


ORIGINAL RESEARCH

# Left Atrial Strain to Predict Stroke in Patients With Acute Heart Failure and Sinus Rhythm

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**BACKGROUND:** Stroke is a major comorbidity in patients with heart failure (HF), especially in those with decreased left atrial (LA) function, and thus, identifying patients highly at risk of stroke can prevent its occurrence. We evaluated the predictive value of global longitudinal strain of LA (LAGLS) in patients with acute HF and sinus rhythm.

**METHODS AND RESULTS:** In this retrospective study, 2461 patients (53.3% men, 69.7±14.4 years old) with sinus rhythm and LAGLS among 4312 consecutive patients with acute HF from 3 tertiary hospitals were included. HF phenotypes were defined as HF with reduced ejection fraction (EF) (left ventricular EF ≤40%), HF with midrange EF (40% <left ventricular EF <50%), and HF with preserved ejection fraction (left ventricular EF ≥50%). Primary outcome was new-onset stroke. The mean left ventricular EF was 39.4%±15.6%. Moreover, 1388 (57.5%), 342 (14.2%), and 682 (28.3%) were classified with HF with reduced EF, HF with midrange EF, and HF with preserved EF, retrospectively. LAGLS was 17.2%±10.4%. During the follow-up duration (mean: 30.3±25.4 months), 100 patients experienced stroke. Patients with stroke had higher LA diameter ( $P=0.031$ ) and lower LAGLS ( $P=0.010$ ) than those without stroke. In the univariate analysis, age, diabetes mellitus, LA diameter, LA volume index, and LAGLS were significant risk factors for stroke. In the multivariate analysis, each 1% decrease in LAGLS was associated with a 3.8% increased risk for stroke (hazard ratio [HR], 1.038; 95% CI, 1.013–1.065;  $P=0.003$ ). When applying a LAGLS cutoff point of 14.5%, patients with LAGLS <14.5% had approximately twice the risk for stroke after adjusting other significant variables (HR, 1.940; 95% CI, 1.269–2.965;  $P=0.002$ ).

**CONCLUSIONS:** In patients with acute HF and sinus rhythm, decreased LAGLS (<14.5%) was associated with an increased risk for stroke, with an annual incidence of 2.38%.

**Key Words:** heart failure ■ strain echocardiography ■ stroke

Stroke is a major cardiovascular disease with high mortality and morbidity. The estimated prevalence of stroke was 2.5% in 2016, and the prevalence of stroke increases with age.<sup>1</sup> Approximately 87% of patients are diagnosed with ischemic stroke, and approximately 91% are associated with modifiable risk factors including hypertension, obesity, hyperglycemia or diabetes mellitus, dyslipidemia, and chronic kidney disease.<sup>2</sup>

Among the risk factors for stroke, atrial fibrillation (AF) is a powerful risk factor that can increase the risk of stroke approximately 5-fold.<sup>3,4</sup> Heart failure (HF) is the second most common risk factor for stroke after

AF and accounts for approximately 9% of stroke.<sup>5,6</sup> Specifically, patients with HF with reduced ejection fraction (HFrEF) have increased risk of thromboembolism because of blood stasis in the dilated left ventricle, impaired release of endothelium-derived vasodilators, hemoconcentration, increased inflammation and thrombin-related pathways, and increased risk of AF.<sup>7–9</sup> The cerebral blood flow may be reduced in patients with HF, which may contribute to further cerebral ischemia in patients with stroke.<sup>10</sup>

Although the anticoagulation value is not well studied, identifying patients highly at risk of stroke can prevent its occurrence. As left atrial (LA) enlargement

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## CLINICAL PERSPECTIVE

### What Is New?

- Decreased left atrial global longitudinal strain (<14.5%) was associated with an increased risk for stroke, with an annual incidence of 2.38%, in patients with acute heart failure and sinus rhythm.
- The risk of stroke corresponds to a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 2 to 3 in patients with nonvalvular atrial fibrillation.

### What Are the Clinical Implications?

- Further clinical evaluation is needed to evaluate the cost-effectiveness of anticoagulant therapy to prevent future stroke in patients with acute heart failure and lower left atrial global longitudinal strain.

## Nonstandard Abbreviations and Acronyms

<b>AHF</b>	acute heart failure
<b>HFrEF</b>	heart failure with reduced ejection fraction
<b>LAGLS</b>	left atrial global longitudinal strain

and dysfunction are associated with an increased risk of AF,<sup>11,12</sup> decreased LA function assessed by LA global longitudinal strain (LAGLS) was associated with increased risk of new-onset AF and mortality.<sup>13–15</sup> Although decreased LAGLS can be associated with LA thrombus formation and subsequent embolic infarction, few studies have shown the association between LAGLS and stroke.

Therefore, we evaluated the predictive value of LAGLS for stroke in patients with acute heart failure (AHF) and sinus rhythm.

## METHODS

Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to Goo-Yeong Cho, MD, PhD (cardioch@snu.ac.kr).

### Study Population

The STRATS-AHF (Strain for Risk Assessment and Therapeutic Strategies in Patients With Acute Heart Failure) registry (ClinicalTrials.gov Identifier 03513653, <https://clinicaltrials.gov/ct2/show/NCT03513653>) is a

large strain registry including 4312 acute HF patients from 3 tertiary university teaching hospitals in Korea between January 2009 and December 2016. Detailed information and primary outcomes are reported elsewhere.<sup>16,17</sup> In this registry, we retrospectively enrolled all admitted AHF patients with symptoms or signs of AHF with either pulmonary edema or objective findings of structural heart disease. We excluded patients with acute coronary syndrome or severe valvular heart disease requiring surgical correction at the time of admission.

This study included only patients with sinus rhythm and LAGLS value. Those with AF at the time of admission were excluded. Although the cardiac rhythm was normal at the time of hospitalization, patients of AF confirmed by the medical history were also excluded from this study. For the detection of new-onset AF during the follow-up period, electrocardiographs of all patients were reviewed. New-onset AF was confirmed when documented in electrocardiographs or when the patient had I48 codes from the *International Classification of Diseases, Tenth Revision* (ICD-10) in their diagnosis. Approximately 16 electrocardiographs per patient (mean: 16.5±15.2 electrocardiographs) were reviewed for AF detection. A total of 397 patients with new-onset AF (16.1%) during the follow-up were also included in the analysis. The institutional review board of each hospital approved this study protocol and waived the consent from the participants.

The study complied with the principles of the Declaration of Helsinki.

### Study Variables and Definitions

Based on echocardiographic findings at the index admission for AHF, patients were categorized as having HFrEF (left ventricular EF [LVEF] ≤40%), HF with mid-range EF (40% <LVEF <50%), and HF with preserved EF (LVEF ≥50%).

The primary outcome was ischemic stroke after discharge from the index admission.

Stroke diagnosis was identified from data in the medical records with patients with regular follow-up. Ischemic stroke was identified as an episode of neurological dysfunction caused by embolism.

### Echocardiographic Examination

We performed echocardiographic examinations using commercial echocardiographic machines and a 2.5-MHz probe using standard echocardiographic techniques, including M-mode, 2-dimensional, and Doppler modalities, as suggested by the American Society of Echocardiography.<sup>18</sup> End-diastolic and end-systolic LV volumes were measured by 2-dimensional Simpson's method from the apical 4- and 2-chamber views, and the LVEF was calculated from these values.

We recorded mitral inflow velocities using the pulsed-wave Doppler method at the mitral valve coaptation point and mitral annular velocities using the tissue Doppler method of the septum of the mitral annulus. We assessed LV diastolic function with the mitral  $E$  and  $A$  velocities,  $E/A$  ratio, deceleration time, and tissue Doppler analysis of septal mitral annular  $E'$  velocity, and  $E/e'$  ratio. Pulmonary artery systolic pressure was calculated from the continuous-wave Doppler-derived peak tricuspid regurgitation jet velocity. The anteroposterior LA diameter was measured from the parasternal long-axis view, and the LA maximal volume was measured at the end-systole frame using the area-length method from the apical 4- and 2-chamber views and presented as LA volume index after adjusting for body surface area.

### Strain Analysis

We measured the strains including LAGLS from the stored echocardiographic images using TomTec-Arena version 4.6 (TomTec, Munich, Germany) from digitally stored echocardiographic images.<sup>19,20</sup> The TomTec program is a vendor-independent software used to measure strain. After the endocardial border was manually traced on the end-systolic frame in the selected image, the software tracked speckles along the endocardial border and myocardium throughout the cardiac cycle automatically.

For the LAGLS analysis, we traced the LA endocardial border manually on the LV end-systolic frame. Subsequently, the software tracked speckles along the endocardial border and myocardium automatically throughout the cardiac cycle. We used R-R gating as the zero-reference point. We defined the LAGLS as the first peak positive deflection demonstrating LA reservoir function. The LAGLS was calculated as the mean value of the 4 segments of each apical view as the average of the GLS values from the apical 4- and 2-chamber views.<sup>13,18</sup> The roof of the LA was not analyzed because of poor delineation and contamination of pulmonary veins. All LAGLS values were analyzed on a single cardiac cycle, and an echocardiographic specialist (PJH) blinded to the clinical data independently measured all LAGLS values.

### Statistical Analysis

We presented continuous variables as means $\pm$ SDs and categorical variables as frequencies. We performed the Student's  $t$ -test for continuous variables and the  $\chi^2$  test for categorical variables for comparisons between groups. We used the Kaplan–Meier method with comparison using the log-rank test in the analysis of survival and multivariate time-dependent Cox-proportional hazard analysis to determine the independent predictors of stroke in the time to first adverse clinical events.

We included all significant variables (with  $P$  value less than 0.05) in the univariate analysis as covariates in the multivariate analysis. However, we excluded variables with multicollinearity with others from the multivariate analysis. Two independent investigators calculated intra- and interobserver variabilities of the LAGLS in 20 random patients by calculating the intraclass correlation coefficient. The data were analyzed using the SPSS version 22 (IBM, Chicago, IL, USA). A 2-sided  $P$  value of  $<0.05$  was considered statistically significant.

## RESULTS

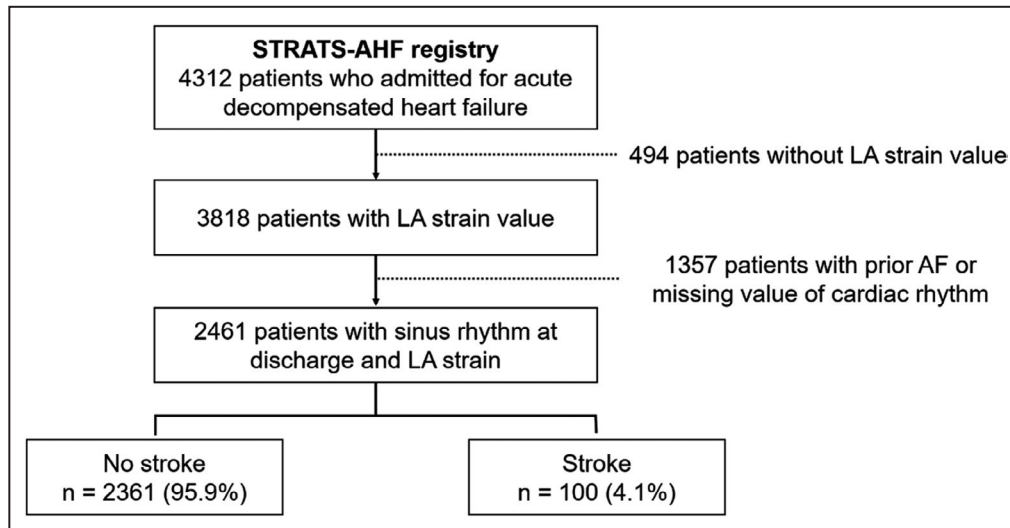
### Patient Characteristics

Initially, we screened all 4312 patients with AHF. We excluded 494 patients without LA strain values and 1357 patients with prior AF or missing values of cardiac rhythm (Figure 1). Thus, we analyzed a total of 2461 admitted patients (1311 men, 69.7 $\pm$ 14.4 years old) with sinus rhythm and adequate echocardiographic images suitable for the measurement of LAGLS. Their baseline characteristics are summarized in Table 1. The mean LVEF was 39.1% $\pm$ 15.6%, and 1388 (57.5%), 342 (14.2%), and 682 (28.3%) patients were classified as having HFrEF, HF HF with midrange EF, and HF with preserved EF, retrospectively. Hypertension was the most common associated cardiovascular risk factor (56.8%), and diabetes mellitus was found in 912 patients (37.1%). LAGLS was 17.2% $\pm$ 10.4%.

### Stroke and Its Determinants

In our registry, 108 patients were lost within 1 year, and additional 157 patients were lost within 2 years. We found 100 stroke events during the follow-up duration (mean duration: 30.3 $\pm$ 25.4 months) from medical records with regular clinical follow-ups and compared variables between the 2 groups according to the presence of stroke (Table 1).

LV end-diastolic dimension and LA diameter in patients with stroke were significantly higher than that in patients without stroke. Although the difference in stroke incidence was not statistically significant according to HF phenotypes, it was highest in the HFrEF group (60 patients [60%] in HFrEF, 11 [11%] in HF with midrange EF, and 29 [29%] in HF with preserved EF groups). During the follow-up duration, 397 patients had new-onset AF. The incidence of new-onset AF was significantly higher in the stroke group (32.0% versus 15.5%,  $P<0.001$ ). Moreover, LAGLS was significantly lower in patients with stroke than in patients without stroke (14.5% $\pm$ 8.8% versus 17.3% $\pm$ 10.5%,  $P=0.010$ ). However, there were no differences between cardiovascular risk factors and LV systolic parameters between the 2 groups. The LA volume index was higher in patients with stroke than



**Figure 1.** Of the 4312 patients who were included in the STRATS-AHF (Strain for Risk Assessment and Therapeutic Strategies in Patients With Acute Heart Failure) registry, 2461 patients with sinus rhythm and left atrial (LA) strain value were analyzed.

During the 5-year follow-up, 100 (4.1%) patients had stroke. AF indicates atrial fibrillation.

that in patients without stroke. However, the difference was not statistically significant between the 2 groups ( $56.6 \pm 28.9$  mL/m<sup>2</sup> versus  $49.8 \pm 24.8$  mL/m<sup>2</sup>,  $P=0.059$ ).

The univariate and multivariate analyses are listed in Table 2. In the univariate analysis, age (hazard ratio [HR], 1.022; 95% CI, 1.006–1.038;  $P=0.005$ ), diabetes mellitus (HR, 1.552; 95% CI, 1.044–2.307;  $P=0.030$ ), LA diameter (HR, 1.032; 95% CI, 1.007–1.056;  $P=0.010$ ), LA volume index (HR, 1.007; 95% CI, 1.002–1.012;  $P=0.007$ ), new-onset AF (HR, 2.494; 95% CI, 1.635–3.805;  $P<0.001$ ), and LAGLS (per 1% decrease, HR, 1.040; 95% CI, 1.017–1.064;  $P=0.001$ ) were significant determinants of stroke. Because LA diameter showed a higher hazard ratio than that of LA volume index (1.032 versus 1.007), we included LA diameter instead of using LA volume index in the multivariate model. In the multivariate analysis, LAGLS (HR, 1.038; 95% CI, 1.012–1.064;  $P=0.003$ ) remained statistically significant after the adjustment of age, diabetes mellitus, LA diameter, and new-onset AF.

We assessed the best cutoff point of LAGLS for the prediction of stroke by performing the receiver operating curve analysis with the Youden index and found that 14.5% was the best cutoff point. The annual incidences of stroke in patients with LAGLS  $<14.5\%$  and  $\geq 14.5\%$  were 2.38/100 person-year and 1.08/100-person-year ( $P=0.008$ ), respectively. After the adjustment of age, sex, diabetes mellitus, cholesterol concentration, LV end-diastolic volume, LA diameter, and new-onset AF, patients with LAGLS  $<14.5\%$  still had a higher incidence of stroke than

patients with LAGLS  $\geq 14.5\%$  (HR, 1.940; 95% CI, 1.269–2.965;  $P=0.002$ ).

In the survival analysis with the Kaplan-Meier method, patients with LAGLS  $\geq 14.5\%$  had significantly higher 5-year stroke-free survival than patients with LAGLS  $<14.5\%$  ( $96.0\% \pm 0.7\%$  versus  $90.4\% \pm 1.4\%$ ,  $P<0.001$ , Figure 2).

### Variability of LAGLS

The intraobserver variability of the intraclass correlation coefficient of LAGLS was 0.957 (95% CI, 0.889–0.982), and interobserver variabilities of the intraclass correlation coefficient was 0.938 (95% CI, 0.844–0.976).

## DISCUSSION

In this study, we showed that LAGLS was an independent predictor of stroke in AHF patients with sinus rhythm and that decreased LAGLS was associated with an increased risk of stroke after the adjustment of other clinically important variables.

Stroke is a major cardiovascular disease with significant disability and mortality. The identification of patients at high risk of developing stroke is important to prevent stroke and to reduce individual and social burden. Control of hypertension is a well-known method to lower stroke risk and prevention.<sup>21</sup> AF is a well-known powerful risk factor for stroke, and anticoagulation therapy in patients with AF can reduce stroke risk.<sup>22</sup> Even without AF, HF itself can increase the risk of stroke because HF patients have body fluid imbalances, endothelial dysfunction, proinflammatory and

**Table 1. Comparison of Baseline Clinical Characteristics and Echocardiographic Data According to the Presence of Stroke**

	Total (n=2461)	No stroke (n=2361)	Stroke (n=100)	P Value
Male sex, %	1311 (53.3%)	1262 (53.5%)	49 (49.0%)	0.414
Age, y	69.7±14.4	69.6±14.5	71.3±12.4	0.188
Body mass index, kg/m <sup>2</sup>	23.3±4.1	23.3±4.1	23.7±4.2	0.323
New York Heart Association functional class IV, %	840 (34.1%)	800 (33.9%)	40 (40.0%)	0.138
Physical examination				
Systolic blood pressure, mm Hg	129.4±27.2	129.2±27.3	132.8±24	0.198
Diastolic blood pressure, mm Hg	74.0±16.2	74±16.3	74.9±13.7	0.583
Heart rate, bpm	84.8±21.7	84.9±21.7	84.2±19.9	0.765
Past medical history				
Hypertension, %	1399 (56.8%)	1337 (56.6%)	62 (62.0%)	0.304
Diabetes mellitus, %	912 (37.1%)	867 (36.7%)	45 (45.0%)	0.112
Ischemic heart disease, %	912 (37.1%)	871 (36.9%)	41 (41.0%)	0.400
Laboratory findings				
Total cholesterol, mg/dL	158.9±44.8	159±44.9	156.5±43.1	0.593
Triglyceride, mg/dL	114.9±75.9	114.9±76.4	115.3±64.6	0.966
High-density lipoprotein-cholesterol, mg/dL	43.4±13.3	43.4±13.4	42.7±11.6	0.668
Hemoglobin, g/dL	12.0±2.3	12.0±2.3	12.1±2.2	0.603
Serum urea nitrogen, mg/dL	25.8±16.8	25.8±16.9	25.4±14.9	0.819
Creatinine, mg/dL	1.7±2.0	1.7±2.0	1.9±2.5	0.361
Glucose, mg/dL	155.1±77.4	154.8±77.3	162.4±79.1	0.347
Echocardiographic findings				
LV end-diastolic dimension, mm	54.1±9.6	54.0±9.6	56.0±10.1	0.044
LV end-systolic dimension, mm	41.8±11.9	41.8±11.8	43.2±13.5	0.273
LV end-diastolic volume, mL	130.4±66.2	129.9±65.7	144.1±76.9	0.107
LV end-systolic volume, mL	86.4±57.8	86.0±57.2	98.3±69.3	0.119
LVEF, %	39.1±15.6	39.1±15.6	38.2±16.5	0.564
LA diameter, mm	42.5±8.1	42.4±8.1	44.2±8.6	0.031
LA volume index, mL/m <sup>2</sup>	50.1±25	49.8±24.8	56.6±29.8	0.059
Mitral E/E' ratio	18.8±11.1	18.9±11.2	18.4±9.3	0.739
Tricuspid regurgitation velocity, m/s	3.0±0.6	3.0±0.6	3.0±0.7	0.735
LA global peak systolic longitudinal strain, %	17.2±10.4	17.3±10.5	14.5±8.8	0.010
Phenotype of HF, %				
HF with reduced EF, %	1437 (58.4%)	1377 (58.3%)	60 (60.0%)	
HF with midrange EF, %	342 (14.2%)	331 (14.3%)	11 (11.0%)	
HF with preserved EF, %	682 (28.3%)	653 (28.2%)	29 (29.0%)	
New-onset atrial fibrillation, %	397 (16.1%)	365 (15.5%)	32 (32.0%)	<0.001

EF indicates ejection fraction; HF, heart failure; LA, left atrial; and LV, left ventricular.

prothrombotic responses.<sup>23,24</sup> A recent population-based study comprising HF patients showed that HF patients had a higher risk of stroke compared with the general population.<sup>25</sup> There are arguments on antiplatelet or anticoagulation therapy in HF with sinus rhythm. In the Warfarin and Antiplatelet Therapy in Chronic Heart Failure trial, warfarin treatment had more favorable effect in reducing all strokes compared with aspirin ( $P=0.0163$ ) or clopidogrel ( $P=0.0164$ ).<sup>26</sup> In the Warfarin Versus Aspirin in Reduced Cardiac Ejection Fraction trial, the incidence of ischemic stroke

was significantly lower with warfarin treatment than that with aspirin treatment.<sup>27</sup> However, the use of warfarin can increase the risk of bleeding.<sup>27</sup> Therefore, with the proper identification of patients with high risk for stroke, the unnecessary use of anticoagulants and the bleeding complications associated with the anticoagulants can be reduced. In a previous meta-analysis, the annual incidence of stroke in patients with HF and sinus rhythm was 1.2%. In our study, the annual incidence of stroke was 1.60%. In patients with LAGLS <14.5%, the annual stroke incidence was 2.38%,

**Table 2. Univariate and Multivariate Analysis of the Prediction of Stroke**

Variable	HR	95% CI	P Value
Univariate analysis			
Age, y	1.022	1.006–1.038	0.005
Male sex	0.838	0.565–1.243	0.380
Body mass index, kg/m <sup>2</sup>	1.001	0.954–1.050	0.963
New York Heart Association functional class IV	1.534	0.995–2.365	0.053
Systolic blood pressure, mm Hg	1.004	0.997–1.011	0.267
Diastolic blood pressure, mm Hg	1.001	0.989–1.013	0.864
Heart rate, /min	1.001	0.992–1.010	0.881
Hypertension	1.285	0.857–1.927	0.225
Diabetes mellitus	1.552	1.044–2.307	0.030
Ischemic heart disease	1.275	0.853–1.905	0.236
Total cholesterol, mg/dL	0.996	0.991–1.001	0.088
Triglyceride, mg/dL	1.000	0.996–1.003	0.835
High-density lipoprotein-cholesterol, mg/dL	0.993	0.974–1.013	0.492
Hemoglobin, g/dL	1.002	0.895–1.122	0.975
Serum urea nitrogen, mg/dL	1.004	0.992–1.015	0.517
Creatinine, mg/dL	1.041	0.971–1.116	0.261
Glucose, mg/dL	1.002	0.999–1.004	0.140
LV end-diastolic dimension, mm	1.017	0.996–1.038	0.115
LV end-systolic dimension, mm	1.007	0.989–1.026	0.434
LV end-diastolic volume, mL	1.003	1.000–1.006	0.053
LV end-systolic volume, mL	1.003	1.000–1.007	0.058
LVEF, %	0.996	0.983–1.008	0.496
LA diameter, mm	1.032	1.007–1.056	0.010
LA volume index, mL/m <sup>2</sup>	1.007	1.002–1.012	0.007
Mitral E/E' ratio	1.001	0.982–1.021	0.907
Tricuspid regurgitation velocity, m/s	1.223	0.780–1.919	0.380
New-onset AF	2.494	1.635–3.805	<0.001
LAGLS (per 1% decrease)	1.040	1.017–1.064	0.001
Multivariate analysis			
Age, y	1.024	1.007–1.041	0.006
Diabetes mellitus	1.655	1.102–2.486	0.015
LA diameter, mm	1.015	0.989–1.043	0.253
New-onset AF	1.557	0.737–3.290	0.246
LAGLS (per 1% decrease)	1.038	1.012–1.064	0.003

AF indicates atrial fibrillation; EF, ejection fraction; HR, hazard ratio; LA, left atrial; LV, left ventricular; and LAGLS, left atrial global peak systolic longitudinal strain.

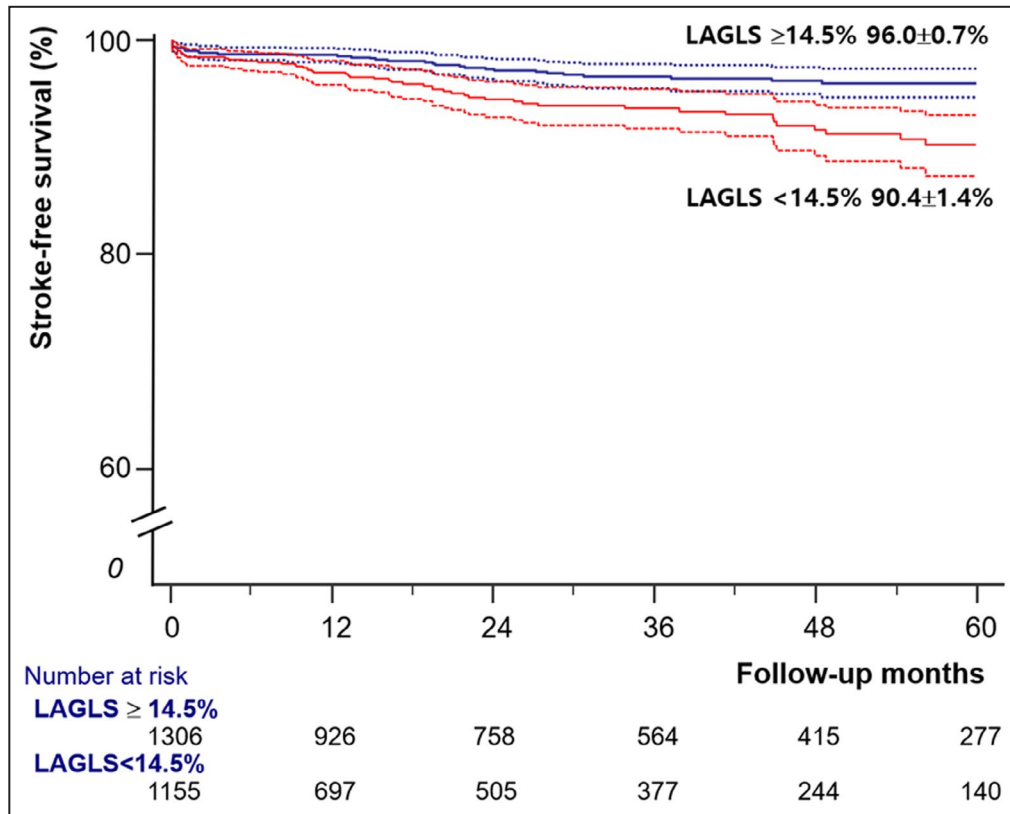
which corresponds to a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 2 to 3. Therefore, further studies are needed to verify the effectiveness of anticoagulation therapy in this group.

LA diameter and LA volume index were also significant predictors of stroke in our study. Although increased LA size and volume were associated with an increased risk of ischemic stroke,<sup>28,29</sup> the mechanisms related to LA enlargement and stroke events have not been fully evaluated. There are several possible hypotheses. First, LA enlargement may precede AF development.<sup>30</sup> In our previous study, we demonstrated that reduced LAGLS (<18.0%) and increased LA volume index were associated with increased risk of new-onset AF in patients with AHF.<sup>15</sup> Second, LA enlargement can be a marker of reduced LV diastolic filling and may promote blood stasis and thrombus formation.<sup>31</sup> Patients with HF have several risk factors of developing AF, and approximately 40% of people with either HF or AF will have the other disease category.<sup>32</sup> Furthermore, HF meets all the criteria of Virchow's triad, which leads to increased risk of thrombus formation. Third, increased LA size and volume can be associated with other risk factors including hypertension and atherosclerosis, which have increased risk of stroke.<sup>33</sup>

Fibrosis of the LA wall can result in LA dysfunction and is influenced by several biological factors, including energy metabolism, neurohumoral factors, and renin-angiotensin-aldosterone system.<sup>34</sup> Increased fibrosis of the LA can provoke AF, correlates with both persistence and burden of AF, and increase subsequent embolic risk. The decreased LA function and blood stasis in LA can increase the risk of thrombus and subsequent risk of embolic infarction.<sup>35</sup> Gadolinium-enhanced magnetic resonance imaging can be used for the detection and quantification of LA fibrosis, but methodological challenges limit its use.<sup>36</sup> Strain analysis can estimate the extent of LA fibrosis, and the lower LAGLS can represent a higher extent of fibrosis.<sup>37</sup> Decreased LAGLS can be used as a poor prognostic factor in several cardiovascular diseases.<sup>14,38</sup> Because LAGLS can detect subclinical LA dysfunction before the development of LA enlargement and may offer unique insights into LA pathophysiology, it is a more sensitive and reproducible marker of LA function than other echocardiographic volumetric indices.<sup>38,39</sup> Therefore, LA strain can be used as a prognostic marker for cryptogenic stroke.<sup>40–42</sup>

## Limitations

This study has several limitations. First, this study was limited by the inherent limitations of its retrospective nature. Thus, residual confounding variables may have affected our findings due to the observational nature of this study. Second, the incidence of stroke may have



**Figure 2.** Event-free survival curve according to a left atrial global longitudinal strain (LAGLS) of 14.5%.

In patients with acute heart failure and sinus rhythm, LAGLS <14.5% had significantly higher stroke risk ( $P < 0.001$  by log-rank test).

been underestimated in our study. In our study, we had 100 patients with stroke (4.1%) during the study period (mean  $30.3 \pm 25.4$  months). This result was similar to that of the previous study performed in Denmark. They found that the incidence of ischemic stroke in patients with HF and sinus rhythm was 1.54% during the first year after HF.<sup>25</sup> Therefore, we might identify nearly all episodes of stroke.

Third, whether a noncardiac source of emboli was identified in all patients with stroke was not confirmed. However, because the main etiology of stroke in HF patients with stroke is an ischemic etiology from the heart,<sup>10</sup> the proportion of nonischemic stroke may be low in our patients. Fourth, we identified the presence of stroke from their medical records during the regular clinical follow-up. Thus, there might be missed cases of stroke in this study. However, because most stroke patients are treated at nearby regional cardiocerebrovascular disease centers, and 3 hospitals in this registry are regional cardiocerebrovascular disease centers, the proportion of missed patients with stroke in this study might be small. Fifth, because this study cohort included only East Asian patients admitted for AHF, the results

may not be generalizable in different clinical settings or to those with other ethnicities.

## CONCLUSIONS

LAGLS was a good predictor of developing stroke despite other risk factors including age, diabetes mellitus, cholesterol concentration, LV volume, and LA volume index in AHF patients with sinus rhythms. In patients with LAGLS <14.5%, the annual stroke incidence was 2.38%.

## ARTICLE INFORMATION

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None.

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