RELATION BETWEEN REPOLARIZATION PARAMETERS AND STROKE LOCALIZATION IN ACUTE ISCHEMIC STROKE

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1. Introduction

Acute stroke is an important cause of morbidity, and mortality and cardiovascular complications are common after an acute stroke (1) (2) . Several ECG abnormalities have been reported in patients following acute cerebrovascular events including QT interval prolongation, ST-segment deviation, and T-wave changes (3). The insula is assumed to play a central regulatory role for the autonomous nervous system. Autonomic nervous system dysregulation after acute cerebrovascular events possibly causes sympathetic activation resulting in cardiac arrhythmia. Ventricular repolarization abnormalities play an important role in the occurrence of arrhythmia. QT dispersion, a marker of repolarization homogeneity, is considered a predictor of sudden cardiac death and mortality in patients with acute ischemic stroke. Despite some controversial data about the positive predictive value of increased QT dispersion, this ECG marker appears to be a powerful tool for risk stratification in patients with impaired left ventricular function after acute ischemic stroke. The T wave is generated by myocardial voltage gradients during the repolarization phase of cardiomyocyte action potentials. QT interval is a measure of repolarization duration, but may not reveal other changes during the repolarization process. T-wave peak to T-wave end (TPE) interval measures terminal repolarization, and has experimentally been linked to arrhythmogenic repolarization dispersion in the myocardium (4). In this study, we aimed to investigate the

relationship between repolarization parameters and stroke localization in acute ischemic stroke patients.

2. Materials and Methods

Study participants and design

Patient Selection

A total of 213 patients (116 men, 97 women, 68 ± 15 years) with acute ischemic stroke were included in the study. Patients were divided into 4 groups according to the clinical ischemic classification (Group 1 (Total anterior circulation infarcts) , n=19 ; Group 2 (Partial anterior sirculation infarcts), n=73; Group 3 (Lacunar infarcts), n= 83 ; Group 4 (Posterior circulation infarcts), n=38. Demographic and baseline clinical data, including neurological deficit severity assessment with NIHSS on admission to the neurology care unit were recorded. Patient clinical data, history of cardiovascular risk factors, and stroke onset were determined, and neurologic examination was conducted at the time of admission. The diagnosis was made based on the neurologic examination and cranial imaging within 24 h of symptom onset. Neuroimaging included description of stroke type, stroke location, and insular involvement. All patients underwent immediate computed tomography after being admitted to the emergency care unit. Troponin levels were measured and electrocardiogram (ECG) was recorded after admission to the neurology care unit. The study was approved by the Ethics Committee of our hospital and informed consent was obtained. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Analysis of QT, Tpe interval

All standard 12-lead ECGs were recorded at 25 mm/s speed and 10 mm/mv gain with Nihon Kohden ECG-9132K electrocardiograph (Nihon Kohden Corporation, Tokyo, Japan). A 12-lead resting ECG was recorded at admission in the neurology care unit for patients with an acute ischemic stroke and then was manually measured with a ruler. All ECGs were manually analyzed by an experienced cardiologist who was unaware of the clinical data. The QT interval was measured from the beginning of the QRS to the end of the T-wave. The end of the T-wave was defined as the point of return to the isoelectric line (5). In cases where the T-wave was interrupted by a U-wave, the end of the T-wave was defined as the nadir between the T- and U-waves. In instances where the T-wave could not be reliably determined due to extremely low voltage (<0.1 mV), measurement of QT interval was not established and consequently, these leads were excluded from the analysis. In order to exclude the effects of heart rate (HR) on the QT interval, the QT interval was corrected according to the Bazett formula (QTc = QT/square

root of RR interval). QTd was defined as the difference between the maximum and minimum QT intervals. T peak to T end (Tpe) was measured with a ruler from the peak of the T-wave to its end; Tpe was corrected for heart rate. The criteria to determine the endpoint of the T-wave were similar to the aforementioned criteria considered for the QT measurement (5).

Definition of stroke and assessment of stroke severity

According to the updated definition of stroke in the American Heart Association/American Stroke Association guidelines, ischemic stroke is diagnosed based on the combination of symptoms and/or signs of typical neurological dysfunction and imaging evidence of central nervous system infarction. Therefore, ischemic stroke is defined as a neurological dysfunction episode caused by focal cerebral, spinal, or retinal infarction on imaging. NIHSS is a simple, valid, and reliable systematic assessment tool that measures acute stroke-related neurologic deficit (6). The NIHSS score is a very important scale for clinical assessment as it enables the determination of appropriate treatment,prediction of lesion size, measurement of stroke severity, and prediction of patient outcome in patients with acute ischemic stroke. The NIHSS comprises 11 different elements evaluating specific ability. Each ability is scored between 0 and 4, where 0 corresponds to normal functioning and 4 corresponds to complete impairment. A patient's NIHSS score is calculated by adding the score for each element of the scale; 42 is the highest score possible. A higher NIHSS score corresponds to greater impairment of cerebral function in a stroke patient.

The higher the NIHSS score, the higher the impairment of a stroke patient. According to NIHSS score, there are five stroke severity groups: NIHSS = 0 (no stroke), NIHSS = 1–4 (minor stroke), NIHSS = 5–15 (moderate stroke), NIHSS = 16–20 (moderate-to-severe stroke), and NIHSS = 21–42 (severe stroke). A baseline NIHSS score greater than 16 indicates a strong probability of patient disability and death (6). Stroke severity at admission to the neurology care unit was assessed by the NIHSS score by a neurologist. Patients were categorized into two groups; Group 1 comprised of patients with nonsevere stroke (NIHSS <16; n = 69), whereas Group 2 comprised of patients with severe stroke (NIHSS ≥16; n = 27).

Statistical analysis

Statistical analysis was conducted with the SPSS statistical package (Version 12.0; SPSS Inc., Chicago, IL, USA). All baseline parameters were analyzed. Continuous variables are expressed as mean ± SD and categorical variables are expressed as percentages. Intraobserver variability was calculated as the absolute difference between the two

measurements as a percentage of their mean. Mann–Whitney U test and Chi-square test were used for comparison of data as appropriate. P values < 0.05 were considered statistically significant. Spearman's correlation was used to determine the relationship between NIHSS and clinical parameters.

3. Results

Baseline characteristics

The baseline characteristics of patients are summarized in Table 1. Clinical characteristics of groups were similar with respect to age, gender, hypertension, diabetes, smoking (P > 0.05).

Electrocardiographic findings

QTc, QTd, QTcd, Tpe values were significantly higher in Group 1 and Group 2 patients than Group 3 and Group 4 patients (Table 2).

Correlation analysis performed to investigate the relationship between NIHSS score and clinical parameters showed a positive correlation between the NIHSS score and QTc, QTd, Tpe, Tpe/QT, age. (Table 3).

4. Discussion

Acute stroke is characterized by profound autonomic dysregulation, including alterations in the autonomic reflex pathways, central autonomic neuroanatomical sites, and hormonal factors (7). Stroke-related sympathetic activation is high in patients with higher NIHSS scores. There is a relationship between the central nervous system and the cardiovascular system during acute cerebrovascular disease (8). The previous studies have reported that a relationship between acute cerebrovascular disease and QT (4) (9). The effect of cerebrovascular events on the cardiovascular system is due to neurogenic myocardial stunning and changes in the autonomic nervous system (increased sympathetic control, reduced parasympathetic control). Significant imbalances between the repolarization and depolarization and of the heart may be associated with arrhythmic conditions. Lazar et al. found that a positive relationship between baseline QTd and NIHSS and modified ranking scores (10). Afsar et al. could not find any differences in the QT dispersion values between rightand left-sided strokes in the 24-hour ECGs (11). In the study by Sander and Klingelhöfer , right-sided infarcts more frequently showed QT prolongation and arrhythmias than left-sided infarcts (12). In a study performed by Colivicchi et al., right insular infarcts were associated with more complex arrhythmias (13). Tokgozoglu et al. concluded that stroke in the region of the insula, especially the right, leads to a decreased heart rate variability (14).

Stead et al. found an increased risk of early death in patients with acute ischemic stroke and a prolonged QTc interval at the time of emergency department presentation (15). Marafioti et al. found that the QTc interval prolongation is mainly a marker of serious cerebral damage (16). Villa et al. found that in patients with ischemic stroke and prolonged QTc interval, the risk of dying could be significantly higher than in patients with normal QTc interval (17). In our study, we found that QT was significantly higher in Group 1 and Group 2 patients than Group 3 and Group 4 patients. Christensen H and et al found that, insular damage, especially right sided insular damage was related to ECG changes in patients with acute stroke. Right insular lesion predicted death within three months of stroke independent of age, severity of stroke, and infarction volume. Patients with insular involvement significantly more often presented with ECG abnormalities(18).

The previous study found that a significant association between changes in QTd and stroke severity quantified by the National Institute of Health Stroke Scale (NIHSS) (19). Larger stroke lesions were associated with greater QTd in the early stages of stroke in the 2 studies (11) (20). Simula et al. found that right MCA ischemic stroke results in prolongation of QT interval (21).

Hypertension, hyperlipidemia, and diabetes mellitus are important risk factors for atherosclerotic cerebrovascular disease. However, Bonardo et al. found that, in young patients with acute ischemic stroke, large infarct volume was not associated with high blood pressure at admission (22). Hendrix et al. found that diabetes mellitus history is an important predictor of stroke severity (23).

5. Conclusions

Our results suggested that, repolarization parameters are associated with stroke localization on admission in patients with acute ischemic stroke. Repolarization parameters can help to evaluate arrhythmia risk in patients with acute neurologic diseases.

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Table 1:Clinical characteristics of patients.

Variables	Group-1 (Total anterior circulation infarcts) n=19	Group-2 (Partial anterior circulation infarcts) n=73	Group-3 (Lacunar infarcts) n=83	Group-4 (Posterior circulation infarcts) n=38	p Value
Age (year)	70.1 ± 12.3	68.7 ± 12.9	68.3± 11.9	69.3± 9.4	NS
Gender (F/M)	11 / 8	41 / 32	38/45	21/17	NS
Hypertension	8 (42%)	34 (45%)	48 (57%)	16 (42%)	NS
Diabetes Mellitus	5 (26%)	19 (26%)	21 (25%)	8 (21%)	NS
Smoking	5 (36%)	20 (32%)	29 (34%)	13 (34%)	NS
Dyslipidemia	6 (31%)	17 (26%)	23 (27%)	11 (28%)	NS

Table 2: Electrocardiographic parameters of patients.

Variables	Group-1 (Total anterior circulation infarcts) n=19	Group-2 (Partial anterior circulation infarcts) n=73	Group-3 (Lacunar infarcts) n=83	Group-4 (Posterior circulation infarcts) n=38	p Value
QTc (ms)	541±75.2	532±76.7	476±48.9	485±53.4	<0.05
QTd (ms)	91.7±3.9	92.4±5.3	61.8±3.1	66.7±3.7	<0.05
QTcd (ms)	95.9±4.3	96.4±3.6	66.2±3.7	67.6±3.7	<0.05
Tpe (ms)	96.3±4.7	95.1±3.5	64.5±3.1	66.4±3.8	<0.05
Tpe / QT	0.18±0.029	0.18±0.032	0.13±0.025	0.14±0.026	<0.05

Table 3: Correlation between NIHSS score and clinical parameters in patients with acute ischemic stroke

Parameters	Pearson's correlation coefficient (r-value)	P-value
QTc	0.342	0.037
QTd (ms)	0.297	0.032
Tpe (ms)	0.346	0.040
Tpe / QT	0.258	0.043
Age	0.320	0.036
* NIHSS: National Institutes of Health Stroke Scale,		