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ORIGINAL RESEARCH

Clinical Usefulness of Left Ventricular Global Longitudinal Strain as a Predictor of Prognosis in Patients With Acute Ischemic Stroke (GLS-STROKE Study)

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BACKGROUND: The prognostic role of left ventricular global longitudinal strain (LV-GLS) in acute ischemic stroke (AIS) remains unexplored despite its established value in cardiovascular conditions. We aimed to investigate the prognostic value of LV-GLS in patients with AIS.

METHODS: In this prospective cohort study, 698 patients with AIS (mean age, 67.6±13.8 years; 60.2% men) underwent transthoracic echocardiography using speckle-tracking to measure LV-GLS within 7 days of admission. The primary end points included all-cause death and recurrent ischemic stroke, with a 3-month modified Rankin Scale score ≥3 considered a poor outcome.

RESULTS: Over a median follow-up of 593 days, the primary end point occurred in 65 patients (9.3%), with significant differences in LV-GLS between those reaching the end point (16.3%) and the others (19.1%; $P<0.001$). Cox regression demonstrated LV-GLS as a statistically significant predictor of outcomes (adjusted hazard ratio, 0.81 [95% CI, 0.74–0.89]; $P<0.001$). Additional analyses showed that LV-GLS enhanced predictive performance for the primary end point, indicated by improvements in global χ^2 and continuous net reclassification index analyses (0.25 [95% CI, 0.01–0.42]; $P=0.044$). Subgroup analysis revealed the prognostic relevance of LV-GLS irrespective of atrial fibrillation status. In predicting a poor functional outcome, LV-GLS also provided incremental value over traditional risk factors and the initial National Institutes of Health Stroke Scale score (continuous net reclassification index, 0.27 [95% CI, 0.09–0.45]; $P=0.004$).

CONCLUSIONS: LV-GLS is a robust predictor of cardiocerebrovascular outcomes in AIS and offers incremental prognostic value beyond traditional risk factors. Incorporating LV-GLS into AIS management may help identify high-risk patients and guide intensive monitoring strategies.

REGISTRATION: URL: https://trialsearch.who.int. Unique identifier: KCT0005780.

Key Words: cohort study ■ global longitudinal strain ■ ischemic stroke ■ left ventricular dysfunction ■ prognosis

Globally, stroke is the second-leading cause of death and the third most common cause of combined death and disability.[1] Over the past decade, stroke-related death has been steadily declining; however, health care expenditures associated with stroke have continued to increase.[1,2] Recurrence

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CLINICAL PERSPECTIVE

What Is New?

- This is the first large-scale prospective cohort study to investigate the prognostic value of left ventricular global longitudinal strain (LV-GLS) in patients with acute ischemic stroke.
- Impaired LV-GLS was independently associated with increased risk of all-cause death and recurrent ischemic stroke, regardless of atrial fibrillation status; LV-GLS provided incremental prognostic value beyond conventional parameters, including left ventricular ejection fraction and stroke severity indices.

What Are the Clinical Implications?

- Incorporating LV-GLS measurements in patients with acute ischemic stroke may help identify individuals at a higher risk of adverse outcomes who may benefit from closer follow-up and intensive management; LV-GLS assessment enables the detection of subclinical cardiac dysfunction, offering a more sensitive prognostic tool than ejection fraction in guiding poststroke care strategies.

Nonstandard Abbreviations and Acronyms

AIS	acute ischemic stroke
LV-GLS	left ventricular global longitudinal strain
mRS	modified Rankin Scale
NIHSS	National Institutes of Health Stroke Scale
TOAST	Trial of ORG 10172 in Acute Stroke Treatment

of ischemic stroke adversely affects patient prognosis and increases the mortality rate.[3] Previous studies have identified several clinical factors contributing to the occurrence and recurrence of ischemic stroke, including stroke subtype, age, hypertension, atrial fibrillation (AF), heart failure (HF), and diabetes.[2,4]

HF is also a risk factor for stroke and is associated with stroke recurrence and death.[5,6] Left ventricular (LV) global longitudinal strain (LV-GLS), a measure of myocardial deformation along the long axis of the left ventricle, is assessed using the speckle-tracking method. It is a sensitive measure of myocardial fiber shortening and has become a reliable parameter for evaluating subtle systolic dysfunction.[7] In patients with acute HF, LV-GLS is frequently reduced regardless of the LV ejection fraction (LVEF), the traditional measure of LV systolic function. LV-GLS has also been shown to be a superior prognostic marker for death than LVEF.[8] Furthermore, in severe mitral regurgitation and severe aortic stenosis, LV-GLS has proven useful as a predictor of postoperative outcomes and a tool for identifying patients who may benefit from early surgical intervention.[9,10] Recent research has demonstrated that LV-GLS can effectively predict incident strokes in patients who are stroke naïve.[11] However, to date, no study has evaluated the prognostic implications of LV-GLS in patients with acute ischemic stroke (AIS) about subsequent cardiovascular outcomes. In this study, we aimed to investigate the prognostic utility of LV-GLS, a novel marker of subclinical LV dysfunction, in patients with AIS.

METHODS

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Participants

This prospective observational cohort study was conducted at Yongin Severance Hospital, a referral hospital (URL: https://trialsearch.who.int; unique identifier: KCT0005780). Eligible participants were patients with AIS hospitalized within 7 days of onset between January 2021 and June 2024, who underwent transthoracic echocardiography within 1 week of admission. During the study period, 768 patients with acute stroke underwent transthoracic echocardiography during hospitalization. Of these, 44 patients who underwent transthoracic echocardiography >7 days after admission and 5 diagnosed with transient ischemic attack were excluded during the screening. Of the 719 patients who provided consent and were enrolled, 21 were subsequently excluded on the basis of the assessment of neurologists who deemed them unsuitable for inclusion in the study. Thus, 698 patients were included in the final analysis (Figure S1). The enrolled patients underwent follow-up assessments at 6 months and 1 year after discharge, followed by annual follow-up. If an outpatient visit occurred within 3 months before or after the scheduled annual follow-up, the visit date was used as a substitute. For patients with irregular outpatient visits, follow-up evaluations were conducted via telephone interviews. All patients were tracked through outpatient visits or telephone calls. Patients who could not be contacted were censored at their last outpatient visit or their most recent successful telephone call. This study was approved by the institutional review board of our hospital (No. 9–2020-0150). Written informed consent was obtained from all participants or their legal guardians before inclusion in the study.

Data Collection

Demographic data; medical, social, and medication history; and laboratory findings were collected. Information on whether intravenous thrombolysis was administered or endovascular thrombectomy was performed was also gathered. Blood pressure and heart rate measurements obtained before transthoracic echocardiography were used. When such measurements were unavailable, vital signs recorded on the morning of the same day were used. Initial stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) score at admission. The presence of AF was determined on the basis of findings from electrocardiography or 24-hour Holter monitoring performed during hospitalization. The modified Rankin Scale (mRS) was evaluated at discharge and 3 months after discharge.

Standard 2-dimensional echocardiographic parameters were obtained at rest using Vivid E9/E95 systems (GE Healthcare, Chicago, IL) and were measured in accordance with the guidelines of the American Society of Echocardiography.[12] LVEF was measured using the biplane Simpson's disc summation method. According to the latest guidelines, a cutoff of ≥50% for LVEF was used for the analysis.[13]

LV-GLS Measurement

LV-GLS was measured using speckle-tracking echocardiography in accordance with the guidelines.[14] The measurements were performed offline at a core laboratory using a vendor-independent postprocessing software (TomTec Arena TTA 2.51 Ultrasound Workspace; TOMTEC Imaging Systems GmbH, Munich, Germany), with the operators blinded to clinical data. Briefly, endocardial borders of the left ventricle were manually delineated on end-systolic frames in the apical 4-chamber, 2-chamber, and 3-chamber views during the LV-GLS measurement. End-systole was defined as the cardiac cycle point with the smallest LV volume. The software tracked speckles along the endocardial border and within the myocardium throughout the cardiac cycle. The LV-GLS was calculated as the average of the global longitudinal strain values obtained from the apical views. As LV-GLS represents myocardial shortening, it is expressed as a negative value. To avoid confusion and facilitate comparison, absolute values are used throughout the article, with lower values consistently described as indicating "reduced" or "impaired" LV systolic function.

Outcomes

The primary end point was a composite of all-cause death and hospitalization due to recurrent ischemic stroke. The secondary outcomes included individual events of all-cause death and recurrent ischemic stroke. The index date was defined as the date of the first hospitalization due to AIS. Recurrent stroke was defined as a new hospitalization for ischemic stroke symptoms after the index event, accompanied by brain magnetic resonance imaging findings consistent with the new symptoms. Patients were followed until the occurrence of the primary composite end point or August 31, 2024, whichever came first. In addition, an mRS score of ≥3 (loss of functional independence) at 3 months was considered a poor functional outcome. Outcomes were assessed through physician interviews, review of medical records, and follow-up telephone interviews conducted by a trained clinical research nurse in a blinded manner.

Statistical Analysis

The participants were categorized into 2 groups based on the primary end point. Continuous variables are reported as mean±SD or median (interquartile range), depending on the data distribution. Categorical variables are summarized as numbers (percentages) and were compared using either the χ^2 test or Fisher's exact test, as appropriate. To assess the ability to discriminate between patients with and without the primary end point, receiver operating characteristic curve analysis was performed for the primary end point. Area under the curve (AUC) comparisons between the models were conducted using the DeLong method. The Youden index was used to determine the optimal cutoff value for LV-GLS.[15]

Cumulative incidence curves for the outcomes were generated for survival analysis. Differences between groups were assessed using the log-rank test. Missing data were imputed using the missForest algorithm.[16] To evaluate the incremental prognostic value of LV-GLS, sequential Cox regression models were constructed: model 1 (including LV-GLS, age, and sex), model 2 (model 1 with the addition of clinical variables), and model 3 (model 2 with the inclusion of laboratory variables). The incremental contribution of LV-GLS in predicting the primary end point was assessed through changes in global χ^2 values from the likelihood ratio test, which was applied sequentially across models incorporating demographic variables (model A), clinical variables (model B), laboratory data (model C), and LV-GLS (model D). To measure the improvement in prediction performance with the addition of LV-GLS, we calculated the continuous net reclassification index between the models. Several logistic regression models were constructed to predict an mRS score of ≥3 at 3 months, and their predictive performance was compared using AUCs. The incremental value of LV-GLS was further evaluated with the continuous net reclassification index. Subgroup analyses were prespecified to evaluate the consistency of the association between LV-GLS and outcomes across

clinically relevant subgroups, including age (<65 versus ≥65 years), sex, history of hypertension, diabetes, AF, initial NIHSS score (<5 versus ≥5), and LVEF (<50% versus ≥50%). All statistical analyses were performed using R software version 4.2.2 (R Development Core Team, Vienna, Austria). A 2-sided *P* value of <0.05 was considered statistically significant.

RESULTS

Baseline Characteristics and Echocardiographic Parameters of the Study Participants

Among the 698 patients (mean age, 67.6±13.8 years), 420 (60.2%) were men, 417 (59.7%) had hypertension, and 186 (26.6%) had diabetes. During a median follow-up of 593 (interquartile range, 226–906) days, the primary composite end point was observed in 65 cases (9.3%): 28 cases of all-cause death and 44 cases of recurrent ischemic stroke. Three patients experienced both recurrent ischemic stroke and all-cause death. For these cases, the initial event of hospitalization due to stroke was considered in the primary end point analysis. The baseline characteristics stratified by LV-GLS <18% versus ≥18% are presented in Table 1. Overall, patients with LV-GLS <18% were older; had more severe strokes; underwent endovascular thrombectomy more frequently; and had higher rates of hypertension, AF, and coronary artery disease than those with LV-GLS ≥18%. Among the laboratory findings, the LV-GLS <18% group exhibited lower estimated glomerular filtration rate, higher levels of C-reactive protein and NT-proBNP (N-terminal pro-B-type natriuretic peptide). The median interval between hospital admission and echocardiography was 2 (interquartile range, 1–3) days. The mean LVEF, a conventional indicator of systolic function, was 61.2±7.6%, and patients with LV-GLS <18% had lower LVEF compared with those with LV-GLS ≥18% (Table 1).

Predictive Performance of LV-GLS for the Primary End Point

The mean LV-GLS was 18.8±2.9%. Patients who reached the primary end point had a more impaired LV-GLS than those who did not (16.3±3.3 versus 19.1±2.7%; *P*<0.001). When constructing the receiver operating characteristic curve for the primary end point (Figure 1), the AUC for LV-GLS (0.753 [95% CI, 0.689–0.818]) was higher than that for the mRS score at discharge (0.563 [95% CI, 0.483–0.643]) or the initial NIHSS score (0.579 [95% CI, 0.497–0.661]; all *P* for difference <0.001). Based on the Youden's index, an LV-GLS of 18% was the optimal cutoff, and the sensitivity and specificity at the cutoff were 64.6% and 71.2%, respectively. In the Kaplan–Meier curves for the primary end point, patients with an LV-GLS <18% had a significantly higher incidence of the primary end point than those with an LV-GLS ≥18% (log-rank *P*<0.001; Figure 2A). Furthermore, the LV-GLS <18% group had higher rates of all-cause death and recurrent ischemic stroke than those of the LV-GLS ≥18% group (all log-rank *P*<0.001; Figure 2B and 2C). In contrast, no significant difference was observed in the incidence of the primary end point between the patient groups based on an LVEF threshold of 50% (log-rank *P*=0.700; Figure 2D).

Prognostic Significance and Incremental Prognostic Value of LV-GLS

Univariable and multivariable Cox regression analyses were performed for the primary end point (Table 2). In the univariable Cox regression analysis, higher LV-GLS, as a continuous variable, was identified as a significant prognostic marker for the primary end point. A spline regression curve revealed an inverse relationship between the risk of the primary end point and LV-GLS (Figure S2). This finding remained consistent in the multivariable Cox regression model, adjusting for demographic, clinical, and laboratory variables (adjusted hazard ratio per 1% increase of LV-GLS: 0.81 [95% CI, 0.74–0.89] Table 2).

To evaluate the incremental value of LV-GLS, several Cox models were constructed, and the improvement in global chi-square values was assessed. Compared with model A, which included age at enrollment and sex, model B, which incorporated the initial NIHSS score and mRS score at discharge, demonstrated superior predictive power for the primary end point. Although model C, which included additional clinical and laboratory variables, showed only a numerical improvement in global χ^2 values (*P*=0.072). However, model D, which incorporated LV-GLS, exhibited incremental value in predicting the primary end point compared with the other models. In the continuous net reclassification index analysis to assess the improvement in prediction performance with the addition of LV-GLS, model D, which included LV-GLS, demonstrated better performance in predicting the primary end point than model C (*P*=0.044; Figure 3).

LV-GLS as a Predictor of Functional Outcome at 3 Months

Among the study participants, additional functional outcome analyses were conducted for 657 patients (94.1%) whose 3-month mRS data were available. Among these, 150 patients (22.8%) had a poor outcome at 3 months (mRS score ≥3), and their LV-GLS

Table 1. Baseline Characteristics of Study Participants

	LV-GLS ≥18% (n=474)	LV-GLS <18% (n=224)	Total population (n=698)	*P* value
Demographics				
Age, y	66.4±13.3	70.2±14.5	67.6±13.8	0.001
Male sex	286 (60.3)	134 (59.8)	420 (60.2)	0.962
Body mass index, kg/m^2	24.3±3.3	24.6±3.5	24.4±3.4	0.332
Systolic blood pressure, mm Hg	140.0±20.9	142.2±24.4	140.7±22.1	0.252
Diastolic blood pressure, mm Hg	82.6±13.7	86.4±15.7	83.8±14.5	0.002
Initial NIHSS score	3.5±4.0	6.4±6.7	4.4±5.2	<0.001
Comorbidities				
Hypertension	268 (56.5)	149 (66.5)	417 (59.7)	0.015
Diabetes	128 (27.0)	58 (25.9)	186 (26.6)	0.827
Chronic kidney disease	16 (3.4)	15 (6.7)	31 (4.4)	0.073
Coronary artery disease	25 (5.3)	32 (14.3)	57 (8.2)	<0.001
Previous stroke	78 (16.5)	34 (15.2)	112 (16.0)	0.750
AF	31 (6.5)	62 (27.7)	93 (13.3)	<0.001
Current smoker	120 (25.3)	52 (23.2)	172 (24.6)	0.612
Medication history				
Antiplatelets	111 (23.4)	58 (26.0)	169 (24.2)	0.516
Renin–angiotensin–aldosterone system inhibitor	143 (30.2)	94 (42.0)	237 (34.0)	0.003
β blocker	44 (9.3)	48 (21.4)	92 (13.2)	<0.001
Calcium channel blocker	144 (30.4)	81 (36.2)	225 (32.2)	0.150
Anticoagulants	11 (2.3)	16 (7.1)	27 (3.9)	0.004
Laboratory findings				
Hemoglobin, g/dL	13.6±1.7	13.4±2.2	13.6±1.9	0.246
Estimated glomerular filtration rate, mL/min per 1.73 m^2	87.7±20.7	79.8±23.8	85.2±22.0	<0.001
Triglyceride, mg/dL	123.6±92.9	129.9±144.1	125.6±111.6	0.554
High-density lipoprotein cholesterol, mg/dL	47.4 ± 13.9	45.5 ± 13.2	46.8 ± 13.7	0.090
Low-density lipoprotein cholesterol, mg/dL	110.8 ± 16.1	110.5 ± 13.5	110.7 ± 15.3	0.797
C-reactive protein, mg/dL	3.8±10.4	10.1±28.1	5.8±18.3	0.001
Troponin T, pg/mL	11.4±11.0	53.2±304.4	24.9±173.6	0.053
NT-proBNP, pg/mL	267.8±648.6	1622.4±3863.6	708.4±2350.4	<0.001
LVEF, %	63.9±4.6	55.4±9.4	61.2±7.6	<0.001
Intravenous thrombolysis	29 (6.1)	24 (10.7)	53 (7.6)	0.047
Endovascular thrombectomy	28 (5.9)	39 (17.4)	67 (9.6)	<0.001
mRS score at discharge	1.7±1.4	2.3±1.6	1.9±1.5	<0.001

Data are presented as n (%) or mean±SD.

AF indicates atrial fibrillation; LVEF, left ventricular ejection fraction; LV-GLS, left ventricular global longitudinal strain; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; and NT-proBNP, N-terminal pro-B-type natriuretic peptide.

values were significantly lower than those in the group with an mRS score of <3 (17.8±3.1% versus 19.2±2.8%, *P*<0.001; Figure S3). Several binary logistic regression models were constructed to predict an mRS score of ≥3 at 3 months, and their AUCs were calculated. Compared with model 1′, which included demographic, clinical, and laboratory variables, model 2′, which additionally incorporated the initial NIHSS score, demonstrated superior performance in predicting an mRS score of ≥3 at 3 months (*P*<0.001). No significant difference in the AUC was observed when comparing the performance of models 2′ and 3′ (addition of LV-GLS; *P*=0.184); however, the continuous net reclassification index (0.268 [95% CI, 0.087–0.449]) highlighted the improvement in predictive performance with LV-GLS (Table 3 and Figure S4).

Subgroup Analyses

Subgroup analyses showed that the association between lower LV-GLS and increased risk of the primary composite end point was consistent across a wide range of clinical subgroups, including age, sex, hypertension, diabetes, coronary artery disease, AF, chronic

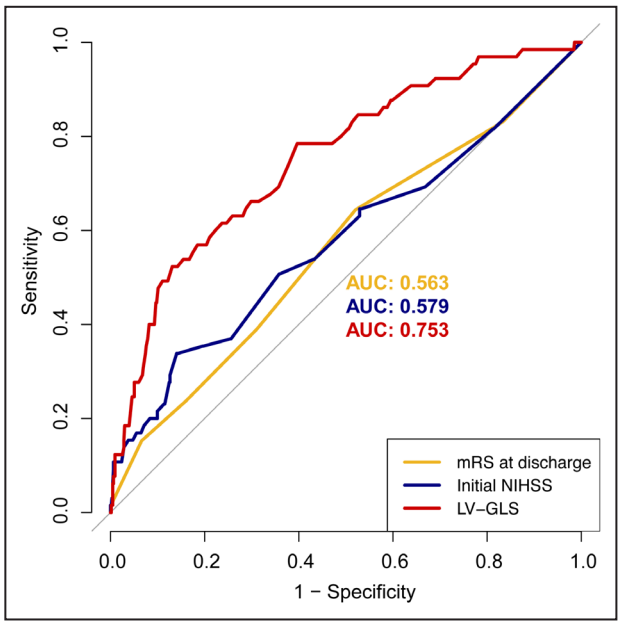

Figure 1. Receiver operating characteristic curves of LV-GLS, initial NIHSS score, and mRS score at discharge for the primary end point.
AUC indicates area under the curve; LV-GLS, left ventricular global longitudinal strain; mRS, modified Rankin Scale; and NIHSS, National Institutes of Health Stroke Scale.

kidney disease, stroke severity (using an NIHSS cutoff score of 5), and stroke classification. While statistical significance was not reached in the coronary artery disease subgroup, likely due to the limited sample size, the direction of association remained uniform. Importantly, no significant interactions were observed in any subgroup, indicating that the prognostic value of LV-GLS was consistent regardless of baseline characteristics (Figure 4). When stratified by the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) stroke classification, LV-GLS demonstrated a consistent association with the primary composite end point across subgroups. Although statistical significance was not observed for all stroke subtypes, the direction of association remained uniform, and no significant interaction was found (Table S1).

DISCUSSION

In this study, we evaluated the prognostic utility of LV-GLS in patients with AIS. The findings suggest that impaired LV-GLS was significantly associated with a higher incidence of all-cause death and recurrent ischemic stroke, regardless of AF status. LV-GLS was also closely associated with functional independence at 3 months. Moreover, LV-GLS demonstrated incremental value over conventional measures, such as LVEF, NIHSS score, and mRS score at discharge, in predicting the primary end point (death and recurrent ischemic stroke). These results collectively highlight the value of assessing subclinical LV systolic function, as determined by LV-GLS, in optimizing risk stratification and guiding management strategies for patients with AIS.

HF is a major risk factor for AIS, and the prognosis is known to be worse when AIS and HF coexist.[17,18] LVEF is the most widely used parameter for assessing systolic function in echocardiography. Patients with AIS, comorbid HF, and reduced LVEF have more than double the risk of in-hospital and overall death compared with those without HF.[19,20] One of the current clinical classifications of HF, HF with reduced ejection fraction, applies to patients with an LVEF <40%. Numerous studies and therapeutic strategies have focused on this patient population. Consequently, several studies investigating AIS have used an LVEF <40% as the cutoff to define LV systolic dysfunction.[19–22] However, recent AIS registries have suggested that the proportion of patients with reduced LVEF is relatively low. One cohort reported that only 3.7% of patients had an LVEF <40%, and another cohort indicated that only 4.5% had an LVEF <55%.[23,24] Previous studies have indicated that an LVEF <40% itself has limited prognostic value, with significant associations with stroke observed only in cases of severe HF, wherein patients have LVEFs <15%.[25] While a severely reduced LVEF increases the likelihood of LV thrombus formation and subsequent cerebral embolism, a mildly reduced LVEF may not share these stroke mechanisms, leading to a weaker predictive power for stroke risk.[11] Furthermore, in the current study, the LVEF did not significantly differ between the group that reached the primary end point and the group that did not.

LV-GLS has the advantage of directly measuring myocardial deformation, enabling earlier detection of myocardial dysfunction in subclinical states compared with LVEF, which is derived from the geometric deformation of the endocardium.[7] In a large-scale study involving 4312 patients hospitalized with acute HF, LV-GLS demonstrated a superior predictive value for death compared with LVEF, as evidenced by a higher c-statistic and a more pronounced inverse relationship between cardiac function and death in a restricted cubic spline analysis.[8] Although LVEF and LV-GLS showed a moderate correlation, LV-GLS values varied widely for a given LVEF. Notably, in patients with myocardial disease severe enough to require hospitalization due to HF, including those with HF with preserved ejection fraction and an LVEF >50%, the average LV-GLS was significantly reduced to 15.2%. Global longitudinal strain has also been suggested to facilitate the detection of subclinical myocardial dysfunction in valvular heart diseases.[23,26,27] When myocardial dysfunction becomes overt due to chronic volume overload, postoperative outcomes deteriorate, with an

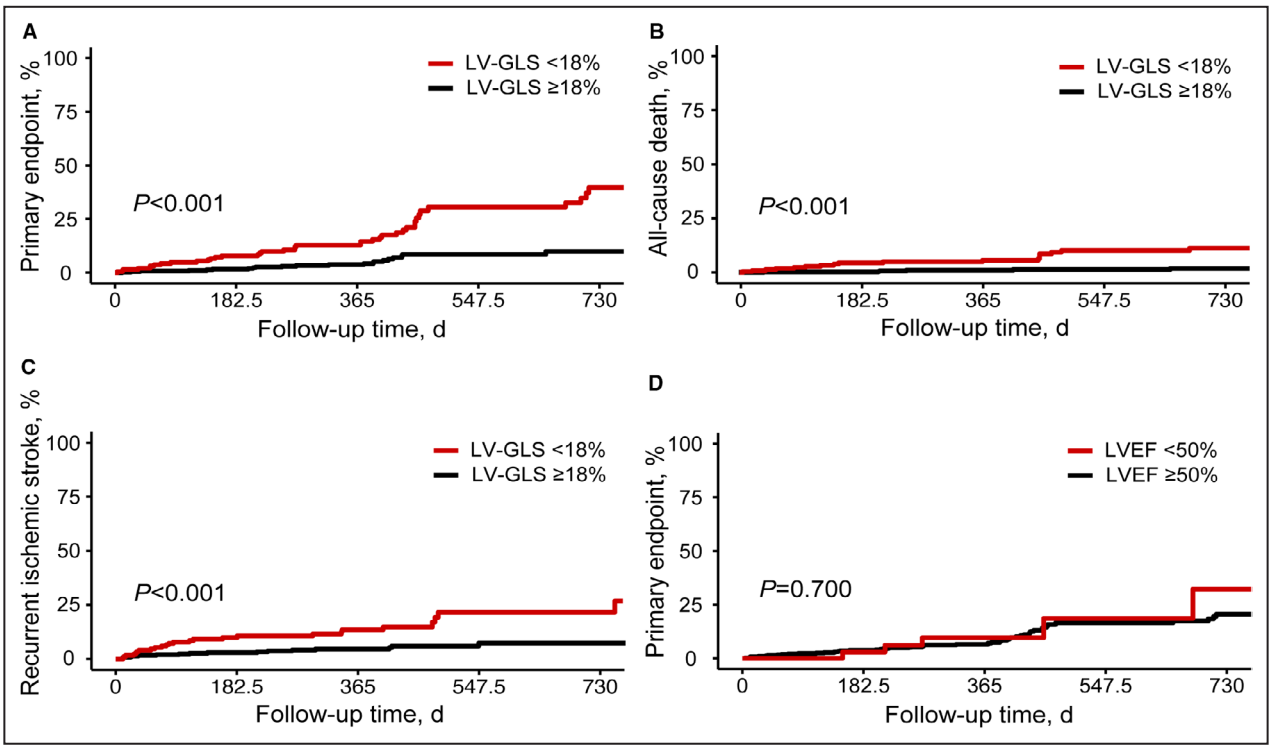

Figure 2. Cumulative incidence curves of the primary end point according to LV-GLS of 18% (A), cumulative incidence of all-cause death (B), and recurrent ischemic stroke (C) according to LV-GLS of 18%, and cumulative incidence of the primary end point according to LVEF of 50% (D).
LVEF indicates left ventricular ejection fraction; and LV-GLS, left ventricular global longitudinal strain.

associated increase in death. Experimental studies have demonstrated a strong correlation between LV-GLS and myocardial fibrosis.[28] This correlation highlights the ability of LV-GLS to detect subtle systolic dysfunction caused by myocardial fibrosis earlier than LVEF, supporting its role in determining the optimal timing for surgery. Importantly, a prospective cardiac magnetic resonance imaging study in patients with AIS demonstrated a significant association between reduced LV-GLS and the presence of myocardial fibrosis, as indicated by late gadolinium enhancement.[29]

Table 2. Cox Regression Analysis With Sequential Adjustments for LV-GLS to Predict the Primary End Point

Model	HR (95% CI)	*P* value
LV-GLS* (unadjusted)	0.81 (0.77–0.87)	<0.001
Model 1 (adjusted for age, sex)	0.82 (0.77–0.88)	<0.001
Model 2 (model 1+clinical variables†)	0.81 (0.75–0.89)	<0.001
Model 3 (model 2+laboratory variables‡)	0.81 (0.74–0.89)	<0.001

HR, hazard ratio; and LV-GLS, left ventricular global longitudinal strain.
*Per 1% increase.
†Hypertension, diabetes, chronic kidney disease, coronary artery disease, history of previous stroke, atrial fibrillation, initial National Institutes of Health Stroke Scale score, and modified Rankin Scale score at discharge.
‡Hemoglobin, glomerular filtration rate, C-reactive protein, and N-terminal pro-B-type natriuretic peptide.

This finding, along with findings from a recent meta-analysis, underscores the prognostic value of LV-GLS across diverse cardiovascular populations and supports our results showing that impaired LV-GLS reflects underlying myocardial disease and is associated with adverse outcomes in patients with AIS.[30]

According to earlier guidelines, the normal reference value for LV-GLS was <20%[12]; however, recent cohort studies suggest a lower threshold of <16%.[7,31] In the present study, the mean LV-GLS in the primary end point group was 16.3%, with a cutoff of 18%, slightly higher than the current reference standard. A previous small-scale study involving 29 patients with AIS reported a mean LV-GLS of 18.8% on day 10 of hospitalization.[32] Similarly, in a large cohort of 900 patients with AIS, the mean LVEF was 65.7%, exceeding the normal reference range of 50% to 55%.[23] This augmented cardiac function compared with established normal references may be attributed to enhanced sympathetic activity, which serves as a compensatory mechanism to improve perfusion in ischemic regions during the acute ischemic stage.[33] Despite this neurohumoral activation, we found that patients with myocardial disease who failed to achieve compensatory hypercontraction during AIS experienced worse outcomes after discharge. These findings align with the concept of stroke–heart syndrome, which encompasses

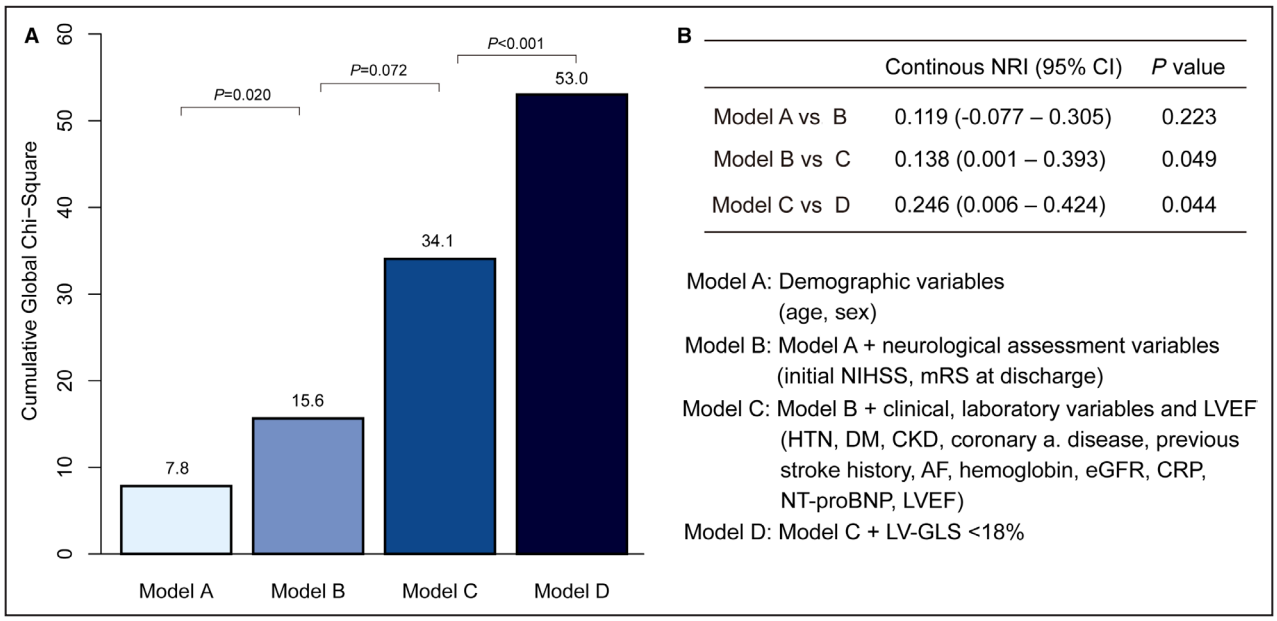

Figure 3. Incremental value of the LV-GLS over demographic, clinical, and laboratory variables for predicting the primary end point by (A) improvement of global χ2 changes in sequential Cox analysis and (B) continuous net reclassification index. Model A: age and sex; model B: model A+initial NIHSS, mRS at discharge; model C: model B+clinical and laboratory variables*; model D: model C+LV-GLS. AF indicates atrial fibrillation CKD, chronic kidney disease; CRP, C-reactive protein; DM, diabetes; eGFR, estimated glomerular filtration rate; HTN, hypertension; LVEF, left ventricular ejection fraction; LV-GLS, left ventricular global longitudinal strain; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; NRI, net reclassification index; and NT-proBNP, N-terminal pro-B-type natriuretic peptide. *Hypertension, diabetes, chronic kidney disease, coronary artery disease, history of previous stroke, atrial fibrillation, hemoglobin, glomerular filtration rate, C-reactive protein, NT-proBNP, left ventricular ejection fraction.

a spectrum of cardiac abnormalities triggered by acute brain injury, including subclinical dysfunction.[34] Recognizing this LV-GLS–detected dysfunction as a manifestation of the broader stroke–heart syndrome underscores the importance of intensive monitoring and proactive follow-up in patients with AIS, with the ultimate goal of improving long-term outcomes.

From a translational perspective, patients with AIS with significantly impaired LV-GLS may benefit from a more tailored management strategy. For example, patients whose LV-GLS falls below the established cutoff could be scheduled for short-term follow-up visits to monitor clinical status, assess medication adherence, and undergo more frequent imaging or laboratory evaluations. This approach is analogous to current practice in the cardio-oncology field, where HF medications are initiated even in asymptomatic patients when a significant decline in LV-GLS is observed during chemotherapy. Similarly, in selected patients with AIS with impaired LV-GLS, initiating HF therapy may be considered, particularly when accompanied by other risk factors or signs of subclinical dysfunction. These strategies highlight the potential of LV-GLS as a prognostic tool and marker guiding individualized management in AIS care. Although LV-GLS assessment is not yet routinely incorporated into clinical care for patients with

Table 3. Incremental Value of LV-GLS Compared With Traditional Variables for Predicting the 3-Month mRS Score ≥3

	Area under the curve		Continuous net reclassification index	
	95% CI	*P* value for difference	95% CI	*P* value for difference
Model 1′ (demographic, clinical, and laboratory variables*)	0.714 (0.666–0.763)			
Model 2 (model 1′+initial NIHSS)	0.797 (0.756–0.838)	<0.001†	0.687 (0.513–0.861)†	<0.001†
Model 3′ (model 2′ +LV-GLS)	0.806 (0.766–0.845)	0.184‡	0.268 (0.087–0.449)‡	0.004‡

LV-GLS indicates left ventricular global longitudinal strain; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.
*Age, sex, hypertension, diabetes, chronic kidney disease, coronary artery disease, previous stroke, atrial fibrillation, hemoglobin, C-reactive protein, N-terminal pro-B-type natriuretic peptide.
†Comparison with model 1′ and model 2′.
‡Comparison between model 2′ and model 3′.

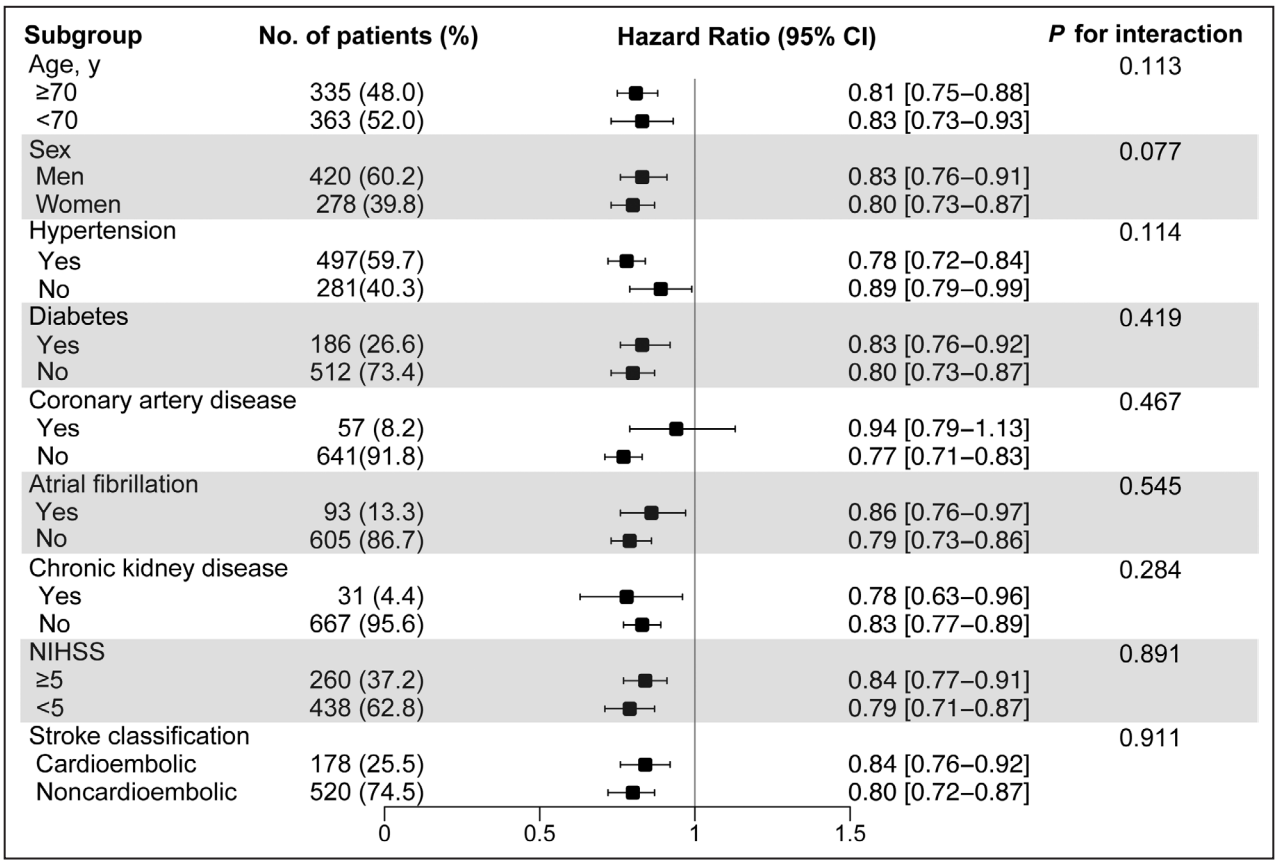

Figure 4. Subgroup analyses of the association between LV-GLS and the primary composite end point.
LV-GLS indicates left ventricular global longitudinal strain; and NIHSS, National Institutes of Health Stroke Scale.

AIS, the prognostic insights offered by this parameter may serve as the basis for future risk-stratification models. This represents an important translational opportunity, where echocardiographic data could guide clinical decision making and potentially shape future guideline recommendations.

This study is significant as the first prospective investigation to evaluate the impact of cardiac function on outcomes in patients with AIS. Furthermore, this is the largest prospective study to date in terms of LV-GLS measurements in hospitalized patients with AIS. The collaboration between cardiologists and neurologists in prospectively collecting research data ensured high accuracy in critical variables, including the NIHSS, mRS, and LV-GLS. Another strength of this study is the demonstration of the utility of LV-GLS in a subgroup of patients without AF. However, this study has certain limitations. First, it was a single-center study involving a homogeneous ethnic population, which may limit its generalizability. While this design provides internal consistency, it may restrict the applicability of our findings to broader clinical settings. External validation in multicenter, multiethnic cohorts is warranted. Second, the LV-GLS cutoff has not been externally validated. Nevertheless, Cox regression analysis addressed this limitation by analyzing LV-GLS as a continuous variable. Third, the study predominantly enrolled patients with relatively mild stroke, as reflected by an average initial NIHSS score of 4.4. Finally, the study is limited by the lack of discussion on potential strategies to improve outcomes based on the findings. Further research is warranted to address these limitations.

CONCLUSIONS

LV-GLS is an independent predictor of all-cause death and recurrent ischemic stroke in patients with AIS, demonstrating incremental prognostic value beyond established risk factors. Evaluating LV-GLS in this population may facilitate the identification of high-risk individuals who would benefit from intensive monitoring, ultimately contributing to the prevention of future cardiocerebrovascular events.

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Supplemental Material

Data S1.
Figures S1–S4.

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