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Prevalence and Prognostic Features of ECG Abnormalities in Acute Stroke: Findings From the SIREN Study Among Africans

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Due to the large number of authors, only the first 30 and the authors affiliated with the University of Kentucky are listed in the author section above. For the complete list of authors, please download this article or visit: <https://doi.org/10.1016/j.gheart.2017.01.002>

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Prevalence and Prognostic features of Electrocardiographic Abnormalities in Acute Stroke among Africans: Findings from SIREN

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Abstract

Background—Africa has a growing burden of stroke with associated high morbidity and a 3-year fatality rate of 84%. Cardiac disease contributes to stroke occurrence and outcomes, but the precise relationship of abnormalities as noted on a cheap and widely available test, the electrocardiogram (ECG), and acute stroke outcomes has not been previously characterized in Africans. We assessed the prevalence and prognoses of various ECG abnormalities among African acute stroke patients encountered in a multisite, cross-national epidemiologic study.

Methods—We included 890 patients from Nigeria and Ghana with acute stroke who had 12-lead ECG recording within first 24 hours of admission and stroke classified based on brain CT scan or MRI. Stroke severity at baseline was assessed using the Stroke severity scale (SLS), while one-month outcome was assessed using the modified Rankin scale (mRS).

Results—Patients mean age was 58.4 (\pm 13.4) years, 490 were male (55%) and 400(45%) females, 65.5% had ischemic stroke, and 85.4% had at least one ECG abnormality. Women were significantly more likely to have atrial fibrillation, or left ventricular hypertrophy (LVH) with or without strain pattern. Compared to ischemic stroke patients, hemorrhagic stroke patients were less likely to have atrial fibrillation (1.0% vs. 6.7%, $p=0.002$), but more likely to have LVH (64.4% vs. 51.4%, $p=0.004$). Odds of severe disability or death at one month was higher with severe stroke (AOR: 2.25; 95% CI :1.44–3.50), or atrial enlargement (AOR: 1.45; CI:1.04–2.02).

Conclusions—About four in five acute stroke patients in this African cohort had evidence of a baseline ECG abnormality, but presence of any atrial enlargement was the only independent ECG predictor of death or disability.

INTRODUCTION

Stroke is a common neurologic condition in all regions of the world. Of the 14.1 million people who died of cardiovascular diseases (CVD) in 2012 in the world, stroke accounted for 6.7 million deaths. (1) Many people who suffer acute stroke have underlying CVD such as hypertension, atrial fibrillation, and ischaemic heart disease. (2) These underlying CVD

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are associated with several pre-existing electrocardiographic (ECG) anomalies such as rhythm and conduction abnormalities, and left ventricular hypertrophy (LVH) with or without ST-T changes.

However, several researchers have postulated the existence of a 'brain-heart axis' whereby structural brain lesions by themselves result in electrocardiographic changes. (3) The precise mechanism that leads to the development of these ECG changes is still uncertain, though increasing evidence suggests that it is mainly due to autonomic nervous system dysregulation.(3, 4) Whereas some authors attribute these ECG changes in acute stroke to underlying CVD, others have demonstrated their presence in acute stroke patients without underlying CVD. (5, 6)

Irrespective of preexisting cardiac diseases or not, observing an abnormal ECG in an acute stroke patients more than doubled their mortality rate at 6 months (5) and these abnormal ECG changes have not been shown to be perfect predictive tool for stroke subtypes.(6, 7) While cardiac arrhythmia such as atrial fibrillation, and LVH has been linked with the occurrence and prognosis of acute stroke, the prognostic value of repolarization changes commonly seen after stroke such as ST segment depression, T-wave and U-wave abnormalities still remains unclear.(8, 9).

Despite the common occurrence of stroke in Africa, there is sparse data on the prevalence and prognostic significance of ECG abnormalities in acute stroke in the region. In addition, there is inadequate data on the contributions of cardiac arrhythmias, conduction abnormalities, LVH, QTc prolongation and QRS prolongation on one-month case fatality in acute stroke especially in the African context. Understanding these interactions will help develop interventions to reduce the morbidity and mortality associated with acute stroke.

We investigated the prevalence of specific baseline ECG abnormalities in Africans with acute stroke and their prognostic effect on severe disability or death at one-month after stroke.

METHODS

Study design

Design of the SIREN study has been described elsewhere.(10) It is a multicenter case-control study involving several sites in Nigeria and Ghana, which has been running since August 2014. Ethical approval was obtained from the institutional ethical committees of all study sites and written informed consent was obtained from all subjects.

Cases included consecutively consenting adults (aged 18 years or older) with first clinical stroke within 8 days of current symptom onset, or 'last seen without deficit' with cranial CT or MRI scan performed to confirm diagnosis within 10 days of symptom onset. We excluded those with stroke mimics, primary subarachnoid hemorrhage and previous strokes that were not radiologically ascertained. Stroke severity was assessed at baseline using the stroke levity scale (SLS). (11) One-month outcome was assessed using the modified Rankin scale

(mRS).(11) Other clinical and laboratory information were obtained according to the SIREN protocol. (10)

Electrocardiography

A standard (resting) 12-lead ECG was performed in each subject using a commercially available ECG machine at 25 mm/s and 1mV/cm calibration. All the 12-lead ECGs were obtained within 24-hours after the onset of stroke. The ECG tracings were independently analyzed by the cardiologists who were unaware of the details of the clinical status of the patients. Abnormalities obtained from the ECGs were defined according to standard criteria as shown in Table 1.(12, 13) Left ventricular hypertrophy was diagnosed using the following criteria: Sokolow-Lyon voltage (sum of the amplitudes of S wave in V1 and R wave in V5 or V6 ≥ 3.5 mV), sex-specific Cornell voltage (sum of the amplitudes of S wave in V3 and R wave in aVL.2.0 mV in women and .2.8 mV in men). Cornell's product (CP) was calculated as the product of Cornell voltage times QRS duration. Repolarization abnormalities in leads V5 and/or V6 indicated typical strain when there was down-sloping convex ST segment with an inverted asymmetrical T-wave opposite to the QRS axis. (14, 15) QT interval was determined using the tangent method.(16) The measured QT interval was corrected for heart rate using the Bazett's formula. Prolonged QT interval was considered present when the QTc was >450 milliseconds and >440 milliseconds in females and males respectively. Presence of other ST-T changes were documented according to standard criteria.(12) ECG definitions of criteria are in Table 1.

Data management and analysis

Quantitative variables were summarized using mean (SD) for normally distributed and median for asymmetric variables. Frequency and percentage was computed for categorical variables. To investigate the statistical significance of the difference in continuous variables according to gender and stroke type, independent samples t-test was employed. For categorical variables, the Chi-square test for the comparison of proportions was employed.

Total mRS scores 0–3 and 4–6 were categorized as good and poor respectively. Association between selected demographic, clinical characteristics and ECG findings was investigated at bivariate and multivariate levels. For bivariate analysis, chi square test was used while binary logistic regression was used for multivariate. Criteria for inclusion of variables in the logistic regression model was a p-value <0.05 in the bivariate or previous report in literature or basic demographic factors (age and sex). Goodness of fit was assessed using the Hosmer-Lemeshow test.

RESULTS

The 12-lead ECGs of eight hundred and ninety subjects were analyzed. There were 490 men (55.1%) and 400 (44.9%) women. The overall mean age of all patients was 58.4 ± 13.4 years with women showing a non-statistically significant trend towards being older ($p=0.057$). Variables with statistically significant gender difference included BMI, diastolic blood pressure, and heart rate. These are shown in table 2. Men were less likely to have atrial fibrillation. The four cases of ventricular tachycardia occurred only in women. Women also

had non-significant longer QT intervals and were more likely to have LVH diagnosed by Cornell voltage or product criteria. Atrial enlargement was significantly more common in men. (Tables 3 and 4)

Tables 5 and 6 depict the comparison of demographic and clinical as well as ECG abnormalities according to stroke types. Subjects with hemorrhagic stroke were significantly younger (by about 7 years) than those with ischemic stroke. They also had higher blood pressures (SBP, DBP, MAP, and PP). In terms of ECG abnormalities, atrial fibrillation was significantly more common in those with ischemic stroke, while LVH was significant in hemorrhagic stroke by any of the ECG-LVH criteria. LVH with strain, QTc duration, QRS duration and axis were comparable across stroke types.

Table 6 shows the demographic and some clinical characteristics of the subjects according to one-month disability status. The presence of sinus rhythm was associated with good mRS. Severe SLS and atrial enlargement on the 12-lead ECG was associated with poor mRS.

In a multivariate logistic regression analysis (Table 7), only severe SLS and presence of atrial enlargement were the independent predictors of one-month outcome.

DISCUSSION

In this ongoing African stroke study, women with stroke appeared older than their male counterpart with higher frequencies of tachycardia, atrial fibrillation and ventricular tachycardia. Men with stroke had higher mean diastolic blood pressure. ECG LVH was more common in women and in those with hemorrhagic stroke. There was no significant difference in the occurrence of conduction abnormalities or QT abnormalities according to gender or stroke type.(13, 17) The pathologic mechanism by which acute stroke generates various ECG abnormalities is still not clear. However, autonomic dysregulation due to sympathetic overactivity have been proposed. Some authors have implicated insular irritation to be responsible for the abnormal cardiac function in acute stroke.(18–23) This is thought to be mediated by impaired inhibition of the sympathetic nervous system leading to increased release of catecholamines.(20, 23)

The management of patients with an acute stroke demands assessment of risk for morbidity and mortality, of which hypertension is major determinant. Studies have shown that elevated BP in acute stroke is associated with poor prognosis.(24) Increased blood pressure increase the risk of bleeding in thrombolytic treatment(25) and increases the bleeding tendency in hemorrhagic stroke. (26) In our study, both systolic and diastolic blood pressures were elevated. The subjects with hemorrhagic stroke had higher mean blood pressure parameter compared with ischemic stroke. This is similar to the findings by Quresh et.al. (26)

While the studies on the pathophysiology of “acute hypertensive response” in stroke have not been exhaustive, severely high blood pressure irrespective of mechanism is associated with poor outcome. (27) Whether the high blood pressure reported in the current study was “acute hypertensive response” or poorly controlled chronic blood pressure was difficult to decipher since pre morbid cardiac state was not known. The same explanation may go for high rate of abnormal ECG findings reported in our study. About four out of five stroke

patients studied had at least one abnormal ECG finding. Irrespective of mechanism, abnormal ECG findings is associated with poor outcome.

Over 20% of our stroke subjects had prolonged QTc. This is not different in men and women and according to stroke type. Previous studies in patients with hypertensive heart diseases or diabetes mellitus have shown that QTc prolongation and QT interval dispersion are related to increased risk of all-cause and cardiovascular mortality through malignant arrhythmias. In a study, it was shown that idiopathic abnormal QTc prolongation was associated with a five-fold increase in the probability of sudden cardiac death.(28)

Except for four cases of ventricular tachycardia (all occurred in women), no case of polymorphic tachycardia especially torsade's de pointes were recorded. This is similar to previous reports.(13) However, this may not have been picked up because continuous ECG monitoring was not carried out in our subjects. Atrial fibrillation is the most common sustained cardiac arrhythmia (29) and its presence increases stroke risk by 5-folds.(30) Interestingly, the prevalence of atrial fibrillation in our study was low. This is in contrast to earlier studies that reported high prevalence of atrial fibrillation especially in ischemic stroke among non-African populations (30, 31). The lower prevalence of atrial fibrillation in African stroke patients may be due to their relatively younger age, or genetic influences. Certain genetic variants have been associated with occurrence of atrial fibrillation especially the familiar type.(32) Also earlier studies have shown a paradoxical relationship between established AF risk factors and AF incidence in people of African descent compared with those of European ancestry. Despite a higher prevalence of many traditional risk factors for AF, including hypertension, diabetes mellitus, heart failure, and larger BMI in African Americans, people of European ancestry had higher incidence of atrial fibrillation.(33) These discrepancies allows for further genomic studies in atrial fibrillation among indigenous African populations which SIREN will explore.

Furthermore, in this study more than half of the patients had LVH. LVH is a well-recognized independent risk factor for hypertensive target organ damage including stroke.(34–36) and when found with stroke it doubles the risk of repeat stroke.(37). In acute stroke therefore, it may not be a new development as it takes long period of blood pressure elevation for clinical LVH to develop; more so that more than half of the stroke patients had atrial enlargement. This suggests that probably more of our subjects had preexisting cardiac anomalies. Our findings are similar to a study by Familoni et.al who found 63% preexisting cardiac disorder in stroke patients with higher prevalence of long QT interval and reported more mortality in patients with preexisting cardiac conditions.(38)

In our study atrial enlargement and severity of stroke were major predictors of one month severe disability or death. While stroke severity is a recognized predictor of stroke outcome with more severe strokes recovering more slowly, atrial enlargement may indicate pre-existing cardiovascular morbidity which impairs stroke recovery at one-month.

Strengths and Limitations

This is the largest study so far of the prognostic implication of ECG abnormalities among indigenous African stroke patients. We provided evidence that any atrial enlargement on baseline ECG is an independent predictor of one-month outcome in this population.

It is not clear if the ECG abnormalities observed in our cohort were related to the acute stroke event since we did not have access to their ECGs prior to the stroke event. Follow up ECG was also not obtained in order to document whether the abnormalities were transient.

Conclusion

Various ECG abnormalities were observed in our stroke subjects. However, only atrial enlargement was an independent ECG predictor of one month stroke outcome. We recommend baseline ECG not only as a tool for detecting cardiac abnormalities in acute stroke patients but also to prognosticate one-month outcome. We will explore this and other ECG variables further when data collection is complete in the SIREN study.

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Highlights

- Four in five acute stroke patients in this African cohort had at least one ECG abnormality
- Atrial fibrillation was rare in the cohort occurring in <5% overall.
- Atrial fibrillation was more common in female stroke patients.
- Presence of any atrial enlargement was the only independent ECG predictor of death or disability.

Table 1

Definitions of Electro-cardiographic (ECG) variables

	ECG variables	Definitions
Rhythm	Atrial Fibrillation	Absent P waves and an irregular ventricular rate
	Atrial Flutter	Rate more than 100/minutes and saw tooth appearance of the p waves
	Sinus Rhythm	Regular p-wave with rate less between 60–100/minutes
	Sinus Bradycardia	Regular p-wave with rate less than 60/minutes
	Sinus Tachycardia	Regular p-wave with rate more than 100/minutes
	Sinus Arrhythmia	Beat-to-beat variation in normal P-P interval
Atrial enlargement	Right atrial enlargement	P wave amplitude > 2.5 millimeters in lead II and duration less than 120mseconds
	Left atrial enlargement	Bifid P wave in lead II with duration more than 120mseconds and amplitude less than > 2.5 millimeters in lead II
	Bi-atrial enlargement	P wave amplitude > 2.5 millimeters in lead II + Bifid P wave with duration more than 120ms in lead II
	Indeterminate	None of above evidence of atrial enlargement
Presence of other arrhythmias	Premature ventricular contraction	QRS > 120mseconds and bizarre QRS shapes
	Supraventricular tachycardia	Evidences of sinus tachycardia, AV Nodal re-entry tachycardia(AVNRT) complexes, Atrial fibrillation, Atrial flutter, Multifocal atrial tachycardia, Accelerated junctional tachycardia, atrial tachycardia
	Ventricular tachycardia	Sustained (5 or more consecutive beats) or non-sustained tachycardia (less than 5 consecutive beats)
	None	None of above other arrhythmias
Presence of conduction abnormalities	First degree AV block	PR duration > 0.20secs with normal P and QRS waves
	Second degree AV block	Progressive PR interval prolongation (> 200msecs) with intermittent failed P wave conduction or wide QRS(greater than 120msecs) with dropped QRS no prior PR prolongation or evidence of advanced block
	Right bundle branch block(RBBB)	Deep S in lead I and V ₆ and tall late R wave in V ₁
	Left bundle branch block(LBBB)	Tall R in lead I and V ₆ and deep S wave in V _I
	Left anterior hemi-block	QRS<120mseconds, left axis deviation, qR pattern in lead I and aVL, rS pattern in lead II, III, aVF and R wave peak time in aVL
	Left posterior hemiblock	QRS<120mseconds, right axis deviation, qR pattern in lead I and aVL, rS pattern in lead II, III, aVF and R wave peak time in aVL
	Bi-fascicular block	RBBB with left anterior hemiblock
	Tri-fascicular block	RBBB, left anterior hemiblock with primary AV block(or RBBB + Left anterior hemi-

ECG variables	Definitions
	block+ left posterior hemiblock)
Complete AV block	Evidence of AV dissociation
Indeterminate intra-ventricular block	>110mseconds with absence of RBBB and LBBB
None	None of the above conduction abnormalities
QT dispersion	QT _C interval
	Prolonged, if duration is greater than > 440ms in men or > 460ms in women
Left ventricular hypertrophy	Cornell Product Criteria
	V3-S +AVL-R>2440 mms (men) V3-S + AVL-R + 8mm > 2440 mms (women)
	Sokolow Lyon Criteria
	V1-S + RV-5 or RV 6 if addition 35mm (whether male or female) there is LVH
	Cornell voltage criteria
	V3-S +AVL-R if addition 20mm(Women) 28mm(men) there is LVH

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Table 2

Demographic and clinical characteristics according to gender

Variable	Total (n=890) Mean (SD)	Males (n=490) Mean (SD)	Females(n=400)	p value
Age (years)	58.4 (13.4)	57.6 (12.0)	59.3 (14.9)	0.057
Height (m)	164.7 (7.8)	167.7 (7.2)	160.9 (6.8)	<0.0001
Weight (kg)	72.4 (14.3)	72.7 (13.6)	72.1 (15.1)	0.678
Body Mass Index (kg/m ²)	26.7 (5.3)	25.7 (4.7)	27.8 (5.7)	<0.0001
Systolic Blood Pressure (mmHg)	162.3 (32.6)	163.1 (31.3)	161.2 (34.1)	0.413
Diastolic Blood Pressure (mmHg)	97.2 (19.2)	98.9 (19.5)	95.1 (18.6)	0.004
Heart Rate	91.3 (27.4)	89.3 (23.9)	93.7 (30.8)	0.042
Mean Arterial Pressure (mmHg)	97.4 (24.6)	97.1 (23.6)	97.8 (25.9)	0.682
Pulse Pressure (mmHg)	65.0 (22.4)	64.1 (21.7)	66.2 (23.3)	0.205
Stroke type: Ischaemic	403 (65.5)	216 (63.3)	187 (68.3)	
Haemorrhagic	212 (35.5)	125 (36.7)	87 (31.8)	0.203

Table 3

ECG abnormalities according to gender

Variable	Total (n=890) frequency(%)	Males 490 (55.1%)	Females 400 (44.9%)	p value
Atrial fibrillation	36 (4.2)	12 (2.5)	24 (6.2)	0.009
Atrial flutter	4 (0.5)	2 (0.4)	2 (0.5)	0.846
Other Arrhythmias	75 (8.9)	38 (8.2)	37 (9.6)	0.466
Conduction abnormality	106 (12.7)	55 (12.0)	51 (13.5)	0.539
Atrial enlargement	466 (55.1)	273 (59.1)	193 (50.4)	0.011
LVH*	397 (54.8)	192 (48.7)	205 (61.9)	<0.001
LVH with ST-T changes	219 (25.5)	124 (26.2)	95 (24.7)	0.607
Prolonged QT _C interval	235 (28.6)	138 (30.3)	97 (26.5)	0.228
Short QT _C interval	49 (6.0)	26 (5.7)	23 (6.3)	0.732
Any ECG abnormality	708 (85.4)	381 (84.5)	327 (86.5)	0.410

* either Sokolow, Cornell voltage or product. LVH: Left ventricular hypertrophy

Table 4

Demographic and clinical characteristics according to stroke type

Variables	Total Mean (SD)	Ischaemic Mean (SD)	Haemorrhagic Mean (SD)	p value
Age (years)	58.3 (13.2)	60.7 (13.1)	53.7 (12.2)	<0.001
Height (m)	164.9 (7.8)	165.1 (8.0)	164.4 (7.4)	0.405
Weight (kg)	73.1 (14.2)	73.2 (14.7)	72.8 (13.1)	0.795
Body Mass Index (kg/m ²)	26.7 (5.3)	26.7 (5.3)	26.9 (5.2)	0.768
Systolic Blood Pressure (mmHg)	161.0 (19.7)	154.1 (30.3)	173.6 (34.1)	<0.001
Diastolic Blood Pressure (mmHg)	96.8 (19.7)	92.6 (18.4)	104.5 (19.8)	<0.001
Heart Rate	92.1 (28.7)	90.6 (27.5)	94.8 (30.6)	0.118
Mean Arterial Pressure (mmHg)	96.5 (25.0)	92.4 (23.2)	103.9 (26.5)	<0.001
Pulse Pressure (mmHg)	64.2 (22.9)	61.5 (21.5)	69.1 (24.6)	<0.001

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Table 5

ECG abnormalities according to stroke type

Variables	Total	Ischaemic	Hemorrhagic	p value
Atrial Fibrillation	28 (4.7)	26 (6.7)	2 (1.0)	0.002
Atrial Flutter	4 (0.7)	4 (1.0)	0 (0.0)	0.304 ^f
Other Arrhythmias	46 (7.8)	34 (8.8)	12 (5.9)	0.222
Conduction abnormality	71 (12.3)	47 (12.4)	24 (12.1)	0.906
Atrial enlargement(any)	340 (58.0)	228 (58.9)	112 (56.3)	0.541
LVH [*]	297 (55.8)	181 (51.4)	116 (64.4)	0.004
LVH with strain	156 (26.2)	94 (24.0)	62 (30.2)	0.102
Prolonged QT _C	171 (29.6)	118 (31.3)	53 (26.4)	0.216
Short QT _C	34 (5.9)	19 (5.0)	15 (7.5)	0.238
QRS duration (median)	84.0	84.0	84.0	0.672
Median QRS Axis	24.0	25.0	23.6	0.321
Any ECG abnormality	488(84.7)	316 (83.9)	172 (87.3)	0.213

^f Fisher's exact test^{*} either Sokolow-Lyon, Cornell voltage or product criteria

Table 6

Demographic and selected clinical characteristics according to one-month disability status.

Variables	Good mRS (n= 254)	Poor mRS (n= 421)	Test statistic	p-value
Age (years, Mean (SD))	58.1 (12.1)	58.8 (14.0)	0.746	0.456
Male gender	161 (59.2)	288 (54.5)	1.574	0.21
Hypertension	255 (93.8)	496 (93.9)	0.011	0.916
Diabetes	106 (38.9)	187 (35.4)	0.977	0.323
Severe SLS	105 (45.5)	294 (60.6)	20.946	0.001
Sinus rhythm	239 (87.9)	427 (80.9)	6.302	0.012
Atrial fibrillation	8 (3.1)	24 (4.7)	1.147	0.284
Other Arrhythmias	24 (9.2)	45 (9.0)	0.013	0.961
Conduction abnormality	33 (13.3)	66 (13.1)	0.003	0.960
Atrial enlargement	101 (38.7)	243 (48.8)	7.046	0.008
LVH	138 (52.9)	276 (53.2)	0.007	0.936
LVH with strain	70 (26.9)	119 (23.3)	1.231	0.267
Prolong QTC	72 (27.6)	139 (29.0)	0.17	0.68
Short QTC	13 (5.0)	27 (5.6)	0.142	0.706
Any ECG abnormality	212 (83.5)	421 (86.5)	1.193	0.275

mRS: modified Rankin Scale. SLS: Stroke levity scale

Table 7

Independent factors associated with one-month disability

Variables	AOR (95% CI)	p-value
Age(years)	1.01 (0.99–1.02)	0.471
Male gender	1.04 (0.75–1.44)	0.806
Hypertension	1.24 (0.62–2.48)	0.549
Diabetes	0.86 (0.61–1.20)	0.377
Stroke severity (SLS)		
Mild	1.00	
Moderate	1.17 (0.73–1.87)	0.506
Severe	2.25 (1.44–3.50)	0.001
Atrial enlargement	1.45 (1.04–2.02)	0.030

SLS: Stroke levity scale

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