed using the Esaote My Lab seven (Getz Healthc are Malaysia) device in the left lateral position. While the TAPSE value was noted down in millimeters by aligning the lateral part of the cursor tricuspid valve with M-mode echocardiography, measuring the peak from the end of diastole to the end of systole (averaging 3 to 5 beats), the PASP value was obtained from the tricuspid regurgitation (TR) jet velocity using the simplified Bernoulli equation. Then, the TAPSE/PASP ratio was calculated by dividing the TAPSE value by the mean pulmonary artery pressure value. Two experienced cardiologists who were blinded to the study protocol took all measurements.

The definition of the AF7;

- Absence of P waves,
- Irregular R-R interval,

The above two criteria are defined as AF if present either  $\geq$  30 seconds on the 24-hour rhythm holter or on the entire 12-lead standard electrocardiogram.

If the AF rhythm terminates spontaneously, it is defined as PAF.6 We decided on PAF according to the presence or absence of the AF criteria mentioned above in the 24hour Holter monitoring and divided the patients into 2 groups according to the presence or absence of AF. (i.e., PAF attack was not observed [without PAF], and PAF attack was observed [with PAF]). In our study, at least 1 AF attack that lasted  $\geq$  30 seconds and ended spontaneously in 24-hour Holter monitoring was considered as PAF. Total duration and number of AF was not calculated in 24-hour Holter monitoring. Patients with at least 1 AF rhythm for  $\geq$  30 seconds in 24-hour Holter monitoring were included in the PAF group. Patients with AF rhythm of < 30 seconds and/or patients without AF rhythm in 24-hour Holter monitoring were included in the group without PAF.

While we defined hypertension (HT) as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and any antihypertensive use as drug therapy8, diabetes mellitus (DM) was defined as fasting blood glucose level  $\geq$ 126 mg/dL, blood glucose level  $\geq$ 200 mg/dL two hours after oral glucose tolerance test, HbA1c value > 6.5, or random blood glucose  $\geq$  200 mg/ dL9. We also recorded the drugs prescribed to the patients for these disorders (antidiabetics, antihypertensives, antiaggregants, and antihyperlipidemics). Finally, while considering complete blood count parameters to be white blood cell (WBC) count, hemoglobin (Hb), hematocrit (HCT), platelet (PLT), mean platelet volume (MPV), red cell distribution width (RDW), and mean cell volume (MCV), we accepted biochemistry parameters as blood glucose, urea, and creatinine levels at admission.

#### **Statistical Analysis**

First off, we resorted to the Kolmogorov-Smirnov test to explore the data distribution. Accordingly, while normally-distributed continuous variables are expressed as means (M) ± standard deviations (SD), we present non-normally distributed continuous variables as medians (interquartile range). Then, we ran the pairwise comparison using independent samples t-test or Mann-Whitney U-test. On the other hand, the categorical variables -demonstrated as absolute and relative frequencies - were compared using the chisquare test. Besides, we performed the receiver operating characteristics (ROC) curve analysis to set the sensitivity, specificity, and cut-off value of the TAPSE/PASP ratio in predicting PAF. Moreover, the variables with a p-value <0.25 in the univariate analysis were considered potential risk factors for PAF attacks and were included in the full model in the multivariate logistic regression analysis. Finally, we performed all statistical analyses on SPSS 22.0 for Windows (Armonk, NY: IBM Corp.) and considered a p-value < 0.05 to be statistically significant.

#### RESULTS

The mean age of the patients, 58 (50.9%) males and 56 (49.1%) females, was found to be  $69.1\pm11.0$  years. We detected DM in 36.8% of the patients, HT in 63.2%, and coronary artery disease (CAD) in 26.3%. The patients' mean body mass index (BMI) was 27.5, and 28.1% were diagnosed with COVID-19. Echocardiographic (echo) findings showed the mean size of the left atrial (LA) to be 37.1±3.9 mm. Besides, ejection fraction was found

to be above 50 % in 86 % of the patients, between 40-50% in 8.8%, and below 4 % in 5.3 BMI%. AF rhythm of  $\geq$  30 seconds was detected in 45.6% of the patients, while 54.4% had no AF rhythm or, if any, it was less than 30 seconds. No abnormal values were observed in their biochemical parameters (**Table 1**).

Table 1. Key clinical characteristics	of the sample (n=114)			
Clinical characteristics	I ( )			
Age (years)	69.1±11.0			
Sex (male), n (%)	58 (50.9)			
Diabetes, n (%)	42 (36.8)			
Hypertension, n (%)	72 (63.2)			
Coronary artery disease, n (%)	30 (26.3)			
Smoking, n (%)	34 (29.8)			
BMI, n (%)	27.5 (25.8-30.6)			
COVID-19, n (%)	32 (28.1)			
Cardiac characteristics				
LA diameter, mm	37.1± 3.9			
PAF, n (%)				
Absence of AF rhythm	62 (54.4)			
≥30 seconds AF rhythm	52 (45,2)			
EF, n (%)				
≥%50	98 (86.0)			
%40-%50	10 (8.8)			
<%40	6 (5.3)			
Heart rate ( per minute)	73.8±11.6			
<b>Biochemical parameters</b>				
HB, g/dL	$12.8 \pm 1.8$			
HCT, %	38.0± 6.9			
PLT, mm3	245.1± 83.4			
MPV, fL	10.1 (9.5-11.1)			
RDW	14.0 (13.3-14.8)			
Urea, mg/dL	$38.4 \pm 18.1$			
Creatinine, mg/dL	0.85 (0.72-1.07)			
Drug use				
ACE-ARB, n (%)	46 (40.4)			
Beta blocker, n (%)	36 (31.6)			
OAD-Insulin, n (%)	40 (35.1)			
Clopidogrel, n (%)	22 (19.3)			
Statin, n (%)	24 (21.1)			
CCB, n (%)	38 (33.3)			
ASA n (%)	42 (36.8)			
Diuretics, n (%)	28 (24.6)			
TAPSE/PASP ratio	$0.70\pm0.10$			
Normally-distributed continuous variables ar	e expressed as means (M)±standard			

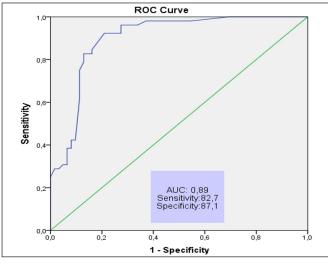
Normally-distributed continuous variables are expressed as means (M)±standard deviations (SD). Non-normally distributed data are presented as medians (interquartile range). Categorical variables are demonstrated as numbers (n) and percentages (%). BMI: body mass index; LA: left atrium; AF: atrial fibrillation; PAF: paroxysmal atrial fibrillation; EF: ejection fraction; HB: hemoglobin; HCT: hematocrit; PLT: platelet count; MPV: mean platelet volume, RDW: erythrocyte distribution width; TAPSE/ PASP: the tricuspid annular plane systolic excursion/mean pulmonary artery systolic pressure ratio; ACE :Angiotensin-converting enzyme; ARB: Angiotensin-2 receptor blockers.

Table 2 presents the analysis findings between patients with and without PAF attacks. Accordingly, the mean age of the patients with PAF attacks was found to be significantly higher. Although we could not detect significant differences between the groups by sex,

DM, CAD, BMI, and COVID-19 history, HT was significantly more prevalent in the group with PAF attacks. Conversely, the PAF-free group hosted more patients persisting in smoking. When it comes to the echo parameters, the LA size was significantly larger in the group with PAF. Except for hemoglobin and hematocrit values (significantly higher in the PAF-free group), the groups did not significantly differ by other biochemical parameters; it was also the case regarding drug use. Nevertheless, there was a significant difference between the groups by TAPSE/PASP ratio; the PAF group had a significantly lower TAPSE/PASP ( $0.62\pm0.07$  vs.  $0.77\pm0.08$ ; p< 0.01)

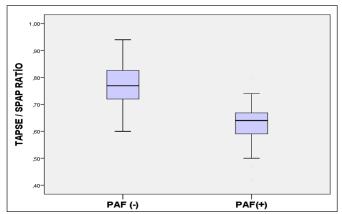
Table 2. Comparison	PAF (-)	PAF(+)	n	
Clinical characteristi			p	
Age (years)	65.7±12.2	73.1±7.7	0.00	
Sex (male), n (%)	32 (51.6)	26 (%50.0)	0.86	
Diabetes, n (%)	20 (32.3)	22 (42.3)	0.80	
Hypertension, n (%)	32 (51.6)	40 (76.9)	0.20	
Coronary artery disease, n (%)	16 (25.8)	14 (26.9)	0.89	
Smoking, n (%)	26 (41.9)	8 (15.4)	0.00	
BMI, n (%)	27.3 (25.9-30.4)	. ,	0.84	
COVID-19, n (%)	14 (22.6)	18 (34.6)	0.15	
Cardiac characteristi		× ,		
LA diameter, mm	$35.3 \pm 2.7$	$39.4 \pm 4.0$	0.00	
EF, n (%)			0.35	
≥%50	56 (90.3)	42 (80.8)		
%40-%50	4 (6.5)	6 (11.5)		
<%40	2 (3.2)	4 (7.7)		
Heart rate	72.8±11.7	74.9±11.6	0.35	
<b>Biochemical paramet</b>	ers			
HB, g/dL	$13.4 \pm 1.7$	$12.0 \pm 1.6$	0.00	
HCT, %	$40.0 \pm 5.1$	$36.7 \pm 4.6$	0.00	
PLT, mm3	$251.4 \pm 92.1$	237.6±71.9	0.38	
MPV, fL	10.0 (9.5-11.4)	10.1 (9.6-11.1)	0.13	
RDW	13.8 (12.9-14.5)	14.2 (13.6-15.1)	0.06	
Urea, mg/dL	37.7±16.9	39.4± 19.6	0.61	
Creatinine, mg/dL	0.82 (0.73-1.04)	0.93 (0.70-1.16)	0.11	
Drug use				
ACE-ARB, n (%)	20 (32.3)	26 (50.0)	0.06	
Beta blocker, n (%)	20 (32.3)	16 (30.8)	0.86	
OAD-Insulin, n (%)	20 (32.3)	20 (38.5)	0.48	
Clopidogrel, n (%)	12 (19.4)	10 (19.2)	0.98	
Statin, n (%)	14 (22.6)	10 (19.2)	0.66	
CCB, n (%)	14 (22.6)	24 (46.2)	0.00	
ASA n (%)	24 (38.7)	18 (34.6)	0.65	
Diuretics, n (%)	14 (22.6)	14 (26.9)	0.59	
TAPSE/PASP ratio	$0.77 \pm 0.08$	$0.62 \pm 0.07$	0.00	

Normally-distributed continuous variables are expressed as means (M)±standard deviations (SD). Non-normally distributed data are presented as medians (interquartile range). Categorical variables are demonstrated as numbers (n) and percentages (%). BMI: body mass index; LA: left atrium; PAF: paroxysmal atrial fibrillation; EF: ejection fraction; HB: hemoglobin; HCT: hematocrit; PLT: platelet count; MPV: mean platelet volume, RDW: erythrocyte distribution width; TAPSE/ PASP: the tricuspid annular plane systolic excursion/mean pulmonary artery systolic pressure ratio The ROC analysis verified the diagnostic value of the TAPSE/PASP ratio in predicting PAF (area under the ROC curve [AUC]=0.89; 82.7%; p< 0.001). Besides, the TAPSE/PASP ratio measured below 0.67 at admission was found to have 87.1% sensitivity and 82.7% specificity in predicting PAF (**Figure 1**).



**Figure 1.** ROC curve of the TAPSE/PASP ratio in predicting PAF (ROC: receiver operating characteristic)

The box-plot plot in Figure 2 also showed that the PAF group had a significantly lower TAPSE/PASP ratio. On the other hand, the error terms were divided into two by the cut-off value of the TAPSE/PASP ratio (0.67), and our findings did not reveal a significant difference between the groups by gender, DM, CAD, BMI, and COVID-19 history. Nonetheless, the group with a TAPSE/PASP ratio <0.67 had a significantly higher mean age, more HT, and less smoking. Besides, the patients with a TAPSE/PASP ratio <0.67 had a significantly higher LA size. Except for hemoglobin and hematocrit values, biochemical parameters were found to be significantly lower in the group with a TAPSE/PASP ratio < 0.67. The groups did not significantly differ by drug use; only the Angiotensin-converting enzyme-Angiotensin-2 receptor blockers (ACE-ARB) ratio was significantly higher in the group with TAPSE/PASP ratio < 0.67 (Table 3).



**Figure 2.** Box-plot of the TAPSE/PASP ratio in the patient groups with and without PAF attacks

	TAPSE/PASPTAPSE/PASP $< 0.67$ $\geq 0.67$		р	
Clinical characteristics				
Age (years)	$72.2 \pm 8.2$	$66.5 \pm 12.3$	0.0	
Sex (male),n (%)	28 (54.9)	30 (47.6)	0.4	
Diabetes, n (%)	23 (45.1)	19 (30.2)	0.1	
Hypertension, n (%)	41 (80.4)	31 (49.2)	0.0	
Coronary artery disease, n (%)	15 (29.4)	15 (23.8)	0.4	
Smoking, n (%)	8 (15.7)	26 (41.3)	0.0	
BMI, n (%)	27.6 (25.3-31.2)	27.3 (25.9-30.4)	0.4	
COVID-19, n (%)	16 (31.4)	16 (25.4)	0.4	
Cardiac characteristics				
LA diameter, mm	$38.8 \pm 4.2$	$35.8 \pm 3.1$	0.0	
EF, n (%)			0.3	
≥%50	41 (80.4)	57 (90.5)		
%40-%50	6 (11.8)	4 (6.3)		
<%40	4 (7.8)	2 (3.2)		
Heart rate	$74.2\pm12.5$	$73.4\pm11.0$	0.6	
<b>Biochemical parameters</b>	3			
HB, g/dL	$12.3 \pm 1.7$	$13.2 \pm 1.8$	0.0	
HCT, %	$37.4 \pm 4.8$	39.4± 5.3	0.0	
PLT, mm3	$243.4{\pm}~67.6$	$246.5{\pm}~94.8$	0.8	
MPV, fL	10.0 (9.6-11.1)	10.3 (9.5-11.2)	0.6	
RDW	14.3 (13.6-15.1)	13.8 (12.9-14.5)	0.1	
Urea, mg/dL	$39.2 \pm 19.3$	37.9± 17.2	0.7	
Creatinine, mg/dL	0.91 (0.70-1.16)	0.82 (0.73-1.04)	0.5	
Drug use				
ACE-ARB, n (%)	27 (52.9)	19 (30.2)	0.0	
Beta blocker, n (%)	18 (35.3)	18 (28.6)	0.4	
OAD-Insulin, n (%)	21 (41.2)	19 (30.2)	0.2	
Clopidogrel, n (%)	11 (21.6)	11 (17.5)	0.5	
Statin, n (%)	11 (21.6)	13 (20.6)	0.9	
CCB, n (%)	25 (49.0)	13 (20.6)	0.0	
ASA n (%)	20 (39.2)	22 (34.9)	0.6	
Diuretics, n (%)	14 (27.5)	14 (22.2)	0.5	

Table 2 Clinical characteristics of the sample by the TADSE/DASD

deviations (SD). Non-normally distributed data are presented as medians (interquartile range). Categorical variables are demonstrated as numbers (n) and percentages (%). BMI: body mass index; LA: left atrium; PAF: paroxysmal atrial fibrillation; EF: ejection fraction; HB: hemoglobin; HCT: hematocrit; PLT: platelet count; MPV: mean platelet volume, RDW: erythrocyte distribution width; TAPSE/PASP: the tricuspid annular plane systolic excursion/mean pulmonary artery systolic pressure ratio

We subjected the risk factors that may affect the presence of PAF and the TAPSE/PASP ratio to univariate and multivariate logistic regression analyses. In univariate analysis, the variables with a p-value <0.25 were identified as potential risk factors for PAF and included in the entire model. Then, the multivariate analysis yielded that the TAPSE/PASP ratio was found to be a significant risk factor for PAF (odds ratio [OR]= 2.971; 95% confidence interval [CI]=1.073-8.959; p=0.000) (Table 4).

Table 4. Results of the univariate and multivariate logistic regression analyses						
	Unadjusted OR	95% Cl	р	Adjusted OR	95% Cl	р
Age	1.074	1.031-1.119	0.001	1.070	1.011-1.133	0.019
Sex	1.067	0.510-2.230	0.864			
Diabetes	1.540	0.716-3.312	0.269			
Hypertension	3.125	1.383-7.060	0.006	1.110	0.346-3.560	0.860
Coroner artery disease	1.059	0.459-2.444	0.893			
BMI	1.005	0.948-1.066	0.865			
TAPSE/PASP	3.225	1.147-9.062	0.000	2.971	1.073-8.959	0.000
BMI: body mass index; CI: Confidence interval; OR: odds ratio. TAPSE/PASP: the tricuspid annular plane systolic excursion/mean pulmonary artery systolic pressure ratio						

## DISCUSSION

Relying on our findings, we concluded that the TAPSE/ PASP ratio is more likely to guide one to detect PAF, a leading etiological cause of acute ischemic stroke. It should be noted that PAF was highly suspected in the patients with a TAPSE/PASP ratio of < 0.67, even if PAF could not be detected in their 24-hour Holter monitoring. Thus, it is highly recommended to check longer-term or recurrent rhythm Holter monitoring among such patients.

In their hallmark Framingham study in 1978, Wolf et al.<sup>10</sup> established the relationship between non-valvular AF and stroke by documenting that patients with AF have a 5-fold higher risk of ischemic stroke compared to those without AF. Moreover, the ACTIVE W trial (Atrial Fibrillation Clopidogrel Trial With Irbesartan for Prevention of Vascular Events) showed the rate of stroke/systemic embolization to be 2.0% in patients with PAF and 2.2% in those with permanent AF.<sup>11</sup> Similarly, SPAF research demonstrated the annual rate of ischemic stroke to be 3.2% among those with PAF and 3.3% in patients with permanent AF.12 Besides, the ENGAGE AF-TIMI 48 (Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation-Thrombolysis In Myocardial Infarction 48) study reported a linear relationship between PAF and stroke risk.<sup>13</sup> However, growing evidence suggests a robust association between the burden of AF and the risk of subsequent ischemic events. In this sense, the detection of PAF may be critical to the emergence of recurrence of acute ischemic stroke. Thus, we carried out this study hinging upon the idea that it would be helpful to explore other predictors other than Holter monitoring to detect PAF.

The literature hosts a plethora of research adopting different echo parameters and biomarkers to predict PAF. For example, XU et al.<sup>14</sup> reported that LA reservoir function, impaired diastolic emptying index, and an elevated BNP level may serve as valuable predictors of PAF relapse in patients undergoing catheter ablation. In this study, we may present several reasons for choosing the TAPSE/PASP ratio as the predictor of PAF. 1) In their study, Guazzi et al.<sup>15</sup> found the TAPSE/PASP ratio (< 0.35) to be significantly lower in patients

with AF. Similar to our study, many other studies on heart failure with preserved ejection fraction (HFpEF) reported AF to be prevalent,<sup>16,17</sup> and associated with the severity of right heart disease. AF and heart failure often emerge together, resulting in increased morbidity and mortality compared to either disorder. One also needs to acknowledge that AF and heart failure share common mechanisms and treatment strategies.<sup>18</sup> 2) In addition, Guazzi et al.<sup>15</sup> observed that the left atrium (LA) size was significantly larger (40.6±16.7 ml/m<sup>2</sup>) in those with a low TAPSE/PASP ratio (<0.35).15 Benjamin et al.<sup>19</sup> documented that every 10 mm increase in LA size among men and women enrolled in the Framingham Heart Study led to ~40% and >100% increases in stroke, respectively. In addition, LA size was previously reported to predict ischemic stroke recurrence in patients with nonvalvular AF.<sup>20,21</sup> The close link between LA size and AF and the inverse correlation between the TAPSE/PASP ratio and LA size inspired our research question of whether the TAPSE/ PASP ratio could be a predictor of PAF. Accordingly, we were able to show LA size to be associated with PAF, overlapping with the previous findings. 3) On the other hand, the relevant research confirmed that some AF may originate in the atrium and characterize right atrial ectopic onset and right-to-left dominant frequency gradients.<sup>22</sup> Furthermore, mapping and extracting complex fragmentation potentials not only for the left atrium and pulmonary veins but also for the left and right atria may contribute to the success rate in patients with permanent and persistent AF,23 which suggests that right atrium-triggered AF may deserve more attention compared to left atrial AF. What is more, recent studies have confirmed that right heart disease can also increase the risk of AF.<sup>24-26</sup> Therefore, further clarification of the pathogenesis of AF is needed to bring more insights into the understanding of AF and to offer novel ideas for AF treatment. In addition to secondary right heart dysfunction led by ischemia, cardiomyopathy, or congenital cardiac structural abnormalities, pulmonary vascular remodelingleading right heart dysfunction is also a right heart disease associated with an increased risk of AF,<sup>24</sup> and its central process in the pathogenesis may be related

to the enlargement of the right atrial cavity caused by pulmonary arterial hypertension (PAH) induced by increased right atrial afterload, tricuspid regurgitation, and right atrial hypertrophy.<sup>25-27</sup> Therefore, we thought that the TAPSE/PASP ratio, which was proven to be closely linked with right heart pathologies in many studies, may be associated with the development of PAF. In this regard, as in our findings, a TAPSE/PASP ratio of <0.67 is likely to signal the presence of PAF.

#### Limitations

Our research is not free of a few limitations. The singlecenter nature of the study restrains the generalizability of our findings. Moreover, we included only acute ischemic stroke patients in the study. In this sense, we believe our results may inspire further multicenter research to focus on multiple disorders.

## CONCLUSION

Overall, the scholarly community should acknowledge the role of a low TAPSE/PASP ratio (<0.67) in predicting PAF in patients. Thus, it may be helpful to consider the TAPSE/PASP ratio along with the Holter monitoring that is commonly adopted for the diagnosis of PAF.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of theBalıkesir University Clinical Researches Ethics Committee (Date: 05.17.2023, Decision No: 2023-55).

**Informed Consent:** All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

## REFERENCES

- 1. GBD 2016 Stroke Collaborators. Global, regional, and national burden of stroke, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurology.* 2019;18(5):439–458.
- Asinger RW, Dyken ML, Fisher M. Cardiogenic brain embolism. The second report of the Cerebral Embolism Task Force. Arch Neurol. 1989;46(7):727–743.
- 3. Bogousslavsky J, Cachin C, Regli F, Despland PA, Van Melle G, Kappenberger L. Cardiac sources of embolism and cerebral infarction-clinical consequences and vascular concomitants: the Lausanne Stroke Registry. *Neurology.* 1991;41(6):855–859.

- Sila CA. Cardioembolic stroke. In: Noseworthy JH, ed. Neurological therapeutics: principles and practice. *New York: Martin Dunitz.* 2003(1):450–457.
- 5. Ferro JM. Cardioembolic stroke: an update. *Lancet Neurol.* 2003;2(3):177-188.
- 6. Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillationexecutive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). [Erratum appears in J Am CollCardiol 2007; 50: 562]. J Am CollCardiol. 2006;48(4):854–906.
- 7. Steinberg JS, O'Connell H, Li S, Ziegler PD. Thirty-Second Gold Standard Definition of Atrial Fibrillation and Its Relationship with Subsequent Arrhythmia Patterns: Analysis of a Large Prospective Device Database. *Circ Arrhythm Electrophysiol.* 2018;11(7):e006274.
- 8. Williams B, Mancia G, Spiering W, et al. ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J.* 2018;39(33):3021-3104.
- 9. American Diabetes Association. Addendum. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. *Diabetes Care*. 2021;44(Suppl 1):15-33
- 10. Wolf PA, Dawber TR, Thomas HE Jr., Kannel WB. Epidemiologic assessment of chronic atrial fibrillation and risk of stroke: the Framingham study. *Neurology*. 1978;28(10):973–977.
- 11. Hohnloser SH, Pajitnev D, Pogue J, et al. Incidence of stroke in paroxysmal versus sustained atrial fibrillation in patients taking oral anticoagulation or combined antiplatelet therapy: an ACTIVE W substudy. *J Am Coll Cardiol.* 2007;50(22):2156–2161.
- 12. Hart RG, Pearce LA, Rothbart RM, McAnulty JH, Asinger RW, Halperin JL. Stroke Prevention in Atrial Fibrillation Investigators. Stroke with intermittent atrial fibrillation: incidence and predictors during aspirin therapy. *J Am Coll Cardiol.* 2000;35(1):183–187.
- 13.Link MS, Giugliano RP, Ruff CT, et al. ENGAGE AF-TIMI 48 Investigators. Stroke and mortality risk in patients with various patterns of atrial fibrillation: results from the ENGAGE AF-TIMI 48 trial (Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation-Thrombolysis in Myocardial Infarction 48). *Circ Arrhythm Electrophysiol.* 2017;10(1):e004267.
- 14.Xu M, Liu F, Ge ZX, Li JM, Xie X, Yang JH. Functional studies of left atrium and BNP in patients with paroxysmal atrial fibrillation and the prediction of recurrence after CPVA. *Eur Rev Med Pharmacol Sci.* 2020;24(9):4997-5007.
- 15. Guazzi M, Dixon D, Labate V, et al. RV contractile function and its coupling to pulmonarycirculation in heart failure with preserved ejection fraction: stratification of clinical phenotypes and outcomes. *JACC Cardiovasc Imaging*. 2017;10(10):1211-1221.
- 16. Mohammed SF, Hussain I, AbouEzzeddine OF, et al. Right ventricular function in heart failure with preserved ejection fraction: a communitybased study. *Circulation*. 2014;130(25):2310-2320.
- 17. Melenovsky V, Hwang SJ, Lin G, Redfield MM, Borlaug BA. Right heart dysfunction in heart failure with preserved ejection fraction. *Eur Heart J.* 2014;35(48):3452–3462.
- 18.Hu CY, Wang CY, Li JY, Ma J, Li ZQ. Relationship between atrial fibrillation and heart failure. *Eur Rev Med Pharmacol Sci.* 2016;20(21):4593-4600
- 19. 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(4):835–841.
- 20.Ogata T, Matsuo R, Kiyuna F, et al. Left atrial size and longterm risk of recurrent stroke after acute ischemic stroke in patients with nonvalvular atrial fibrillation. *J Am Heart Assoc.* 2017;6(8):e006402.

- 21.Yaghi S, Moon YP, Mora-McLaughlin C, et al. Left atrial enlargement and stroke recurrence: the Northern Manhattan Stroke Study. *Stroke*. 2015;46(6):1488–1493.
- 22. Hasebe H, Yoshida K, lida M, et al. Right-to-left frequency gradient during atrialfibrillation initiated by right atrial ectopies and its augmentation by adenosine triphosphate: implications of right atrial fibrillation. *Heart Rhythm.* 2016;13(2):354–363.
- 23. NademaneeK, McKenzie J, Kosar E, et al. A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologicsubstrate. *J Am CollCardiol*. 2004;43(11):2044–2053.
- 24. Rajdev A, Garan H, Biviano A. Arrhythmias in pulmonary arterial hypertension. Prog Cardiovasc Dis. 2012;55(2):180–186.
- 25.Goudis CA. Chronic obstructive pulmonary disease and atrial fibrillation: an unknown relationship. *J Cardiol.* 2017;69(5):699–705.
- 26. Drakopoulou M, Nashat H, KempnyA, et al. Arrhythmias in adult patients with congenital heart disease and pulmonary arterial hypertension. *Heart*. 2018;104(23):1963–1969.
- 27.Iram R, Naud P, Xiong F, et al. Right atrial mechanisms of atrialfibrillation in a rat model of right heart disease. *J Am CollCardiol.* 2019;74(10):1332–1347.