

## Echocardiographic Abnormalities and Determinants of 1-Month Outcome of Stroke Among West Africans in the SIREN Study

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**Background**—Little is known about the relationship between echocardiographic abnormalities and outcome among patients with acute stroke. We investigated the pattern and association of baseline echocardiographic variables with 1-month disability and mortality among patients with stroke in the SIREN (Stroke Investigative Research and Education Network) study.

**Methods and Results**—We enrolled and followed up consecutive 1020 adult patients with acute stroke with baseline transthoracic echocardiography from west Africa. To explore the relationship between echocardiographic variables and 1-month disability (using modified Rankin scale >3) and fatality, regression models were fitted. Relative risks were computed with 95% CIs. The participants comprised 60% men with a mean age of  $59.2 \pm 14.6$  years. Ischemic stroke was associated with smaller aortic root diameter (30.2 versus 32.5,  $P=0.018$ ) and septal (16.8 versus 19.1,  $P<0.001$ ) and posterior wall thickness at systole (18.9 versus 21.5,  $P=0.004$ ). Over 90% of patients with stroke had abnormal left ventricular (LV) geometry with eccentric hypertrophy predominating (56.1%). Of 13 candidate variables investigated, only baseline abnormal LV geometry (concentric hypertrophy) was weakly associated with 1-month disability (unadjusted relative risk, 1.80; 95% CI, 0.97–5.73). Severe LV systolic dysfunction was significantly associated with increased 1-month mortality (unadjusted relative risk, 3.05; 95% CI, 1.36–6.83).

**Conclusions**—Nine of 10 patients with acute stroke had abnormal LV geometry and a third had systolic dysfunction. Severe LV systolic dysfunction was significantly associated with 1 month mortality. Larger studies are required to establish the independent effect and unravel predictive accuracy of this association. (*J Am Heart Assoc.* 2019;8:e010814. DOI: 10.1161/JAHA.118.010814.)

**Key Words:** echocardiography • left ventricular geometry • morbidity/mortality • stroke

Africa is undergoing sociodemographic and lifestyle changes leading to epidemiological transition, which is currently driving an increased burden of stroke in the region.<sup>1,2</sup> Ischemic stroke includes cardioembolic stroke and accounts for about 20% of all strokes.<sup>3,4</sup> While atrial fibrillation, which accounts for half of all cardioembolic strokes,<sup>5</sup> can be diagnosed with electrocardiography, other

nonarrhythmic cardioembolic diseases and cryptogenic stroke require echocardiography. Although transesophageal echocardiography is more sensitive in excluding intracardiac/left atrial appendage clot in cardioembolic stroke, transthoracic echocardiography is more widely available and is more commonly used in low-resource settings such as sub-Saharan Africa.<sup>6</sup> Certain transthoracic echocardiography features such

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## Clinical Perspective

### What Is New?

- The role of echocardiography in the management of acute stroke among African populations has not been well studied.
- Nine of 10 patients with acute stroke of African descent had abnormal left ventricular geometry and a third had left ventricular systolic dysfunctions.
- Patients with acute stroke with severe left ventricular systolic function were 3 times at risk of 1-month mortality.

### What Are the Clinical Implications?

- Routine echocardiographic diagnosis and management of cardiac dysfunction during acute stroke may be helpful in preventing worse outcome.

as left atrial volume, spontaneous echo contrast or “smoke,” increased left ventricular (LV) mass, and poor LV functions have been previously associated with stroke and stroke outcome.<sup>7</sup> Early detection of these conditions may be of therapeutic value in the management of stroke. Despite the aforementioned, the current recommendations for the management of acute stroke does not consider echocardiography as an essential test in patients with stroke.<sup>8</sup> This may be the result of global dearth of data on the usefulness of echocardiography in the management of stroke. Therefore, the purpose of this study was to describe the pattern of echocardiographic abnormalities and predictors of outcome in a large cohort of indigenous Africans with acute stroke.

## Methods

### Data Availability

The data, methods used in analysis, and materials that support the findings of this study are available from the corresponding author upon reasonable request.

### Study Design

The SIREN (Stroke Investigative Research and Education Network) study is a multicenter case-control investigation that involves 15 sites in Ghana and Nigeria. The details of the study protocol have been published elsewhere.<sup>9</sup> Participants who were 18 years and older with clinical (within 8 days of current symptoms onset) and radiological evidence of stroke were consecutively recruited. Using a pretested case report form completed by trained research assistants and clinicians, basic demographic and lifestyle data including ethnic origin of the participants, socioeconomic status, and anthropometric measurements were obtained. The current analysis was

restricted to 1020 participants with stroke who completed echocardiographic assessment at baseline. We used validated instruments such as the Stroke Leivity Scale, modified Rankin Scale (mRS), modified National Institute of Health Stroke Scale (NIHSS), and Barthel Index to assess stroke outcome. In this report, 30-day functional outcome was measured using the mRS. Poor outcome was defined as an mRS >3. Lipid profile and other clinical and laboratory information were obtained according to the SIREN protocol.<sup>9</sup>

Metabolic syndrome was defined according to International Diabetic Federation criteria by the presence of waist circumference  $\geq 94$  cm in men and  $\geq 80$  cm in women and any 2 of the following characteristics: triglycerides  $\geq 150$  mg/dL, high-density lipoprotein cholesterol  $< 40$  mg/dL in men and  $< 50$  mg/dL in women, blood pressure  $\geq 130/85$  mm Hg, and fasting glucose  $\geq 100$  mg/dL.

## Echocardiography

Experienced cardiologists at the participating centers performed transthoracic echocardiographic examination of patients in a partial left lateral decubitus position using machines equipped with a 3.5-MHz transducer. Standard echocardiographic measurements were obtained in accordance with the guidelines of the American Society of Echocardiography (ASE) and European Association of Cardiovascular Imaging.<sup>10</sup> Two-dimensional guided M-mode echocardiograms were obtained according to the recommendations of the committee on M-mode standardization of the ASE.<sup>11</sup> Left atrial end-systolic diameter was assessed from the trailing edge of the posterior aortic–anterior left atrial complex.<sup>12,13</sup>

LV mass was calculated using the formula of Devereux and Reichek<sup>14</sup>:  $LV\ mass = 0.8 \{ 1.04 [(IVS + LVIdD + PWTd)^3 - (LVIdD)^3] + 0.6$ ; where LVIdD=LV internal diameter in end diastole, PWTd=LV posterior wall thickness in end diastole, and IVSTd=interventricular septal wall thickness in end diastole. Measurements from this closely related to autopsy measurements ( $r=0.90$ )<sup>15</sup> and showed good interobserver reproducibility ( $\rho=0.93$ ) in one study.<sup>16</sup>

LV mass index (LVMI) was calculated by dividing the value of LV mass by height to its allometric growth rate of 2.7.<sup>17,18</sup> The partition value of 51 g/height<sup>2.7</sup> was used since this was the only criterion that was demonstrated as the optimal threshold value for LV hypertrophy in blacks irrespective of sex in 2 previous studies.<sup>19,20</sup>

Relative wall thickness (RWT) was derived from  $2 \times$  posterior wall thickness/LV end-diastolic internal diameter. Increased RWT was considered to be present when RWT exceeded 0.42. This represents the 97.5th percentile in normal patients.<sup>21</sup> LV geometry was stratified using LVMI and RWT. Normal geometry was defined as normal LVMI and RWT, concentric remodeling as normal LVMI and increased RWT,

**Table 1.** Demographic and Clinical Characteristics According to Sex

Variables	All Participants (N=1020)	Men (n=608)	Women (n=412)	P Value
Mean age, y	59.2 (14.6)	59.0 (13.9)	59.6 (15.5)	0.473
Education, %				
No formal education	15.3	7.5	26.6	0.001*
Primary	20.5	18.5	23.4	
Secondary	27.5	28.7	25.6	
Higher	36.7	45.2	24.4	
Height, m	1.66 (0.08)	1.69 (0.07)	1.62 (0.074)	0.001*
Weight, kg	73.5 (14.4)	73.9 (13.5)	72.8 (15.6)	0.331
BMI, kg/m <sup>2</sup>	26.6 (5.26)	25.8 (4.66)	27.8 (5.87)	0.001*
Systolic BP, mean (SD), mm Hg	155.0 (30.06)	155.0 (29.8)	155.0 (30.5)	0.979
Diastolic BP, mean (SD), mm Hg	93.9 (18.3)	94.7 (18.8)	92.7 (17.4)	0.097
Hypertension, %	75.3	76	74.3	0.533
Diabetes mellitus, %	13	13	13.1	0.958
Dyslipidemia, %	60.2	59.7	60.9	0.696
Stroke type, %				
Ischemic	80	77.9	83	0.049*
Hemorrhagic	20	22.1	17	
Family history of stroke, %	19.4	20.1	18.3	0.463
Metabolic syndrome, %	42.5	29.8	61.5	<0.001*
Waist circumference, cm	90.2 (14.0)	88.8 (12.7)	92.3 (15.5)	0.0002*
Triglyceride, mg/dL	133.9 (96.7)	133.8 (96.6)	134.3 (97.0)	0.937
Total cholesterol, mg/dL	193.4 (52.3)	188.1 (56.8)	200.9 (62.0)	0.0015*
HDL cholesterol, mg/dL	50.3 (22.5)	48.7 (24.2)	52.6 (19.7)	0.022*
LDL cholesterol, mg/dL	121.0 (50.4)	117.1 (46.0)	126.4 (55.6)	0.0081*
Lipids ratio: total cholesterol/HDL cholesterol	4.46 (2.23)	4.58 (2.34)	4.29 (2.08)	0.091
Lipids ratio: total cholesterol/LDL cholesterol	1.75 (0.62)	1.76 (0.66)	1.75 (0.57)	0.799

BMI indicates body mass index; BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

\* $P<0.05$ .

eccentric hypertrophy as increased LVMI and RWT  $<0.45$ , and concentric hypertrophy as increased LVMI and RWT  $\geq 0.45$ .

LV dimensions and systolic function (ejection fraction [EF] and fractional shortening) were derived from 2-dimensional-guided M-mode measurements and, where impossible as a result of regional wall motion abnormalities, the modified Simpson's method was used in assessing LV systolic function. The degree of LV systolic dysfunction has been classified according to ASE guidelines as normal range (52 to 72), mildly abnormal (41 to 51), moderately abnormal (30 to 40), and severely abnormal ( $<30$ ) for men, while normal range (54 to 74), mildly abnormal (41 to 53), moderately abnormal (30 to 40), and severely abnormal ( $<30$ ) for women.<sup>22</sup>

We also assessed for presence of valvular dysfunction by semiquantitative method according to international guidelines.<sup>23,24</sup> Other abnormalities assessed for included presence

of pericardial effusion and interventricular and interatrial abnormalities (asymmetric wall motion abnormalities, septal defects, presence of patent foramen ovale, interatrial septal aneurysm).

Measurements were obtained in up to 3 cardiac cycles according to the ASE convention.<sup>11</sup>

Experienced cardiologists performed all echocardiography in the various centers; intraobserver concordance correlation coefficient and measurement error have been reported.<sup>25,26</sup>

### Data Management and Statistical Analysis

We reported mean and SD or median and interquartile range (IQR) for continuous variables, and categorical variables were summarized using counts and percentages. These descriptive measures were reported by sex (male versus female) and stroke

type (ischemic versus hemorrhagic). Comparisons between these categories were performed using the 2-sample *t* test for continuous variables or Mann–Whitney *U* test depending on whether the variable was symmetrical (normally distributed) or not. Chi-square test was employed for categorical variables. To explore the relationship between echocardiographic parameters and 1-month disability and fatality, univariate and multivariable generalized linear models were fitted. In order to obtain relative risk (RR), which is the appropriate measure for a prospective study, a generalized linear model with binomial distribution and log-link function was employed. Both unadjusted RRs and adjusted RRs were computed and reported with their corresponding 95% CIs. Predictive model was fitted separately for 1-month disability and fatality using backward selection with removal of *P* value set at 0.20. Goodness of fit of the final model was assessed using residual analysis and Hosmer-Lemeshow test. To assess the predictive power of the fitted model, cross-validation was performed and area under the receiver operating characteristic curve (AUC) was estimated with its 95% CI.<sup>27</sup> Statistical significance was assessed at a level of 0.05. Analysis was performed using Stata MP version 14 (StataCorp).<sup>28</sup>

## Ethical Approval

Ethical approval for the study was obtained from the joint University of Ibadan/University College Hospital ethical review committee as the primary site and institutional review board of each other participating institution. Informed consent was obtained from each participant.

## Results

### Clinical and Echocardiographic Characteristics of the Study Population

A total of 1020 patients with stroke comprising 60% men with mean age of  $59.2 \pm 14.6$  years were studied (Tables 1 and 2). Women were heavier, with higher mean waist circumference and total and low-density lipoprotein cholesterol levels. Forty-three percent of the participants had metabolic syndrome, with a female preponderance (61.5% versus 29.8%,  $P=0.001$ ). Compared with ischemic stroke, hemorrhagic stroke occurred in younger ages, was more common in men, and was associated with higher mean systolic blood pressure, diastolic blood pressure, mean arterial pressure, and prevalence of hypertension (86.3% versus 72.6%;  $P<0.001$ ) Table 2.

### LV Structure and Functions

Echocardiographic features varied across sex and stroke types (Tables 3 and 4). Male participants had larger mean aortic root

**Table 2.** Clinical Characteristics According to Stroke Type

Variables	Ischemic (n=814)	Hemorrhagic (n=204)	<i>P</i> Value
Mean age, y	60.5 (14.7)	54.0 (13.0)	<0.001*
Sex, %			
Male	58.1	65.7	0.049*
Female	41.9	34.3	
Education, %			
No formal education	11.9	11.2	0.09
Primary	18.8	19.2	
Secondary	34.2	34.6	
Higher	35.1	35.1	
Height, m	1.66 (0.078)	1.67 (0.087)	0.5074
Weight, kg	73.2 (14.7)	74.9 (14.4)	0.2179
BMI, kg/m <sup>2</sup>	26.5 (5.28)	27.0 (5.57)	0.3346
Mean systolic BP, mm Hg	151.8 (29.2)	167.7 (29.1)	<0.001*
Mean diastolic BP, mm Hg	91.6 (17.3)	102.7 (18.7)	<0.001*
MAP, mm Hg	90.8 (21.7)	99.2 (22.1)	<0.001*
PP, mean, mm Hg	60.2 (19.6)	65.0 (20.6)	0.0039*
Hypertension, %	72.6	86.3	<0.001*
Diabetes mellitus, %	13.8	9.8	0.133
Dyslipidemia, %	61.6	54.4	0.063

BMI indicates body mass index; BP, blood pressure; MAP, mean arterial pressure; PP, pulse pressure.

\* $P<0.05$ .

diameter ( $P<0.0001$ ), LV internal dimension at systole ( $P<0.0377$ ) and diastole ( $P<0.0001$ ), and septal wall thickness at systole ( $P=0.0007$ ). A greater proportion of women than men had left atrial enlargement (21.4% versus 16.6%;  $P=0.006$ ). Ischemic stroke was associated with smaller aortic root diameter, septal and posterior wall thickness at systole, and poorer LV systolic function. Spontaneous echo contrast and abnormal wall motion abnormalities were more common among patients with ischemic stroke. Over 90% of patients with stroke had associated abnormal LV geometry with eccentric hypertrophy predominating. Abnormal LV geometry was worse in men than women and patients with hemorrhagic versus ischemic stroke.

### Predictors of 1-Month Disability and Fatality

After adjusting for variables that had significant bivariate association, age was an independent predictor of 1-month disability and fatality (Tables 5 and 6). Patients 60 years and older had a higher risk of having disability (adjusted RR,

**Table 3.** Echocardiographic Parameters According to Sex

Variables, Mean (SD), mm	All Participants (N=1020)	Men (n=608)	Women (n=412)	P Value
Left atrial diameter	29.7 (20.3)	30.3 (23.5)	28.9 (14.2)	0.295
Aortic root diameter	30.6 (11.6)	31.9 (14.5)	28.5 (4.4)	0.000*
Aortic valvular opening	19.2 (7.3)	20.1 (8.8)	17.8 (3.6)	0.000*
LVID	44.0 (9.9)	45.8 (10.1)	41.4 (8.9)	0.000*
LVIDs	32.2 (29.1)	33.9 (33.2)	29.7 (21.2)	0.038*
IVSTD	14.6 (8.1)	14.9 (7.8)	14.2 (8.6)	0.198
IVSTS	17.3 (5.5)	17.8 (6.0)	16.5 (4.6)	0.000*
LVPWTD	14.5 (7.4)	14.6 (7.4)	14.3 (7.5)	0.668
LVPWTS	19.5 (11.5)	19.3 (10.2)	19.9 (13.3)	0.427
EF, %	62.2 (30.8)	61.2 (31.6)	63.6 (29.6)	0.234
FS, %	35.2 (24.0)	33.5 (16.3)	37.8 (32.2)	0.007*
LVM, g	240.0 (108.3)	261.2 (113.7)	207.7 (90.5)	0.000*
LVM/height <sup>2.7</sup>	61.6 (27.0)	64.5 (26.8)	57.1 (26.8)	0.000*
LVH, %	62.1	66.3	55.5	0.006*
LV wall motion abnormality, No. (%)	137 (15.4)	88 (16.5)	49 (13.8)	0.292
Pericardial effusion, No. (%)	83 (9.5)	55 (10.4)	28 (8.1)	0.252
Mitral valve disease, No. (%)	128 (12.6)	84 (13.8)	44 (10.7)	0.143
Aortic valve disease, No. (%)	97 (9.5)	64 (10.5)	33 (8.1)	0.184
Spontaneous echo contrast, No. (%)	58 (6.3)	43 (7.8)	15 (4.1)	0.022*
Intracardiac clots, No. (%)	11 (1.2)	4 (0.7)	7 (1.9)	0.128
LV geometry, %				
Normal	9.4	8.9	10.3	0.053*
Concentric remodeling	25.3	22.1	30.2	
Concentric hypertrophy	9.1	10.6	6.9	
Eccentric hypertrophy	56.1	58.4	52.7	
LV systolic dysfunction, %				
None	68.3	67.6	69.4	0.362
Mild	20.7	19.9	22	
Moderate	6.3	7.0	5.3	
Severe	4.7	5.5	3.4	
Left atrial enlargement, %				
None	81.5	83.4	78.6	0.006
Mild	12.6	12.2	13.1	
Moderate	3.9	3.5	4.3	
Severe	2.1	0.9	4	

EF indicates ejection fraction; FS, fractional shortening; IVSTD, interventricular septal thickness at end diastole; IVSTS, interventricular septal thickness at end systole; LV, left ventricular; LVH, left ventricular hypertrophy; LVID, left internal dimension at diastole; LVIDs, left internal dimension at systole; LVM, left ventricular mass; LVPWTD, left ventricular posterior wall thickness at diastole; LVPWTS, left ventricular posterior wall thickness at systole.

\* $P < 0.05$ .

1.42; 95% CI, 1.06–1.88) and fatality (adjusted RR, 1.84; 95% CI, 1.06–3.18) compared with younger patients. Women were more likely to have functional disability (unadjusted RR 1.26; 95% CI, 1.05–1.51). While secondary

school education was protective, hypertension (unadjusted RR: 1.27; 95% CI, 1.00–1.62) and LV posterior wall thickness were associated with disability (unadjusted RR, 1.08; 95% CI, 1.07–1.069).

**Table 4.** Echocardiographic Parameters According to Stroke Type

Variables, Mean (SD), mm	Ischemic (n=814)	Hemorrhagic (n=204)	P Values
Left atrial diameter	29.5 (13.1)	29.9 (14.9)	0.991
Aortic root diameter	30.2 (7.2)	32.5 (22.7)	0.018*
Aortic valvular opening	18.9 (4.1)	19.0 (4.3)	0.805
LVID	44.2 (9.9)	42.6 (10.2)	0.062
LVIDs	32.5 (30.9)	29.9 (22.9)	0.292
IVSTD	14.4 (8.2)	15.4 (7.8)	0.192
IVSTS	16.8 (5.3)	19.1 (5.4)	0.000*
LVPWTD	14.2 (7.7)	14.8 (4.7)	0.2663
LVPWTS	18.9 (11.9)	21.5 (10.4)	0.004*
EF, %	59.7 (15.6)	62.9 (15.4)	0.009*
FS, %	32.9 (11.3)	35.0 (11.4)	0.029*
LVM, g	236.5 (106.7)	254.7 (113.9)	0.059
LVM/height <sup>2.7</sup>	60.6 (26.5)	65.4 (28.6)	0.063
LVH, %	61.1	65.4	0.356
Wall motion abnormality, No. (%)	107 (15.1)	30 (16.8)	0.576
Pericardial effusion, No. (%)	66 (9.4)	17 (10.1)	0.759
Mitral valve disease, No. (%)	107 (13.1)	21 (10.3)	0.282
Aortic valve disease, No. (%)	79 (9.7)	18 (8.9)	0.716
Spontaneous echo contrast, No. (%)	37 (5.0)	21 (11.4)	0.002*
Intracardiac clots, No. (%)	9 (1.2)	2 (1.1)	0.614
LV geometry, %			
Normal	10.6	5	0.015*
Concentric remodeling	25.1	25.9	
Concentric hypertrophy	10.4	4.3	
Eccentric hypertrophy	53.9	64.8	
LV systolic dysfunction, %			
None	67.8	70.8	0.741
Mild	20.7	20.8	
Moderate	6.6	4.9	
Severe	4.9	3.5	

EF indicates ejection fraction; FS, fractional shortening; IVSTD, interventricular septal thickness at end diastole; IVSTS, interventricular septal thickness at end systole; LV, left ventricular; LVH, left ventricular hypertrophy; LVID, left internal dimension at diastole; LVIDs, left internal dimension at systole; LVM, left ventricular mass; LVPWTD, left ventricular posterior wall thickness at diastole; LVPWTS, left ventricular posterior wall thickness at systole.

\* $P < 0.05$ .

Abnormal LV geometry was weakly associated with disability, with concentric hypertrophy having the strongest effect size (unadjusted RR, 1.80; 95% CI, 0.97–5.73). After cross-validation, the AUC for disability was 0.58 (95% CI, 0.52–0.64). Severe LV systolic dysfunction was associated with 1-month mortality (unadjusted RR, 3.05; 95% CI, 1.36–6.83). The AUC obtained from cross-validation was 0.56 (95% CI, 0.52–0.64).

## Discussion

This study demonstrated the clinical risk factor profile for stroke as earlier reported.<sup>29,30</sup> Low LVEF, sex, and age were independently associated with poor stroke outcome.

LV systolic dysfunction as defined by low EF has been shown in several studies to be a strong determinant of stroke outcome.<sup>31</sup> This study revealed that the risk of fatality at

**Table 5.** Clinical Features Associated With 1-Month Disability

Variables	Good mRS, (n=626), %	Poor mRS (n=394), %	Unadjusted Risk Estimates		Adjusted Risk Estimates			
			RR	95% CI	P Value	RR	95% CI	P Value
Age (mean), y	57.7 (13.9)	62.4 (14.4)	1.01	1.01–1.02	<0.0001	...	...	...
Age >60 y	45.1	59.4	1.43	1.18–7.73	<0.0001	1.42	1.06–1.88	0.017*
<b>Sex</b>								
Male	61.7	52.5						
Female	38.3	47.5	1.26	1.05–1.51	0.015*	1.05	0.80–1.39	0.720
<b>Education</b>								
No formal education	12.6	16.4	1.00	...	...	1.00	...	...
Primary	15.3	24.7	1.12	0.85–1.47	0.420	0.91	0.62–1.33	0.622
Secondary	30.8	23.6	0.72	0.54–0.97	0.030*	0.65	0.42–0.99	0.046*
Higher	41.3	35.3	0.78	0.59–1.02	0.068	0.77	0.53–1.11	0.163
Hypertension	73	79.7	1.27	1.00–1.62	0.047*	1.22	0.87–1.71	0.246
Diabetes mellitus	14.3	9.8	0.76	0.55–1.06	0.107	...	...	...
Dyslipidemia	62.5	67	1.13	0.93–1.38	0.216	...	...	...
BMI	26.8 (5.19)	26.5 (5.41)	0.99	0.97–1.01	0.425	...	...	...
<b>Echo parameters</b>								
Left atrial diameter	3.07 (2.68)	3.01 (1.26)	0.99	0.95–1.04	0.808	...	...	...
Aortic root diameter	3.05 (0.76)	3.00 (0.54)	0.93	0.79–1.10	0.403	...	...	...
Aortic valvular opening, cm	1.99 (0.99)	1.90 (0.47)	0.85	0.65–1.12	0.261	...	...	...
LVID	4.44 (0.95)	4.32 (1.06)	0.91	0.82–1.01	0.082	0.99	0.75–1.31	0.977
LVIDs	3.18 (1.78)	3.35 (4.65)	1.02	1.01–1.02	<0.0001	0.97	0.75–1.24	0.789
IVSTD	1.45 (0.98)	1.43 (0.58)	0.98	0.86–1.13	0.828	...	...	...
IVSTS	1.66 (0.57)	1.69 (0.56)	1.06	0.88–1.26	0.549	...	...	...
LVPWTD	1.43 (0.81)	1.53 (0.76)	1.07	0.97–1.18	0.0189	...	...	...
LVPWTS	1.88 (1.04)	2.17 (1.62)	1.08	1.07–1.069	0.010*	1.11	1.07–1.15	<0.001*
EF, %	63.0 (27.3)	61.9 (34.7)	0.99	0.99–1.00	1.00	...	...	...
EF <50%	16.9	20.4	1.15	0.91–1.44	0.248	...	...	...
FS, %	34.0 (11.4)	36.2 (28.6)	1.00	0.98–1.01	0.989	...	...	...
LVM indexed by height	244.5 (107.8)	237.9 (108.2)	0.99	0.99–1.01	0.800	...	...	...
Abnormal LVM	63.6	63.0	0.98	0.72–1.34	0.915	...	...	...
<b>LV geometry</b>								
Normal	14	7.7	1.00	...	...	1.00	...	...
Concentric remodeling	23.5	26.8	1.66	0.98–2.82	0.062	1.35	0.74–2.47	0.325
Concentric hypertrophy	7.3	9.5	1.80	0.97–5.73	0.058	1.77	0.89–3.52	0.103
Eccentric hypertrophy	55.2	56	1.54	0.94–3.56	0.095	1.48	0.86–2.55	0.158
<b>LV systolic dysfunction</b>								
None	72.8	69.1	1.00	...	...	...	...	...
Mild	18.6	20.7	1.17	0.92–1.48	0.207	...	...	...
Moderate	5.7	6	1.11	0.81–1.52	0.529	...	...	...
Severe	3	4.2	1.30	0.80–2.12	0.292	...	...	...

BMI indicates body mass index; EF, ejection fraction; FS, fractional shortening; IVSTD, interventricular septal thickness at end diastole; IVSTS, interventricular septal thickness at end systole; LV, left ventricular; LVID, left internal dimension at diastole; LVIDs, left internal dimension at systole; LVM, left ventricular mass; LVPWTD, left ventricular posterior wall thickness at diastole; LVPWTS, left ventricular posterior wall thickness at systole; mRS, modified Rankin Scale; RR, relative risk.

\* $P < 0.05$ .

**Table 6.** Clinical Characteristics by 1-Month Fatality

Variables	No Fatality (n=926)	Fatality (n=94)	Unadjusted Risk Estimates			Adjusted Risk Estimates		
	%	%	RR	95% CI	P Value	RR	95% CI	P Value
Age, mean, y	59.0 (14.2)	64.2 (14.3)	1.02	1.01–1.04	0.005*			
Age >60 y	49.3	63.6	1.71	1.06–2.76	0.029*	1.84	1.06–3.18	0.029*
Sex								
Male	58.6	54.6						
Female	41.4	45.4	1.16	0.73–1.84	0.530	...	...	...
Education								
No formal education	13.9	15.2	1.00	...	...	...	...	...
Primary	18.6	22.7	1.11	0.52–2.37	0.785	...	...	...
Secondary	27.9	30.3	1.00	0.49–2.05	1.000	...	...	...
Higher	39.6	31.8	0.76	0.37–1.55	0.449	...	...	...
Hypertension	75	80.3	1.32	0.74 to 2.36	0.348	...	...	...
Diabetes mellitus	12.6	10.6	0.83	0.39–1.77	0.637	...	...	...
Dyslipidemia	63.8	68.2	1.20	0.73–1.96	0.480	...	...	...
BMI	26.6 (5.3)	27.8 (4.9)	1.03	0.98–1.09	0.194	...	...	...
Echo parameters, mean (SD)								
Left atrial diameter	3.03 (2.33)	3.21 (0.96)	1.02	0.95–1.09	0.600	...	...	...
Aortic root diameter	3.03 (0.69)	3.04 (0.55)	1.02	0.75–1.39	0.894	...	...	...
Aortic valvular opening	1.97 (0.88)	1.88 (0.39)	0.76	0.39–1.45	0.402	...	...	...
LVID	4.42 (0.96)	4.21 (1.20)	0.81	0.64–1.03	0.088	0.88	0.67–1.14	0.336
LVIDs	3.14 (1.59)	4.22 (9.13)	1.04	1.03–1.04	<0.001	1.01	0.99–1.03	0.394
IVSTD	1.44 (0.86)	1.55 (0.86)	1.09	0.89–1.35	0.384	...	...	...
IVSTS	1.67 (0.55)	1.69 (0.71)	1.09	0.72–1.65	0.687	...	...	...
LVPWTD	1.46 (0.81)	1.48 (0.59)	1.03	0.77–1.36	0.850	...	...	...
LVPWTS	1.98 (1.30)	2.13 (1.34)	1.06	0.92–1.23	0.412	...	...	...
EF, %	61.5 (15.3)	57.9 (15.6)	0.99	0.97–1.00	0.060	0.98	0.94–1.01	0.228
EF <50%	17.5	25.8	1.56	0.92–2.67	0.102			
FS, %	34.0 (11.4)	31.9 (12.1)	0.98	0.96–1.01	0.154	...	...	...
LVM indexed by height	62.7 (28.8)	55.9 (24.7)	1.00	0.97–1.01	0.520	...	...	...
Abnormal LVM	63.8	58.3	0.81	0.37–1.76	0.594	...	...	...
LV geometry								
Normal	12.3	6.7	1.00	...	...	...	...	...
Concentric remodeling	24.4	26.7	1.92	0.56–6.52	0.298	...	...	...
Concentric hypertrophy	8	8.9	1.95	0.46–8.22	0.364	...	...	...
Eccentric hypertrophy	55.3	57.8	1.84	0.58–5.88	0.302	...	...	...
LV systolic dysfunction								
None	72.2	93	1.00	...	...	1.00	...	...
Mild	19.3	20.4	0.77	0.37–1.60	0.488	0.56	0.20–1.38	0.191
Moderate	5.6	7.4	1.38	0.68–2.82	0.372	0.71	0.20–2.49	0.589
Severe	2.8	9.3	3.05	1.36–6.83	0.007*	0.96	0.16–5.75	0.968
Left atrial enlargement	19.9	14.3	0.69	0.35–1.36	0.288	...	...	...

EF indicates ejection fraction; FS, fractional shortening; IVSTD, interventricular septal thickness at end diastole; IVSTS, interventricular septal thickness at end systole; LV, left ventricular; LVID, left internal dimension at diastole; LVIDs, left internal dimension at systole; LVM, left ventricular mass; LVPWTD, left ventricular posterior wall thickness at diastole; LVPWTS, left ventricular posterior wall thickness at systole; RR, relative risk.

\* $P < 0.05$ .

1 month was significantly higher at lower EFs. While some studies have shown significant association with low EF and poor clinical outcome, especially in cardioembolic stroke, others have shown that the association is merely a reflection of old age, increasing cardiac comorbidities, and more severe clinical presentation than the EF alone.<sup>32,33</sup> Similar to our findings, Wira et al<sup>31</sup> reported higher in-hospital mortality rates in patients with stroke with LVEF <50%. The higher mortality rate may be a result of loss of intrinsic cerebral vascular autoregulation, making cerebral blood flow dependent on cardiac function, which, if poor, will result in reduced cerebral blood flow and poorer outcome.

While findings of association between low EF and worse stroke outcome have been consistent, there are conflicting reports with regard to the predictive accuracy of low EF and mortality. In this study, low EF was associated with 1-month fatality, with an AUC of 0.56, which is not strong.<sup>34</sup> Similarly in the ASTRAL (Acute Stroke Registry and Analysis of Lausanne) study, despite an increased rate of morbidity and death among patients with stroke with low EF, the AUC was 0.50.<sup>33</sup> In some studies, predictive accuracy of low EF was only improved when combined with the NIHSS and lipid disorders.<sup>35,36</sup> Nevertheless, early detection and management of patients with stroke with low EF through routine echocardiography and aggressive treatment of LV dysfunction in patients with acute stroke may improve post-stroke morbidity and death and prevent stroke recurrence.

The reasons for sex differences in stroke outcomes remain unclear. In this study, men were more prone to functional disability with no difference in mortality at 1 month. This differs from findings from the Fukuoka Stroke Registry in Japan, where women older than 70 years were more prone to poor functional disability but no difference was seen in those younger than 70 years.<sup>37</sup> The reason for worse outcome among men in our study may be partly caused by higher frequency of LV systolic dysfunction among men. In addition, this disparity may be the result of the sex-specific association, with major cardiovascular risk factors similarly reported in other studies<sup>38,39</sup>; hormonal influences; and the effect of Y chromosome on cardiovascular diseases.<sup>40</sup>

Elderly patients experiencing stroke generally have poor functional outcomes afterwards.<sup>41</sup> Our finding of increased risk of functional disability and death among patients older than 60 years was not surprising. Elderly patients were more prone to having atrial fibrillation and poor cardiac function, as well as having a high likelihood comorbid conditions.<sup>42</sup> In another study, biological rather than chronological age was a better predictor of worse stroke outcome.<sup>43</sup> Biological age can be modified by lifestyle and dietary practices such as consumption of green leafy vegetables, which demonstrated a strong protective effect against stroke occurrence and severe stroke.<sup>29</sup>

The clinical significance of LV geometry has been explored in many populations.<sup>44</sup> Despite the increased risk of stroke in the presence of abnormal LV geometry, information on the prognostic implications of LV geometry in patients with ischemic stroke is scanty. This study provides the first data among indigenous Africans on the prognostic role of LV geometric pattern in acute stroke. Over 90% of our study participants had associated abnormal LV geometry with eccentric hypertrophy predominating. Contrary to earlier reports, abnormal LV geometry demonstrated in this study was not associated with worse stroke outcome.<sup>45,46</sup> Similar to the current study findings, Field et al<sup>47</sup> in the SPS3 (Secondary Prevention of Small Subcortical Strokes) trial showed that 70% of the participants with lacunar stroke had abnormal LV geometry with no significant association with worse stroke outcome. The reasons for this discrepancy may be a result of our small sample size and short follow-up duration.

### Strengths, Limitations, and Future Direction

To the best of our knowledge, this is the largest echocardiographic study among indigenous African patients with stroke ever reported.<sup>2</sup> We provide evidence that LV systolic dysfunction on baseline echocardiography is associated with 1-month outcome in this population. We could not establish whether these factors were independent predictors of outcome because of low predictive accuracy for low EF and abnormal LV geometry (AUC 0.56 and 0.58, respectively). Larger studies are required to establish their independent effects and investigate mediators of such an effect. However, aggressive management of LV systolic dysfunction and abnormal geometry by cardiologists and stroke experts may improve stroke outcome among the identified at-risk population.

A limitation of our study is our inability to assess diastolic function because of incomplete tissue Doppler imaging data. Follow-up echocardiography was not obtained in order to document whether the abnormalities were transient.

Given the observed association of age, male sex, low EF, and abnormal geometry with worse outcome, coupled with our earlier reported ECG determinants of stroke outcome,<sup>48</sup> we plan to develop a post-stroke outcome prediction tool that will be validated for use in people of African ancestry.

### Conclusions

This study demonstrated strong relationships between echocardiographic data and stroke outcome. LV systolic dysfunction may be a useful determinant of outcome in acute stroke among indigenous Africans. Routine echocardiographic diagnosis and management of cardiac dysfunction during acute stroke may be helpful in preventing worse outcome.

Larger longitudinal studies are required for confirmation of these findings.

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## Disclosures

None.

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