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Evaluation of cardiac-electrophysiological balance according to National Institutes of Health Stroke Scale score at admission and discharge in acute ischemic stroke patients: A pilot study

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SUMMARY

OBJECTIVE: The main objectives of this investigation were to determine whether there were any relationships between corrected cardiac-electrophysiological balance value and National Institutes of Health Stroke Scale scores at admission and discharge in patients with acute ischemic stroke and to assess whether cardiac-electrophysiological balance value was an independent predictor of high National Institutes of Health Stroke Scale scores (National Institutes of Health Stroke Scale score ≥5).

METHODS: In this retrospective and observational study, 231 consecutive adult patients with acute ischemic stroke were evaluated. The cardiac-electrophysiological balance value was obtained by dividing the corrected QT interval by the QRS duration measured from surface electrocardiography. An experienced neurologist used the National Institutes of Health Stroke Scale score to determine the severity of the stroke at the time of admission and before discharge from the neurology care unit. The participants in the study were categorized into two groups: those with minor acute ischemic stroke (National Institutes of Health Stroke Scale score=1–4) and those with moderate-to-severe acute ischemic stroke (National Institutes of Health Stroke Scale scores ≥5).

RESULTS: Acute ischemic stroke patients with National Institutes of Health Stroke Scale score ≥5 had higher heart rate, QT, corrected QT interval, T-peak to T-end corrected QT interval, cardiac-electrophysiological balance, and cardiac-electrophysiological balance values compared with those with an National Institutes of Health Stroke Scale score of 1–4. The cardiac-electrophysiological balance value was shown to be independently related to National Institutes of Health Stroke Scale scores ≥5 (OR 1.102, 95%CI 1.036–1.172, p<0.001). There was a moderate correlation between cardiac-electrophysiological balance and National Institutes of Health Stroke Scale scores at admission (r=0.333, p<0.001) and discharge (r=0.329, p<0.001).

CONCLUSIONS: The findings of this study demonstrated that the cardiac-electrophysiological balance value was related to National Institutes of Health Stroke Scale scores at admission and discharge. Furthermore, an elevated cardiac-electrophysiological balance value was found to be an independent predictor of National Institutes of Health Stroke Scale score ≥5.

KEYWORDS: Cardiac Arrhythmia. Ischemic stroke. Cardiac electrophysiologic study. Acute ischemic stroke.

INTRODUCTION

Acute ischemic stroke (AIS) is a complex clinical entity associated with major cardiovascular complications as a result of autonomic dysfunction and disruption of neurohormonal pathways[1]. Remarkably, the risk of developing cardiac complications increases with the severity of AIS[2]. Similarly, worsened cardiac functions as a consequence of AIS may result in poor neurological outcomes[3].

The National Institutes of Health Stroke Scale (NIHSS) is a simple, effective, and reliable tool for measuring acute stroke-related neurologic impairments[4]. The NIHSS score is a useful scale for clinical evaluation in patients with AIS since it allows for the identification of appropriate therapy, prediction of lesion size, measurement of stroke severity, and prediction of patient prognosis.

The electrocardiographic (ECG) measures of ventricular repolarization, such as QT, Tp-e, and Tp-e/QTc, were studied in AIS patients to predict the probability of ventricular arrhythmia[5]. The cardiac-electrophysiological balance (iCEB), which is determined on surface ECG by dividing the QT interval by QRS duration, is a noninvasive index that can be used to determine malignant ventricular arrhythmias[6]. Since iCEB is considered the cardiac wavelength analog, the iCEB values have been linked to ventricular arrhythmia risk. Nevertheless,

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there is a scarcity of data in the existing medical database on the values of iCEB based on NIHSS scores at admission and discharge in patients with AIS. As a result, we aimed to determine whether there were any relationships between iCEBc values and NIHSS scores at admission and discharge in patients with AIS and whether high iCEBc values were an independent predictor of high NIHSS scores.

METHODS

Participants and design of the study

A total of 231 consecutive patients from a single stroke center who were diagnosed with an AIS between January 2018 and November 2020 were included in the study. This was a retrospective and observational study. The exclusion criteria of the study were as follows: patients with moderate-to-severe heart valve disease, a history of cardiac valve surgery, electrolyte imbalance, a history of a pacemaker or implantable cardioverter-defibrillator implantation, and those with bundle branch block and using drugs that affect the cardiac conduction system (n=38). The diagnosis of AIS was determined based on a neurologic examination and cranial imaging. All patients underwent a computed tomography scan and magnetic resonance imaging after being admitted to the emergency service. The Ethics Committee authorized the study, and the study was carried out in conformity with the principles of the Helsinki Declaration (decision number: HNEAH-KAEK-2021/KK/55).

Echocardiographic examination

According to the American Society of Echocardiography guidelines, all patients had a complete transthoracic echocardiographic examination within the first 24 h. The usual biplane Simpson approach was used to assess the left ventricular ejection fraction (LVEF). The end-systolic, end-diastolic, and left atrial anteroposterior diameters were recorded from the parasternal long-axis view. The left atrial volume index (LAVI) was calculated using the modified biplane area-length method, which was then corrected for body surface area.

Analysis of electrocardiography parameters

The standard 12-lead ECG was recorded at 25 mm/s speed and 10 mm/mV gain upon admission to the hospital. All ECG records were digitally scanned at 300 dpi scanning and 10× amplification. The ECG records were evaluated by two expert cardiologists. The EP Calipers application (EP Studios, USA) was applied to calculate the amplitudes and time periods in ECG recordings. The QT interval was determined from the onset of the QRS to the end of the T wave. The end point of the T wave was recognized as the point of return to the isoelectric line. To remove the effect of heart rate on the QT interval, the QT interval was corrected using Bazett's approach (QTc=square root of the QT/RR interval). T-peak to T-end (Tp-e) was measured from the peak to the end of the T wave. To compute iCEB, the QT/QRS ratio from ECG recordings was utilized, and iCEBc was obtained by dividing the QTc by the QRS.

Assessing the severity of stroke

AIS was defined as a neurological impairment caused by a cerebral, spinal, or retinal infarction on imaging. The NIHSS score was utilized by an expert neurologist to identify the severity of the stroke at the time of admission and before discharge from the neurology care unit. Patients were divided into two subgroups: those with minor AIS (NIHSS score=1–4) and those with moderate-to-severe AIS (NIHSS score ≥5).

Statistical analysis

The statistical analysis was carried out using the SPSS statistics program (version 12.0; SPSS Inc., Chicago, IL, USA). Qualitative variables were represented using frequencies and percentages. To analyze categorical data between groups, the chi-square analysis was applied. The distribution of all continuous variables was non-normal. As a result, these variables were reported as medians [interquartile ranges (IQR)]. To assess the normality of variable patterns, the Kolmogorov-Smirnov test was chosen. To compare continuous variables between groups, the Mann-Whitney U test was employed. The independent predictors for NIHSS score ≥5 were determined using univariable and multivariable logistic regression analysis (backward entry method). Parameters having a p-value of 0.05 in univariable analysis were included in the multivariate logistic regression analysis. The association between iCEBc levels and NIHSS scores at admission and discharge was determined using Spearman's correlation analysis. All findings were presented as odds ratios (OR) and 95% confidence intervals (95%CI). The level of statistical significance was specified at $p<0.05$. The goodness-of-fit test presented adequate calibration for the multivariate model (Hosmer-Lemeshow goodness-of-fit=10.158, p=0.412). The effect size (Cohen's d) and power value (1–β) were calculated using the G*Power software (version 3.1.9.2). The effect size and power value were 0.82 and 0.94, respectively.

RESULTS

This investigation involved 231 patients with AIS. Participants of the study were divided into two groups: those with an NIHSS score of 1–4 (n=94) and those with NIHSS ≥5 (n=137).

Clinical characteristics and echocardiographic findings are summarized in Table 1. Patients with NIHSS ≥5 were older and smokers. The other clinical characteristics of the groups were similar in terms of gender, hypertension, diabetes, insulin dependency, hyperlipidemia, chronic obstructive pulmonary disease, cancer, and dementia. With regard to echocardiographic data, LVEF, left ventricular end-diastolic dimension, left ventricular end-systolic dimension, left atrial anteroposterior diameter, and LAVI were similar in both groups.

With regard to laboratory measurements, both groups were similar (Table 2). When ECG recordings were analyzed, patients with NIHSS ≥5 had higher heart rate, QT, QTc, Tp-e/QTc, iCEB, and iCEBc values compared with those with an NIHSS score of 1–4.

To find potential predictors of NIHSS ≥5, both univariable and multivariable logistic regression analyses were conducted. Age, smoking, LAVI, heart rate, QRS, QTc, and iCEBc were predictors of NIHSS ≥5 according to univariable logistic regression analysis. After incorporating all of the aforementioned variables into a multivariable logistic regression analysis, age, smoking, LAVI, and iCEBc (OR 1.102; 95%CI 1.036-1.172; p<0.001) were shown to be independently related to NIHSS ≥5. There was a moderate correlation between iCEBc and NIHSS scores at admission (r=0.333; p<0.001) and discharge (r=0.329; p<0.001) (Figure 1).

DISCUSSION

The study findings revealed that the iCEBc value calculated at admission was associated with NIHSS scores at admission and discharge. Furthermore, a high iCEBc value was an independent predictor of NIHSS ≥5.

Both ischemic and pro-arrhythmic ECG changes are common in the first 24 h after AIS[7]. One of the primary mechanisms involved in stroke-heart mixing is the hypothalamic-pituitary-adrenal axis (HPA). When a central regulatory region in the brain is affected, several pathways are activated based on the affected area and the severity of the lesion. Stimulation of the frontal lobe's orbital surface and the cingulate gyrus, for example, affects blood pressure and heart rate regulation; ischemic lesions of the insular cortex affect blood pressure control; and trigger serious cardiac complications, such as arrhythmias and autonomic dysfunction[7,8]. Furthermore, cerebral infarction in the left hemisphere is linked to a higher risk of negative cardiac outcomes and long-term mortality[9].

Table 1. Baseline clinical characteristics and echocardiographic findings of all patients according to the National Institutes of Health Stroke Scale score.

	National Institutes of Health Stroke Scale score 1–4 (n=94)	National Institutes of Health Stroke Scale score ≥5 (n=137)	p-value
Age, years	63 (54–74)	72 (63–78)	0.006
Gender, male, n (%)	65 (69.1)	85 (62.0)	0.266
Risk factors			
Hypertension, n (%)	65 (69.1)	105 (76.6)	0.204
Diabetes mellitus, n (%)	36 (38.3)	53 (38.7)	0.952
Insulin dependency, n (%)	10 (10.6)	10 (7.3)	0.379
Hyperlipidemia, n (%)	40 (42.6)	57 (41.6)	0.886
Smoker, n (%)	12 (12.8)	35 (25.5)	0.015
Chronic renal failure, n (%)	11 (11.7)	14 (10.2)	0.722
Coronary artery disease, n (%)	19 (20.2)	39 (28.5)	0.155
Chronic obstructive pulmonary disease, n (%)	9 (9.6)	15 (10.9)	0.736
Cancer, n (%)	4 (4.3)	9 (6.6)	0.446
Dementia, n (%)	9 (9.6)	18 (13.1)	0.403
Echocardiographic data			
Left ventricular ejection fraction, %	58 (58–59)	58 (57–58)	0.114
Left ventricular end-diastolic dimension, mm	46 (45–48)	46 (44–49)	0.601
Left ventricular end-systolic dimension, mm	25 (24–29)	25 (24–32)	0.117
Left atrial anteroposterior diameter, mm	36 (35–40)	37 (35–40)	0.912
Left atrial volume index, mL/m^2	22 (21–26)	23 (21–27)	0.113

Continuous variables are presented as median (IQR), and nominal variables are presented as frequency (%).

In 60–90% of AIS patients, ECG abnormalities can occur[10]. T-wave inversion (35%), ST depression (33%), a longer QTc interval (29%), and U waves (28%) are the most common findings[11]. The most frequent arrhythmias after AIS consist of atrial fibrillation, supraventricular tachycardia, ventricular ectopic beats, ventricular tachycardia, and sinus tachycardia[11].

Table 2. Laboratory variables and electrocardiography findings of all patients according to the National Institutes of Health Stroke Scale score.

	NIHSS score 1–4 (n=94)	NIHSS score ≥5 (n=137)	p-value
Laboratory data			
Hemoglobin, g/dL	13.8 (11.9–14.8)	13.1 (12.0–14.0)	0.120
Red cell distribution width, %	12.9 (12.5–13.5)	13.3 (12.36–14.4)	0.191
White blood cell count, cells/μL	8.7 (6.9–10.7)	8.4 (6.3–9.3)	0.113
Platelet count, mm^3	237 (192–278)	226 (181–286)	0.232
Mean platelet volume, fL	9.6 (8.7–10.1)	9.2 (8.2–10.8)	0.838
Creatinine, mg/dL	1.0 (0.8–1.2)	0.9 (0.8–1.1)	0.171
Urea, mg/dL	37 (30–48)	36 (26–47)	0.136
Thyroid-stimulating hormone, mIU/L	1.2 (0.7–2.0)	1.2 (0.5–2.3)	0.770
Aspartate aminotransferase, U/L	22 (19–29)	21 (16–44)	0.267
Alanine aminotransferase, U/L	23 (15–37)	25 (15–34)	0.870
Albumin, mg/dL	3.8 (3.6–4.2)	3.8 (3.4–4.4)	0.812
Glucose, mg/dL	110 (91–156)	105 (87–145)	0.150
Electrographic data			
Heart rate, beats/min	77 (63–88)	82 (72–94)	0.006
QRS, ms	101 (87–110)	96 (78–108)	0.057
QT, ms	399 (365–436)	455 (404–478)	<0.001
QTc, ms	452 (420–479)	511 (455–581)	<0.001
Tp-e, ms	88 (69–94)	90 (78–95)	0.118
Tp-e/QT	0.21 (0.17–0.24)	0.20 (0.16–0.23)	0.058
Tp-e/QTc	0.19 (0.16–0.20)	0.17 (0.14–0.20)	0.015
iCEB (QT/QRS)	4.0 (3.4–4.5)	4.6 (4.2–5.5)	<0.001
iCEBc (QTc/QRS)	4.5 (4.0–5.0)	5.6 (4.9–6.2)	<0.001
NIHSS score at admission	3 (2–4)	8 (6–10)	<0.001
NIHSS score at discharge	2 (1–3)	9 (6–11)	<0.001

Continuous variables are presented as median (IQR), and nominal variables are presented as frequency (%). QTc: corrected QT; Tp-e: T-peak to T-end; iCEB: cardiac-electrophysiological balance; NIHSS: National Institutes of Health Stroke Scale.

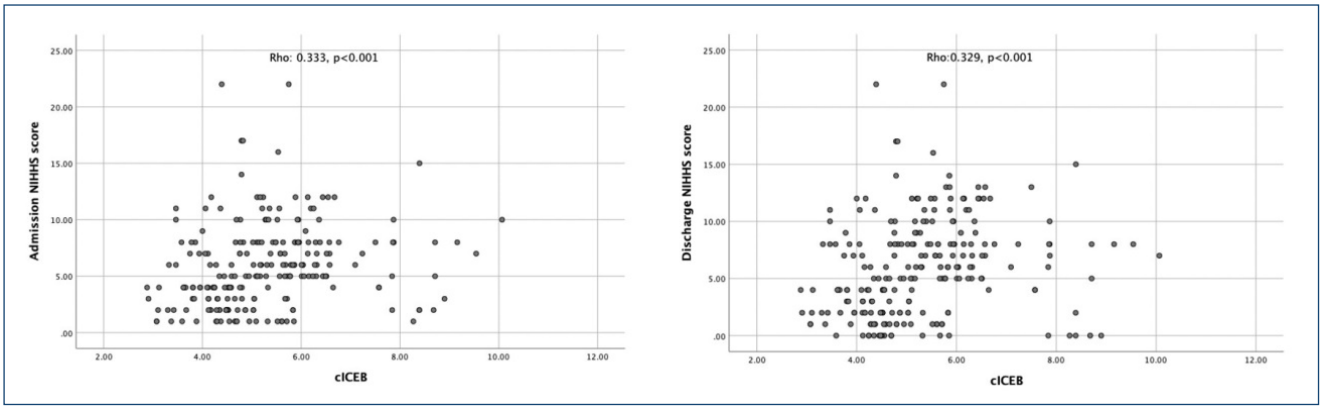

Figure 1. A correlation analysis between and NIHSS scores at admission and discharge. corrected cardiac-electrophysiological balance; National Institutes of Health Stroke Scale.

Acute hemodynamic instability is frequently associated with conduction abnormalities, which is linked to higher morbidity and death following AIS[12]. Moreover, a history of heart failure, the severity of the AIS, the QTc interval, and ventricular extrasystoles might be the risk factors for major cardiac events following an AIS[13]. Villa et al. discovered that patients with AIS with a longer QTc interval had a considerably higher mortality rate than patients with a normal QTc interval[14]. A prior study discovered a link between increases in QTd and the severity of stroke as measured by the NIHSS[15]. In our study, we revealed that both QT and QTc were substantially longer in patients with NIHSS ≥5. However, none of them were independent predictors of high NIHSS scores.

The iCEBc has been proposed as a novel noninvasive index for predicting lethal arrhythmia risk[6]. It was proposed that maintaining the electrical stability of the ventricles requires a careful balance between depolarization (QRS duration) and repolarization (QT interval), in which the deterioration of this balance may lead to arrhythmias. Sivri et al. revealed that after hemodialysis, elevated iCEBc values suggested a higher risk of TdP-mediated cardiac arrhythmia in patients with end-stage renal diseases[16]. Asoğlu et al. showed that iCEBc could be a new noninvasive and simple biomarker to detect the increased risk of pro-arrhythmia in COVID-19 patients[17]. In our study, we discovered that patients with AIS with a high NIHSS score had significantly higher iCEB values. No study showed a link between iCEB values at admission and NIHSS scores at discharge of patients with AIS when we searched through the literature. In addition, we found that high iCEBc levels were independently correlated with high NIHSS scores.

Our results, we believe, would be valuable in a clinical setting. Because patients with a high NIHSS are at a higher risk of arrhythmia, the iCEBc levels can be implemented to identify high-risk individuals. Furthermore, iCEBc levels, which are cheaply and quickly acquired, might be employed for risk assessment and follow-up plans for AIS with NIHSS ≥5 after discharge from hospital.

In our study, although iCEBc is found to be an independent predictor of higher NIHSS scores, their clinical importance of them appears to have a need to be supported with larger cohorts. As a result, new clinical scoring systems, including iCEBc, should be formed to increase the precision of future predicting systems.

Limitations

There were several limitations to our investigation. First, the study was conducted retrospectively, which might be considered a major weakness. Second, because consecutive AIS patients from a single institution were enrolled, the results may be limited in their relevance to a larger population and produce a susceptibility to selection bias. This limitation, however, might be minimized by the relatively large number of individuals in our study. Third, we were unable to assess in-hospital and long-term arrhythmias among patients with high iCEBc and NIHSS scores. However, we believe that our study may be a pilot study in this field. Finally, even though ECG recordings were anonymously evaluated by two experienced cardiologists, computer analyses of the traces were not employed, which might have resulted in human error in the results.

CONCLUSIONS

This study concluded that iCEBc levels were an independent predictor of NIHSS ≥5 and were correlated with both the NIHSS scores at admission and discharge.

AUTHORS' CONTRIBUTION

YK: Conceptualization, Writing – original draft, Writing – review & editing. **MİH:** Conceptualization, Formal Analysis, Writing – review & editing. **MS:** Conceptualization, Data curation, Writing – review & editing. **VÇ:** Data curation, Funding acquisition, Writing – review & editing. **SD:** Data curation, Funding acquisition, Writing – review & editing. **MMA:** Supervision, Writing – review & editing. **TÇ:** Conceptualization, Supervision, Writing – review & editing.

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