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QT intervals and QT dispersion in patients with subarachnoid hemorrhage

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Abstract
Purpose. To clarify the clinical significance of QT dispersion and the longest QT intervals (L-QTc) in patients with subarachnoid hemorrhage (SAH).
Methods. ECGs, clinical features, and laboratory data were analyzed in 38 patients with SAH (R) and 30 with unruptured cerebral aneurysms (U). Standard 12-lead ECGs obtained on admission were analyzed manually, and the longest QT interval (L-QTc) and the QT dispersion (difference between longest and shortest QTc) were compared between groups.
Results. There were no differences between groups R and U in age, sex, or location of aneurysms. The QT dispersion and L-QTc were greater in R than in U (109 ± 49 *vs* 64 ± 21 ms and 503 ± 63 *vs* 435 ± 38 ms, respectively; $P < 0.01$). The QT dispersion and L-QTc were longer in patients with premature ventricular contractions (PVCs) than in patients without PVCs (185 ± 30 *vs* 85 ± 41 ms and 586 ± 47 *vs* 467 ± 59 ms, respectively; $P < 0.01$). There were positive correlations between QT dispersion or L-QTc and preoperative Hunt and Hess grade ($rs = 0.560$ and $rs = 0.615$, respectively; $P < 0.01$). QT dispersion and L-QTc tended to correlate negatively with serum K^+ ($r = -0.365$ and $r = -0.376$, respectively).
Conclusion. QT dispersion in patients with SAH is prolonged, especially in high-grade cases.

Key words Subarachnoid hemorrhage · Arrhythmia · QT Dispersion · ECG

Introduction

In many patients with subarachnoid hemorrhage (SAH) abnormalities in the ECG morphology and rhythm are seen [1], and more than 90% of the patients show abnormalities on Holter ECG [2,3]. Inverted T waves, elevated or depressed ST segments, and prolongation of the QT interval are the most common changes, and long QT is seen in about 30% of patients with SAH [4]. Fatal arrhythmias, such as torsades de pointes and ventricular fibrillation, associated with QT prolongation occur in some cases [2,3,5].

The relationships between the QT interval and arrhythmias and prognosis were studied in the 1980s, and it was revealed that QT intervals among the 12 leads were different. Mirvis et al. investigated the differences in QT intervals among the 12 leads in patients with acute myocardial infarction [6] and found that the difference between the longest and shortest QT (QT dispersion) was greater in patients with the long QT syndrome associated with arrhythmias [7]. Thus, QT dispersion is defined as the difference between the longest and shortest QT on the 12-lead ECG and is considered as arrhythmogenic [8,9].

Abnormalities of the ECG in patients with SAH have been reported in several articles; however, there have been only a few reports of QT dispersion. Randell et al. investigated QT dispersion in 26 patients with SAH and 16 with unruptured cerebral aneurysms [10]. The QT dispersion in patients with SAH was longer than in patients with unruptured aneurysms (78 *vs* 25 ms). QT dispersion correlated with the levels of catecholamine metabolites, and these authors concluded that catecholamine release after SAH might lead to enlargement of QT dispersion.

To clarify the clinical significance of QT dispersion in patients with SAH, ECGs were analyzed retrospectively.

Materials and methods

Thirty-eight patients with SAH due to ruptured cerebral aneurysms (R) and 30 with unruptured cerebral

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Table 1. Hunt and Hess grading system for patients with cerebral aneurysms

Grade	Description
0	Unruptured aneurysm
I	Asymptomatic or minimal headache and slight nuchal rigidity
II	Moderate to severe headache, nuchal rigidity, but no neurologic deficit other than cranial nerve palsy
III	Drowsiness, confusion, or mild focal deficit
IV	Stupor, mild to severe hemiparesis, possible early decerebrate rigidity, vegetative disturbance
V	Deep coma, decerebrate rigidity, moribund appearance

Serious systemic diseases, such as hypertension, diabetes, severe arteriosclerosis, chronic pulmonary disease, and severe vasospasm seen on arteriography, result in placement of the patients in the next less favorable category.

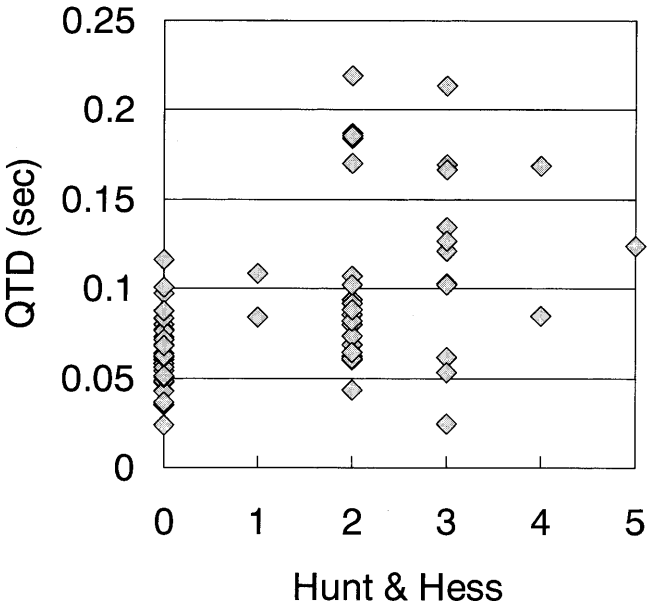

Fig. 1. Correlation between preoperative grade and QT dispersion. Positive correlations were found between QT dispersion *QTD* and Hunt and Hess grade ($rs = 0.560$, $P < 0.01$)

aneurysms (U) admitted to Kohnan Hospital from March to December 1999 were included in this study. The ages ranged from 34 to 86 years (mean, 59 years), and 44 women and 24 men were involved. In group R, the locations of the aneurysms were the middle cerebral artery in 7 patients, the internal carotid artery in 8, the anterior communicating artery in 9, the anterior cerebral artery in 2, the basilar artery in 4, and the vertebral artery in 8. In group U, the numbers of patients with aneurysms in these locations were 11, 9, 8, 1, 1, and 0, respectively.

The QT and RR intervals of the standard 12-lead ECG on admission were measured manually, and the corrected QT intervals (QTc) were calculated ($QTc\text{-}QT/(RR)^{1/2}$) according to Bazett [11]. The QT dispersion, the difference between the longest and shortest QTc, was compared between groups U and R. Correlations between QT dispersion and the Hunt and Hess grade [12] (Table 1), serum K^+, serum Mg^{2+}, and white blood cell count (WBC) were investigated. In group R, the relationship between QT dispersion and the location of the ruptured aneurysms was studied.

A comparison of the location of aneurysms and the sex distribution between groups U and R was made using the chi-square test. Correlations between QT dispersion and the Hunt and Hess grade were analyzed by Spearman's rank correlation coefficient. Correlations between QT dispersion and serum K^+, serum Mg^{2+}, and WBC were analyzed using Pearson's correlation coefficient. Differences of QT dispersion among locations of ruptured aneurysms were analyzed by one-factor analysis of variance (ANOVA). Other comparisons between the two groups were made with the unpaired *t*-test. A *P* value less than 0.05 was considered to be statistically significant.

Results

There were no differences between R and U in age (58.8 ± 5.0 years in R and 59.1 ± 11.2 years in U), sex distribution (female : male, 23 : 15 in R and 20 : 10 in U), or location of aneurysms. QT dispersion was larger in R than in U (109 ± 49 ms in R and 64 ± 21 ms in U; $P < 0.01$), and the longest QTc was larger in R than in U (503 ± 63 ms in R and 435 ± 38 ms in U; $P < 0.01$). In 21 patients in R (55%) and 5 in U, the QTc was prolonged (≧500 ms). The QT dispersion and the longest QTc in patients with premature ventricular contractions (PVCs) were longer than in those without PVCs (QT dispersion: 185 ± 30 *vs* 85 ± 41 ms; L-QTc: 586 ± 47 *vs* 467 ± 59 ms, $P < 0.01$). Sudden onset ventricular fibrillation was seen in one patient with a QT dispersion of 169 ms and L-QTc of 682 ms.

Positive correlations were found between QT dispersion or L-QTc and Hunt and Hess grade ($rs = 0.560$ and $rs = 0.615$; $P < 0.01$, respectively) (Figs. 1 and 2). QT dispersion and L-QTc tended to correlate negatively with serum K^+ and positively with WBC, but the correlation did not achieve statistical significance (Table 2).

The QT dispersion was longest in patients with ruptured aneurysms of the basilar artery (169 ± 53 ms) and the shortest in patients with aneurysms of the anterior cerebral artery (82 ms) (Table 3). The QT dispersion was longer in patients with ruptured aneurysms of the basilar artery than in patients with ruptured aneurysms in other locations ($P < 0.05$). There was no difference in

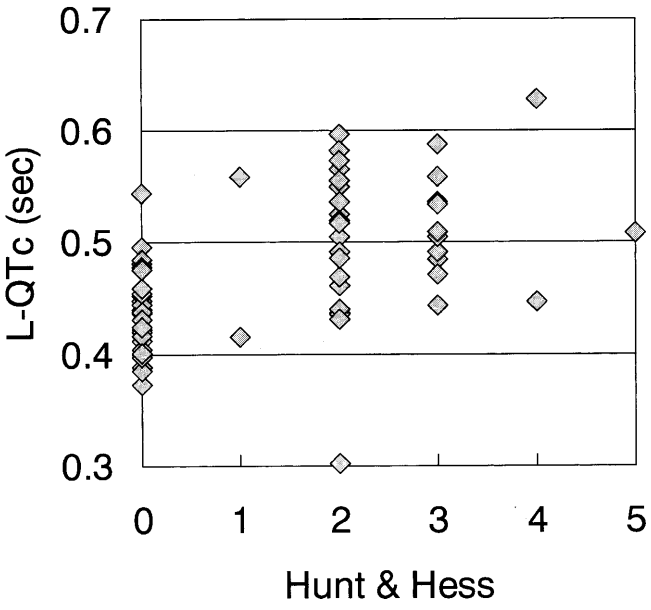

Fig. 2. Correlation between preoperative grade and longest QT interval. Positive correlations were found between longest QTc (*L-QTc*) and Hunt and Hess grade ($rs = 0.615$, $P < 0.01$)

Table 2. Correlation between ECG findings and laboratory data

Factors	*r*	*P*
K: QTD	−0.365	1.998
K: L-QTc	−0.376	1.999
Ca: QTD	−0.050	1.311
Ca: L-QTc	−0.100	1.573
Mg: QTD	0.057	0.652
Mg: L-QTc	0.049	0.702
WBC: QTD	0.363	0.002
WBC: L-QTc	0.355	0.003
HR: QTD	0.260	0.032
HR: L-QTc	0.408	0.000

QT dispersion and longest QTc tended to correlate negatively with serum K^+ and positively with WBC but did not achieve statistical significance. L-QTc, Longest QT interval; HR, heart rate; WBC, white blood cell count; QTD, QT dispersion; *r*, correlation coefficient

Table 3. Differences in ECG findings among ruptured aneurysms in different locations

		QTD (s)		L-QTc (s)	
Location	*n*	Mean	SD	Mean	SD
ACA	2	0.082	0.028	0.458	0.038
AcomA	9	0.109	0.059	0.507	0.059
BA	4	0.169*	0.053	0.529	0.053
ICA	8	0.118	0.050	0.519	0.061
MCA	7	0.084	0.040	0.478	0.096
VA	8	0.098	0.022	0.501	0.045

* $P < 0.05$

QT dispersion was longest in patients with ruptured aneurysms of the basilar artery (169 ± 53 ms) and shortest in patients with aneurysms of the anterior cerebral artery (82 ms). QT dispersion was longer in patients with ruptured aneurysms of the basilar artery than in patients with ruptured aneurysms in other locations ($P < 0.05$). ACA, Anterior cerebral artery; AcomA, anterior communicating artery; BA, basilar artery; ICA, internal carotid artery; L-QTc, longest QTc; QTD, QT dispersion, SD, standard deviation; VA, vertebral artery

the L-QTc among patients with ruptured aneurysms in different locations. The QT dispersion in patients with ruptured aneurysms at the internal carotid artery and the anterior communicating artery, (considered to supply the hypothalamus) was 113 ± 54 ms and was not larger than that in patients with ruptured aneurysms at other locations.

In group U, the QT dispersion was longer in women than in men (66 ± 22 *vs* 59 ± 18 ms; $P < 0.01$), and there was no difference in group R between women and men (103 ± 45 *vs* 119 ± 56 ms). There was no difference in L-QTc according to sex.

Discussion

In this study, we found that the QTc and the QT dispersion were prolonged in patients with SAH compared with those with unruptured aneurysms. There were positive correlations between L-QTc, QT dispersion, and preoperative Hunt and Hess grade. QT dispersion tended to correlate negatively with serum K^+. The results of this study are consistent with a previous report [10], and this is the first report that has revealed the correlation between QT dispersion and the Hunt and Hess grade and differences of QT dispersion in SAH patients with and without ventricular arrhythmias. Therefore it is advisable to assess the standard 12-lead ECG for QT dispersion to prevent and treat fatal arrhythmia, especially in patients with high-grade SAH. Hypokalemia should be treated in these patients.

The long QT syndrome is present when the QT is prolonged on the standard 12-lead ECG and when ventricular arrhythmia, such as torsades de pointes, occurs. It is classified into congenital and acquired types. The congenital type is caused by abnormalities of K^+ and Na^+ channels, which act on myocardial repolarization [13,14]. Hypokalemia, hypomagnesemia, and some drugs, such as antiarrhythmic agents, major tranquilizers, antidepressants, antihistamines, and some antibiotics, may induce the long QT syndrome. Myocarditis, myocardial ischemia, and cerebrovascular diseases may also be causes. Such drugs may act on the K^+ channel in the myocardium; however, the relationship between such factors and the long QT syndrome is unknown. In patients with SAH, hypokalemia and hypomagnesemia are often seen, and some patients suffer from a strong catecholamine release after the attack [15], which is

likely to cause a QT prolongation. In this study, 55% of SAH cases exhibited a long QT (QTc ≧ 500 ms). Patients with a long QT are more likely to have a fatal arrhythmia, such as ventricular fibrillation, especially with concomitant hypokalemia [2,3]. Abnormal depolarization during the third phase of the action potential may lead to torsades de pointes [16]. K^+ channel blockers, acidosis, and catecholamines accelerate this process and may cause elevation of extracellular K^+. Ca^{2+} antagonists, class Ib antiarrhythmic agents, and K^+ channel openers inhibit it [17]. Therefore, hypokalemia and acidosis should be promptly treated in patients with SAH. Consideration should also be given to the use of a Ca^{2+} antagonist, a K^+ channel opener, or a β-blocker.

Impairment of the hypothalamus may contribute to the long QT syndrome in patients with cerebrovascular disease [4]. Catecholamines are more elevated in patients with ruptured cerebral aneurysms in the vessels supplying the hypothalamus [18]. In this study, however, there was no difference in QT dispersion between the patients with ruptured aneurysms of the internal carotid artery or the anterior communicating artery, both of which supply the hypothalamus. It is possible that impairment of the cerebral circulation immediately after the onset of SAH may affect all of the brain, and therefore a difference among the locations of ruptured cerebral aneurysms was not seen. Further investigations with measurements of catecholamine levels are required to resolve this issue.

Sympathetic hyperactivity is seen in patients with SAH [18,19] and is considered to cause some of the abnormalities of the ECG [20]. Therefore, β-blockers are a logical choice to treat patients with SAH. Bonner et al. reported prolonged QT intervals and QT dispersion in patients with cardiac failure who improved with β-blocker therapy [21]. Previous reports of administration of β-blockers to patients with SAH investigated only blood pressure and heart rate [22,23]. The effects of β-blockers on the ECG and cardiac function require further investigation.

In conclusion, QT dispersion is prolonged in patients with SAH and correlates with the Hunt and Hess grade. QT dispersion should be evaluated on the standard 12-lead ECG in order to identify patients at risk and start early treatment.

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