Acta Cardiologia Indonesiana

Web page: jurnal.ugm.ac.id/v3/jaci

pISSN:2460-5700

eISSN:2579-4345

ASSOCIATION OF LEFT ATRIAL STRAIN WITH ATRIAL FIBRILLATION IN ACUTE ISCHEMIC STROKE PATIENTS

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Manuscript submitted: 22 Feb 2023
Revised and accepted: 10 Jun 2024

Keywords: left atrial strain; atrial fibrillation; ischemic stroke; speckle tracking echocardiography

ABSTRACT

Background: Acute ischemic stroke due to cardio-embolism associated with atrial fibrillation (AF) has been known to have the highest risk of recurrence and increased patient morbidity and mortality. However, the detection rate of AF rhythm in acute ischemic stroke patients using electrocardiograms and Holter monitoring was still quite low. Functional changes in the left atrium have been associated with an increased incidence of AF. Left atrial strain measurement using speckle tracking echocardiography 2D (STE-2D) can detect left atrial dysfunction associated with AF.

Aim: To determine the association between left atrial strain and atrial fibrillation in patients with acute ischemic stroke.

Research Methods: This analytical observation study was conducted with a cross-sectional design, using secondary data from medical records at RSUP Dr. Sardjito within January 2020–December 2022 on the population with acute ischemic stroke patients who underwent an electrocardiogram and transthoracic echocardiography examination.

Results: During the observation period 142 acute ischemic stroke patients underwent an electrocardiogram and transthoracic echocardiography examinations. A total of 72 patients diagnosed with acute ischemic stroke met the inclusion criteria as study subjects, there were 49 subjects (68%) with sinus rhythm and 23 subjects (32%) with AF rhythm. The left atrial strain value was found to be lower in the AF rhythm group (13,02 ± 8,49%) than in the sinus rhythm group (25,12 ± 8,36%) and was statistically significant (p <0,001). Determination of the optimal cut-off value using the Youden Index obtained a left atrial strain value < 16,25% with a sensitivity of 85,7%, specificity of 73,9%, and area under the curve (AUC) value of 84% (p < 0,001, 95% CI 0,74 – 0,95). The results of the multivariate analysis test showed that left atrial strain was an independent predictor related to the occurrence of AF rhythm (p = 0,001, OR 18,68; 95% CI 3,22 – 108,45).

Conclusion: Decreased left atrial strain is associated with atrial fibrillation rhythms in acute ischemic stroke patients. Acute ischemic stroke patients with a left atrial strain value < 16.25% have a higher prevalence of atrial fibrillation rhythm.

INTISARI

Latar Belakang: Stroke iskemik akut akibat kardioemboli yang berkaitan dengan irama fibrilasi atrium (FA) telah diamati memiliki risiko terbesar untuk kambuh dan meningkatkan morbiditas serta mortalitas pasien. Namun, angka deteksi irama FA pada pasien stroke iskemik akut menggunakan modalitas elektrokardiogram dan pemantauan holter masih cukup rendah. Perubahan fungsional pada atrium kiri telah dikaitkan dengan meningkatnya kejadian FA. Pengukuran strain atrium kiri menggunakan speckle tracking echocardiography 2D (STE-2D) dapat mendeteksi gangguan fungsi atrium kiri yang berkaitan dengan kejadian FA.

Tujuan: Mengetahui hubungan nilai strain atrium kiri dan kejadian fibrilasi atrium pada pasien dengan stroke iskemik akut

Metode Penelitian: Studi observasi analitik ini dilakukan secara potong lintang menggunakan data sekunder catatan medis di RSUP Dr. Sardjito sejak periode Januari 2020–Desember 2022, pada populasi pasien stroke iskemik akut yang dilakukan pemeriksaan elektrokardiogram dan ekokardiografi transtorakal

Hasil: Selama periode observasi, sebanyak 142 pasien stroke iskemik akut dilakukan pemeriksaan elektrokardiogram dan ekokardiografi transtorakal. Sebanyak 72 pasien terdiagnosis stroke iskemik akut yang memenuhi kriteria inklusi sebagai subjek penelitian, terdapat 49 subjek (68%) dengan irama sinus dan 23 subjek (32%) dengan irama FA. Nilai strain atrium kiri didapatkan lebih rendah pada kelompok irama FA (13,02 ± 8,49%) dibandingkan kelompok irama sinus (25,12 ± 8,36%) dan secara statistik berbeda signifikan (p <0,001). Penentuan nilai titik potong optimal menggunakan Indeks Youden didapatkan nilai strain atrium kiri < 16,25% memiliki nilai sensitivitas 85,7% dan spesifisitas 73,9% dengan nilai area under the curve (AUC) sebesar 84% (p < 0,001, IK95% 0,74 – 0,95). Hasil uji analisis multivariat didapatkan bahwa strain atrium kiri merupakan prediktor independen yang berhubungan dengan kejadian irama FA (p = 0,001, OR 18,68; IK95% 3,22 – 108,45).

Simpulan: Nilai strain atrium kiri berhubungan dengan irama fibrilasi atrium pada pasien stroke iskemik akut. Pasien stroke iskemik akut dengan nilai strain atrium kiri < 16,25% memiliki prevalensi irama fibrilasi atrium lebih besar.

INTRODUCTION

Stroke is a common disease, with one in four people affected over their lifetime, and is the second leading cause of death and third leading cause of disability in adults worldwid[1]. Based on the results of Riskesdas in 2007, 2013 and 2018 in Indonesia, acute ischemic stroke has the highest prevalence rate in the category of non-communicable diseases and is the most common cause of death in the category of non-communicable diseases. The highest proportion of stroke events in Indonesia was found at the age of 75 years and over[2].

Cardiac thromboembolism associated with atrial fibrillation (AF) is one of the main causes up to 30% of the total cases of acute ischemic stroke. This proportion increases with age which is related to the increasing prevalence of AF with age. Atrial fibrillation associated strokes are more fatal or disabling and carry a higher mortality risk than acute ischemic stroke from other causes[3]. Acute ischemic stroke due to cardio-embolism has been observed to have the greatest risk of recurrence[4]. The majority of acute ischemic stroke cases associated with AF can be prevented with the use of oral anticoagulants. This has been the reason it is important to investigate undetected AF after stroke to reduce recurrence of acute ischemic stroke[5].

Cardiac monitoring should be performed for at least the first 24 hours after acute ischemic stroke to screen for AF and other potentially serious cardiac arrhythmias that would necessitate emergency cardiac interventions. Based on the results of recent studies, monitoring of heart rhythm using an ECG with a longer duration is currently being considered in post stroke patients to increase the detection rate of heart rhythm abnormalities, especially AF[6]. New AF detection rates after cerebral ischemia are approximately 2-5% with standard 12 lead ECG and 2-9.2% with 24-hour Holter monitoring[7]. Longer monitoring and using more sophisticated monitoring tools can generally increase AF detection with the overall detection rate after all phases of cardiac monitoring reaching 23.7%[8]. However, AF that occurs is often asymptomatic and paroxysmal making it difficult to detect. Studies suggest that longer cardiac rhytm monitoring can be beneficial in detecting AF, but identifying the right patients for prolonged monitoring is important[9].

Functional changes in the left atrium (LA) have been associated with atrial fibrillation rhythms. LA function is complex, comprising of three main components: reservoir function in systole when blood fills the left atrium, as a conduit in early diastole corresponding to passive left ventricular filling and as an active contractile chamber in late diastole[10]. Strain analysis has been used to evaluate left atrial function and can be measured throughout the cardiac cycle, making it possible as an instrument for evaluating all three functions of the left atrium. Strain measurements are fractional changes in the length of myocardial segments and represent myocardial deformation[11]. Left atrial strain during the reservoir phase and contraction phase has been widely studied as an index of left atrial function in a number of clinical trials. There is evidence supporting LA strain as a measure of subclinical LA dysfunction with incremental value for prediction of AF in cardioembolic and cryptogenic stroke over traditional clinical and echocardiographic parameters[12]. Recently, studies have shown that LA strain correlate well with LA fibrosis and left ventricular (LV) filling pressure and therefore hypothesize that left atrial strain is a strong predictor of AF[13].

Detection of AF rhythm in patients with acute ischemic stroke can reduce the stroke recurrence rate by administering oral anticoagulant therapy. However, the detection rate of FA rhythm after acute ischemic stroke using Holter and ECG is still quite low, making it difficult to detect. This study aims to determine the association between left atrial strain and atrial fibrillation in patients with acute ischemic stroke. The result from this study is expected to be a consideration for post-acute ischemic stroke patients who will get benefit from longer and more intensive rhythm monitoring to detect clinical AF.

METHODS

This study is an analytical observational with a cross-sectional method conducted in RSUP Dr. Sardjito Yogyakarta after receiving permission from FK-KMK UGM medical ethical committee. Study subject data was taken secondarily from RSUP Dr. Sardjito medical records that have fulfilled inclusion and exclusion criteria since January 2020-December 2022. The study subject is acute ischemic stroke patients who underwent an electrocardiogram and transthoracic echocardiography examination when hospitalized in RSUP Dr. Sardjito.

Inclusion criteria in this study consist of 1) patient's age > 18 years old, 2) diagnosed with acute ischemic stroke based on clinical presentation and radiological examination, 3) patients who have 12-lead ECG examination data at the time of hospitalization, 4) patients with sinus rhythm from a 12-lead ECG examination who had a Holter examination with a minimum duration of 24 hours during hospitalization or no later than 4 weeks from the event of acute ischemic stroke, and 5) patients who have performed a transthoracic echocardiography examination.

Exclusion criteria in this study are: 1) patients with echocardiographic examination results that have poor or incomplete image quality, 2) patients with echocardiographic image < 40 frames per second (fps), 3) patients with chronic heart failure with reduced left ventricular ejection fraction with an ejection fraction of ≤ 40%, 4) patients with a heart rate > 110 beats per minute, 5) patients with any degree of mitral stenosis, 6) patients with hyperthyroidism, and 7) patients with incomplete clinical data.

RESEARCH PROTOCOL

Study subjects were collected from patients diagnosed with acute ischemic stroke based on clinical presentation and radiological examination, with a maximum onset of 7 days from clinical signs of stroke. Inclusion and exclusion criteria were screened for acute ischemic stroke patients who were hospitalized and transthoracic echocardiography was performed at RSUP Dr. Sardjito Yogyakarta from 2020-2022. Based on the results of the 12-lead ECG examination, we identified subjects who were included in the AF rhythm and sinus rhythm patient groups. In the sinus rhythm group, we are tracking the holter monitor results for a minimum duration of 24 hours, which were carried out at the time of hospitalization or no later than 4 weeks from the event of acute ischemic stroke, and if AF rhythms (both persistent and paroxysmal) were obtained from the holter monitor results, the subject moved into the AF rhythm group. Patient data obtained from medical records for the baseline characteristics of the study subjects are sex, age, blood pressure, heart rate frequency during echocardiography examination, body mass index (BMI), CHA2DS2-VASC score, kidney function and electrolyte values, complaints of dizziness, comorbid hypertension, diabetes, ischemic heart disease, chronic heart failure, valvular heart disease, chronic kidney disease, and previous history of stroke. The echocardiographic examination data obtained are the left atrial volume index (LAVI), left ventricular mass index (LVMI), relative wall thickness (RWT), left ventricular systolic function, and mitral valve abnormalities.

Left atrial reservoir strain was obtained by echocardiographic examination using the 2D speckle tracking echocardiography (2D-STE) method using Echo-PAC software version 202 (GE Healthcare, Wisconsin, USA). This study uses calculations of the left atrial strain in the reservoir phase. The calculation procedure uses an apical four-chamber view and an apical two-chamber view with a zero reference point in the R wave (ventricular cycle) according to the 2018 EACVI/ASE consensus recommendations (14). The image quality for the calculations is an echocardiography image with a minimum frame rate > 40 frames per second (fps). Steps to measure left atrial strain are: (1) marking the systolic phase of opening and closing of the aortic valve; (2) manual tracing of the left atrial endocardial margin; (3) evaluation and approval of left atrial tracking using the apical four chamber view and apical two chamber view (twelve segments), if there are two or more segments that do not agree on one view, then repeat step number 2; (4) using the mean strain curve to get the left atrial strain value of the reservoir. Strain values are expressed in percent (%). In all subjects with both sinus rhythm and AF, 3 cycles of measurement were carried out, and the average measured reservoir strain value was taken. The reservoir strain value is calculated from the average value of the reservoir strain taken from the apical four-chamber view and the apical two-chamber view. Examination of left atrial strain was carried out by researchers and other cardiologists who were blind to this study to obtain inter-observer variability.

STATISTICAL ANALYSIS

Data were analyzed with Statistical Package for the Social Science (SPSS) International Business Machine (IBM) software version 23. Univariate analysis was used to describe descriptively the baseline characteristics of the subject. Univariate analysis numeric variable using Kolmogorov-Smirnov/Shapiro-Wilk test where $p > 0{,}05$ showed normally distributed data. Numeric variables with normal distribution will be shown as mean + standard deviation (SD). Meanwhile, data without normal distribution will be shown as median (minimum-maximum).

The inter-observer variability test was analyzed using the ICC (Intraclass Correlation Coefficient) test on the left atrial strain measurement data between the two observers. An analysis with the receiver operating characteristic (ROC) curve was performed to determine the value of the area under the curve (AUC) of the left atrial strain value to detect atrial fibrillation rhythms. The AUC value will describe the strength of the resulting diagnostic value. After the AUC value is obtained, the optimal cut-off point is determined for the left atrial strain to detect atrial fibrillation rhythm based on the ROC curve. The optimal cut point value is determined based on the Youden Index.

Numeric variable with normal distribution will be bivariate analysis with independent T-test, meanwhile without normal distribution will be tested with non- parametric test Mann-Whitney. The categorical variable will be analyzed with the Chi- Square test; if there were less than five expected counts from one cell Fisher test will be used. Multivariate analysis was then performed on variables with a significance of $p < 0.25$ in bivariate analysis using the logistic regression test to determine factors that significantly influence the rhythm of atrial fibrillation.

RESULT

Baseline Characteristic of Study Subjects

From January 2020 to December 2022, there were 142 patients with an acute ischemic stroke who were hospitalized and underwent a transthoracic echocardiography examination at RSUP Dr. Sardjito. A total of 72 patients fulfilled inclusion and exclusion criteria and were included as study subjects, there were 49 subjects (68%) with sinus rhythm and 23 subjects (32%) with AF rhythm (Figure 1).

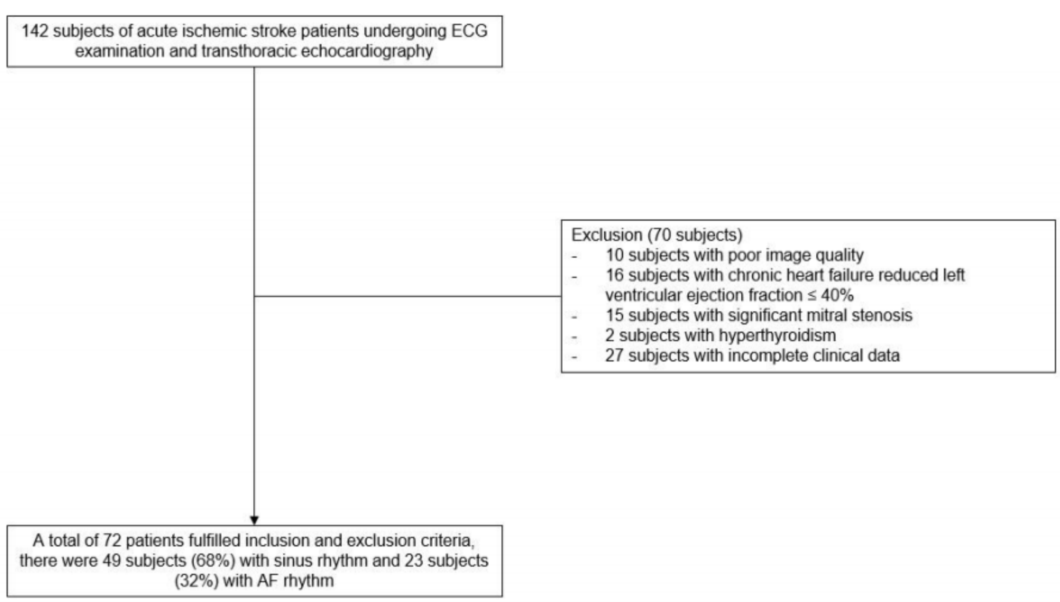

Figure 1. Flowchart of study population inclusion, exclusion, and distribution

The research subjects consisted of 42 male subjects (58.3%) and 30 female subjects (41.7%). The mean age of the study subjects was 63.82 ± 10.49 years with a median body mass index of 23.7 (15-43) kg/m2. The subjects' mean systolic blood pressure was 155.85 ± 29.37 mmHg and diastolic blood pressure was 84.61 ± 14.56 mmHg. The subjects had normal kidney function and electrolytes with mean GFR values of 70.94 ± 26.24 ml/min/m2, sodium values of 138 ± 5 mmol/L, and potassium values of 4 ± 0.5 mmol/L. The median CHAD2VASC score of the study subjects was 3 (1-8). Dizziness complaints were found in 26 subjects (36.1%) and a history of previous stroke was found in 18 subjects (25%). Subjects with comorbid hypertension were 71 subjects (98.6%), those with diabetes were 30 subjects (41.7%), those with ischemic heart disease were 18 subjects (25%), those with chronic heart failure were 10 subjects (13.9%), and those with heart valve disease were 6 subjects (8.3%). Paroxysmal AF rhythm was found in 11 subjects (15.3%). The number of subjects who had > 1 comorbidity was found to be 52 (72.2%) (Table 1).

Data of echocardiography parameters in this study showed that the mean left atrial strain was 21.26 ± 10.09%, the average LAVI value was 31 ± 13.75 ml/m2, the average left ventricular ejection fraction was 66.28 ± 9.82%, the average LVIDD was 43.90 ± 8.84 mm, and the average heart rate during the echocardiography examination was 74.82 ± 14.14 beats per minute. Subjects with significant mitral regurgitation disorder were 3 (4.2%). The subjects' median LVMI value was 97.1 (31.4-218.6) g/m2 and their median RWT value was 0.5 (0.2-1.26) (Table 1).

Table 1. Baseline Characteristic

Variable	Subject (n=72)
Demographic Parameters	
Sex	
- Male	42 (58.3%)
- Female	30 (41.7%)
Age	63.82 ± 10.49
Clinical Parameters	
BMI (kg/m^2)	23.7 (15-43)
Systolic Blood Pressure (mmHg)	155.85 ± 29.37
Diastolic Blood Pressure (mmHg)	84.61 ± 14.56
GFR (ml/min/m^2)	70.94 ± 26.24
CHAD2VASC	3 (1-8)
Natrium (mmol/L)	138 ± 5
Kalium (mmol/L)	4 ± 0.5
Dizziness	26 (36.1%)
Sinus Rhythm	49 (68%)
AF Rhythm	23 (32%)
Paroxysmal AF Rhythm	11 (15.3%)
Comorbidities	
Hypertension	71 (98.6%)
Diabetes	30 (41.7%)
Ischemic Heart Disease	18 (25%)
Chronic Heart Failure	10 (13.9%)
Valvular Heart Disease	6 (8.3%)
History of Stroke	18 (25%)
1 Comorbidity	20 (27.8%)
> 1 Comorbidity	52 (72.2%)
Echocardiography Parameters	
LAVI (ml/m^2)	31 ± 13.75
Left Atrial Strain (%)	21.26 ± 10.09
EF (%)	66.28 ± 9.82
LVMI (g/m^2)	97.1 (31.4-218.6)
RWT	0.5 (0.2-1.26)
LVIDD (mm)	43.90 ± 8.84
Mitral Regurgitation	3 (4.2%)
Heart rate during examination (bpm)	74.82 ± 14.14

GFR: glomerular filtration rate, AF: atrial fibrillation, LAVI: left atrium volume index, EF: ejection fraction, LVMI: left ventricular mass index, RWT: relative wall thickness, LVIDD: left ventricular internal diameter end diastole

Inter-observer Variability Test of Left Atrial Strain

Reliability of left atrial strain measurements was assessed by analysis of the ICC (Intraclass Correlation Coefficient) test on strain measurement data between the two observers to test the consistency of the examinations. The average left atrial strain measurement by observer 1 was 21.26 and observer 2 was 22.26. The left atrial strain measurement between the two observers obtained an ICC value of 0.918, which indicated that the left atrial strain measurement between the two observers had excellent reliability (Table 2).

Table 2. Intraclass Correlation Coefficient Test of Left Atrial Strain

	Mean ± SD	ICC	CI 95%
Observer 1	21.26 ± 10.09	0,918	0,87 – 0,95
Observer 2	22.26 ± 10.22		

SD: standard deviation, ICC: intraclass correlation coefficient, CI: confidence interval

ROC Analysis and Cutoff Value of Left Atrial Strain

Analysis using the receiver operating characteristic (ROC) curve was performed to determine the area under the curve (AUC) of the left atrial strain value to detect atrial fibrillation rhythms. From the ROC curve, it appears that the left atrial strain examination has an AUC value of 84% (p <0.001, 95% CI 0.74 – 0.95) which indicates a diagnostic value with good statistical power (Figure 2). Determination of the optimal cutoff value using the Youden Index showed that the left atrial strain had an optimal cutoff point of 16.25% with a sensitivity of 85.7% and a specificity of 73.9%.

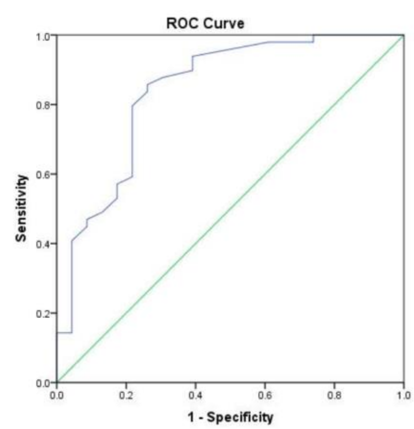

Figure 2. ROC Curve and AUC of Left Atrial Strain Measurement

Hypothesis Analysis of Left Atrial Strain with Atrial Fibrillation

Subjects with a left atrial strain value < 16.25% experienced atrial fibrillation in 17 subjects (70.8%) more than those with a left atrial strain value > 16.25% with a significant statistical difference (p< 0.001). The prevalence ratio value was 5.67 (p <0.001, 95% CI 2.57 – 12.5) which means that subjects with a left atrial strain value <16.25 had a prevalence of atrial fibrillation that was 5.67 times higher (Table 3).

Table 3. Association of Left Atrial Strain with AF Rhythm

		Rhythm				p	PR	CI 95%
		AF		Sinus				
		n=23	%	n=49	%			
Strain	<16.25	17	70.8%	7	29.2%	<0,001	5,67	2,57-12,50
	>16.25	6	12.5%	42	87.5%			

AF: atrial fibrillation, PR: prevalence rate, CI: confidence interval

Bivariate & Multivariate Analysis of Left Atrial Strain with Confounding Factors

This bivariate analysis tests several variables such as age, body mass index, systolic and diastolic blood pressure, history of hypertension, diabetes mellitus, ischemic heart disease, chronic heart failure, chronic kidney disease, valvular heart disease, previous history of stroke, electrolyte value, multiple comorbidities, LAVI, left ventricular EF, and mitral regurgitation. Bivariate analysis showed p < 0.25 for systolic blood pressure, diabetes, valvular heart disease, history of stroke, LAVI, left ventricular ejection fraction, and mitral regurgitation (Table 4). Variables with a significance level of p <0.25 were then followed by multivariate analysis together with left atrial strain values using the logistic regression test to determine factors that significantly influence atrial fibrillation rhythms.

Table 4. Bivariate Analysis of Research Variables with AF Rhythm

Variable	Rhythm (n=72)		p
	AF (n=23)	Sinus (n=49)	
Age	65.69 ± 10.09	62.94 ± 10.65	0,302
BMI (kg/m^2)	25.8 (17-35.1)	23.5 (15-43)	0,923
Systolic BP (mmHg)	146.47 ± 31.81	160.24 ± 27.39	0,063*
Diastolic BP (mmHg)	82.39 ± 15.36	85.65 ± 14.22	0,379
Hypertension	22 (95.6%)	49 (100%)	0,319
Diabetes	3 (13%)	27 (55.1%)	0,01*
Ischemic Heart Disease	6 (26.1%)	12 (24.5%)	0,884
Chronic Renal Failure	6 (26.1%)	17 (34.7%)	0,465
Chronic Heart Failure	5 (21.7%)	5 (10.2%)	0,273
Valvular Heart Disease	4 (17.4%)	2 (4.1%)	0,078*
History of Stroke	10 (43.5%)	8 (16.3%)	0,013*
Natrium (mmol/L)	139 ± 4	137 ± 6	0,413
Kalium (mmol/L)	4 ± 0.4	4 ± 0.5	0,922
Multiple Comorbidities	15 (65.2%)	37 (75.5%)	0,363
Left Atrial Strain	13.02 ± 8.49	25.12 ± 8.36	< 0,001*
LAVI	38.78 ± 18.56	27.73 ± 9.06	0,008*
EF	63.91 ± 10.80	67.39 ± 9.23	0,163*
Mitral Regurgitation	3 (100%)	0 (0%)	0,030*

*) significant p < 0.25, BP: blood pressure, AF: atrial fibrillation, LAVI: left atrium volume index, EF: ejection fraction

Based on multivariate analysis, systolic blood pressure, diabetes, valvular heart disease, history of stroke, LAVI, left ventricular ejection fraction, and mitral regurgitation were not statistically significant in association with atrial fibrillation rhythm (p > 0.05). The results of multivariate analysis showed that the left atrial strain showed a significant association with atrial fibrillation rhythm, with an OR of 18.68 (p = 0.001, 95% CI 3.22 – 108.45). Patients with a left atrial strain value < 16.25% are at risk of experiencing atrial fibrillation rhythm of 18.68 times (Table 5).

Table 5. Multivariate Analysis of Research Variables with AF Rhythm

Variable (n=72)	p	OR	CI 95%
Left Atrial Strain < 16,25 %	0.001*	18.68	3,22-108,45
Systolic BP (mmHg)	0.669	0.99	0,97-1,02
Diabetes	0.334	0.21	0,1-7,25
Valvular Heart Disease	0.541	0.37	0,02-9,16
History of Stroke	0.367	2.14	0,41-11,09
LAVI	0.997	1.0	0,94-1,07
EF	0.881	1.01	0,93-1,09
Mitral Regurgitation	0.999	-	0-∞

BP: blood pressure, AF: atrial fibrillation, LAVI: left atrium volume index, EF: ejection fraction

DISCUSSION

Acute ischemic stroke associated with cardio-embolism with FA rhythm is known to have the greatest risk of recurrence. As an effort to reduce the stroke recurrence rate is to detect AF rhythm. In patients with acute ischemic stroke, the diagnosis of AF may reduce the incidence of stroke recurrence with long-term oral anticoagulant treatment[15]. In this study, it was found that more research subjects were male, the average age was 64 years, and more than 90 percent of the subjects had a history of hypertension. A history of other comorbidities was found with a lower prevalence, such as 41.7% DM, 25% ischemic heart disease, 13.9% chronic heart failure, and 8.3% valvular heart disease. The prevalence data found in this study are similar to studies in the stroke population using a previous prospective cohort method[4].

In this study, it was found that the number of subjects who had multiple comorbidities was higher which is 52 subjects (72.2%) than subjects who only had single comorbidity. The proportion of subjects with multiple comorbidities was found to be higher in the sinus rhythm group than in the FA rhythm group (65% vs 75%) but not statistically significant. This could be due to the smaller proportion of AF rhythm subjects when compared to the number of sinus rhythm subjects. In the AF rhythm group, multiple comorbid subjects were found to be more than 15 of 23 subjects (65%) who only had single comorbid.

AF is frequently linked to both cardiac and noncardiac comorbidities as well as cardiac illness. The most frequent diseases associated with AF are hypertensive heart disease (22%-36%), coronary heart disease (14%-32%), valvular heart disease (12%-26%), and cardiomyopathy (6%-10%), while the most common comorbidities are hypertension (67%-76%), heart failure (22%-42%), diabetes (20%-24%), obesity (20%-35%), thyroid dysfunction (8%-11%), and renal failure (11%-22%). In particular, one third of AF patients have three or more co-morbid conditions; one fifth and one quarter of patients, respectively, have neither co-morbidity nor heart illness[16]. Stroke survivors generally have more than one comorbid condition, and these may arise for a variety of biopsychosocial reasons. In a population study, stroke survivors who experienced more than one comorbidity were found to be twice as likely as the control group[17]. Those with higher long-term comorbidity rates have poorer clinical outcomes and will use health services more frequently. The presence of multiple comorbid conditions also adds to the complexity of disease management. Multimorbidity in stroke patients is also associated with polypharmacy which can increase the risk of drug interactions[18].

History of previous stroke in the subjects of this study was found in 18 subjects (25%). Of the 18 subjects with a history of stroke, as many as 10 subjects (43.5%) were in the AF rhythm group, so that the proportion of subjects with a history of recurrent stroke was found to be higher in the AF rhythm group, which also differed statistically significant. The increased risk of stroke recurrence due to AF rhythm is caused by a process of blood stasis, endothelial dysfunction, hypercoagulability, and systemic inflammation resulting in conditions that increase the risk of thromboembolism[19].

In this study, the mean left atrial strain value of all subjects in the acute ischemic stroke population was 21.26 ± 10.09%. In the AF rhythm group, the mean left atrial strain value was lower 13.02 ± 8.49 % compared to the sinus rhythm group, which was 25.12 ± 8.36. The difference in scores between the two groups was statistically significant. The findings in this study are in accordance with studies regarding left atrial strain in the stroke population without AF rhythm, which also show a decrease in left atrial strain values. The process of left atrial remodeling in stroke patients is caused by several factors, such as aging, cardiovascular risk factors, and comorbidities (e.g., chronic kidney disease). These factors cause a pathological process in the left atrium, which is characterized by chamber dilation, fibrosis, and stiffness thereby reducing the left atrial strain value[20].

The inter-observer reproducibility of the left atrial strain examination obtained in this study resulted in high reliability and is in accordance with previous studies in healthy populations with sinus rhythm, which have an ICC value of 0.86[21]. In another study with diverse populations, including those with cardiac abnormalities in the form of acute coronary syndrome, heart failure, and heart valve disease, left atrial strain examination had good inter-observer agreement with an ICC value of 0.81[22]. In another prospective cohort study with the FA rhythm population, the left atrial strain examination also had good inter-observer agreement with an ICC value of 0.99[23].

New echocardiographic examination techniques, such as measurement of left atrial strain using the speckle tracking echocardiography 2D (STE 2D) technique, have better accuracy in evaluating left atrial function (Leung et al., 2018). The results of this study indicated that subjects with a left atrial strain value < 16.25% had a higher prevalence of atrial fibrillation 5.67 times, with a good AUC value of 84%, a sensitivity of 85.7% and a specificity of 73.9%. This figure is almost similar to a prospective cohort study in the hypertensive population where left atrial strain with a value of 19% can predict the emergence of AF rhythms in hypertensive patients with an AUC value of 88%, a sensitivity of 86%, and a specificity of 76%[24]. The left atrial strain parameter associated with AF rhythm with good value of sensitivity and specificity. Left atrial strain measurement may be considered for use in acute ischemic stroke patients as an indicator of patients requiring long-term rhythm monitoring, such as an implantable loop recorder (ILR) or repeated Holter monitoring at regular intervals. Using this parameter will improve the detection of patients diagnosed with AF rhythm and receiving anticoagulant treatment for the prevention of recurrent stroke.

The results of the multivariate analysis found that the left atrial strain still showed a significant relationship with atrial fibrillation rhythm. With a left atrial strain value < 16.25%, the risk of experiencing atrial fibrillation rhythm was 18.68 times. This is similar to what was found in other studies in the general population, where examination of left atrial strain independently predicts AF. These findings remained consistent even in participants with normal left atrial size and normal left ventricular systolic function[25]. In other population studies, left atrial strain examination was also an independent predictor of AF recurrence in subjects undergoing cardioversion and catheter ablation[26].

Another echocardiographic parameter that is often used is LAVI to assess left atrial dilatation, left atrial structural remodeling, and cardiovascular prognostic markers. The average LAVI value in all study subjects was 31 ± 13.75 ml/m2, with the average LAVI value in the FA rhythm group being greater, which is 38.78 ± 18.56 ml/m2 when compared to the sinus rhythm group with 27.73 ± 9.06 ml/m2. The difference in LAVI values between the two groups was statistically significant. This study shows that in the AF rhythm group of stroke patients, there has been structural remodeling in the form of chamber dilatation in the left atrium. The process of atrial remodeling causes electrical disturbances between muscle fibers and conduction fibers in the atrium, and is a triggering factor as well as a perpetuating factor for AF. This electro-anatomical substrate facilitates the reentry circuits that perpetuate arrhythmias. Once AF is started, it causes further changes in the atrial structure, thereby exacerbating cardiomyopathy[27]. This shows that an increase in left atrial size is an important factor for the occurrence of AF rhythm[28].

This study has several limitations. First, subjects with AF rhythm were only measured for 3 cycles and the average measured strain value was taken, while the guidelines suggested doing at least 5 cycles. Second, the results showed a wide confidence interval because the number of subjects with an AF rhythm was lower even though they met the minimum number of samples required. Third, this is a cross-sectional study, so the association between left atrial strain and AF rhythm still needs to be re-examined using a prospective cohort study method. Fourth, the NIH Stroke Scale (NIHSS) score is a parameter related to the degree of stroke severity that is often associated with FA rhythms. A high NIHSS score is associated with the possibility of acute ischemic stroke caused by FA rhythm, but researchers cannot collect NIHSS data due to a lack of data and time limitations. Finally, left atrial longitudinal 2D-STE tracking also suffers from the limitations of conventional speckle tracking, such as its reliance on good imaging quality (all kinds of ultrasonic noise reduce tracking quality) and the temporal stability of the tracking pattern.

CONCLUSION

Decreased left atrial strain is associated with atrial fibrillation rhythms in acute ischemic stroke patients. Acute ischemic stroke patients with a left atrial strain value < 16.25% have a higher prevalence of atrial fibrillation rhythm.

ACKNOWLEDGEMENTS

The authors would like to thank all staff and residents of the Department of Cardiology and Vascular Medicine, Faculty of Medicine, Public Health and Nursing, Gadjah Mada University, for the discussion and suggestions regarding this research.

FUNDING SOURCES

This research did not receive funding from any source.

DISCLOSURES AND ETHICS

The authors have no conflicts of interest to declare. This study has been approved by the medical ethics committee of Faculty of Medicine, Public Health and Nursing, Gadjah Mada University number KE/FK/1044/EC/2022.

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