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Impaired heart rate recovery as a predictor for poor health-related quality in patients with transient ischemic attack

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Abstract

We aimed to investigate heart rate recovery (HRR) in patients with transient ischemic attack (TIA) and the relationship between HRR and health-related quality of life (HRQOL).

All available patients were enrolled during the enrollment period. A total of 120 patients with TIA and 120 healthy controls were included in this study. A treadmill stress test was performed to calculate the HRR. The HRR were calculated as follows: HRR 1, 2, 3, and 5 minutes = heart rate at peak during exercise − heart rate at 1, 2, 3, and 5 minutes at rest. All patients enrolled were asked to fill in the Short Form 36 Health Survey to calculate HRQOL.

We found that the maximum heart rate of TIA patients was significantly higher than that of healthy controls (166 ± 11 vs. 162 ± 14 beats/min, $P = .015$). Similarly, maximum systolic blood pressure (SBP) and diastolic blood pressure (DBP) were higher in TIA group compared with healthy control group (SBP: 172 ± 15 vs. 165 ± 14 mm Hg, $P < .001$; DBP: 102 ± 12 vs. 93 ± 16 mm Hg, $P < .001$). The HRR were significantly lower in TIA group compared with control group (TIA vs. controls, HRR1: 17 ± 7 vs. 30 ± 8 beats/min, HRR2: 32 ± 11 vs. 49 ± 9 beats/min, HRR3: 43 ± 13 vs. 63 ± 12 beats/min, HRR5: 54 ± 16 vs. 73 ± 15 beats/min, all $P < .001$). Multivariate analysis showed that older age ($P = .03$) and high BMI ($P = .04$) were risk factors associated with abnormal HRR in patients with TIA. With regard to HRQOL, we found that role limitations due to physical problems, general health, vitality, and role limitations due to emotional problems were significantly lower in patients with abnormal HRR compared with patients with normal HRR. Multivariate analysis showed that older age ($P = .04$) and abnormal HRR ($P = .03$) were predictors for poor HRQOL in TIA patients.

HRR was impaired in patients with TIA. In addition, TIA patients with abnormal HRR suffered from a significantly poorer HRQOL. Hence, given the prognostic value of HRR, patients with TIA should be monitored to prevent cardiovascular events and to improve HRQOL.

Abbreviations: BMI = body mass index, BP = blood pressure, BP = bodily pain, DBP = diastolic blood pressure, GH = general health, HDL = high-density lipoprotein, HRQOL = health-related quality of life, HRR = heart rate recovery, HRR2 = heart rate recovery at 2 minutes, LDL = low-density lipoprotein, MH = mental health, PF = physical functioning, RE = role limitations due to emotional problems, RP = role limitations due to physical problems, SBP = systolic blood pressure, SF = social functioning, SF-36 = Short Form 36 Health Survey, TIA = transient ischemic attack, VT = vitality.

Keywords: health-related quality of life, heart rate recovery, risk factor, transient ischemic attack

1. Introduction

Transient ischemic attack (TIA) is transient neurological dysfunction caused by ischemia of the brain.[1] TIA is one of the most common ischemic cerebrovascular diseases. TIA affects more than 14 million people worldwide each year, and the morbidity and mortality rates are high.[1–3] Moreover, the risk of stroke after TIA is very high. Therefore, TIA is an early warning signal for stroke intervention, and detection of TIA is also an important opportunity for secondary prevention of stroke. The symptoms of TIA are mild, but if not treated in time, it can cause serious consequences.[4,5] It can lead to severe strokes and even mortality within 5 years. In essence, TIA and cerebral infarction are different stages of a dynamic process of ischemic brain injury.[6] Although the TIA episode is transient and reversible, 70% of patients are at an unstable and high-risk state, with a higher risk of relapse or short-term progression to stroke.[7,8] TIA patients are prone to developing cerebral infarction and myocardial infarction. The overall risk of TIA recurrence, myocardial infarction, and death within 90 days after TIA occurrence is as high as 25%.[9–11] Therefore, preventing the

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The Institutional Review Board had approved this study. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Informed consent was obtained from all patients for inclusion in the study.

The authors have no conflicts of interest to disclose.

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occurrence of advanced stroke, improving the health-related quality of life (HRQOL) of patients with TIA, and improving the prognosis are important therapeutic endpoints for patients with TIA.

Heart rate recovery (HRR) is defined as the decreased heart rate after exercise.[12,13] HRR abnormalities are often seen in patients with metabolic disorders, including cardiovascular disease, fatty liver, and diabetes.[14–17] HRR is estimated by calculating heart rates at minutes 1, 2, 3, and 5 during the recovery period after maximal heart rate in a patient undergoing a maximal stress test. Impaired HRR has been reported as an independent predictor of mortality.[12,13] Although impaired HRR has been reported in patients with cardiovascular diseases, it has not been reported in patients with cerebrovascular diseases, especially patients with TIA. Whether the HRR is impaired in patients with TIA and its relationship with HRQOL is currently unknown.

Hence, the purpose of this study is to investigate HRR among patients with TIA. We also evaluated the relationship between HRR and HRQOL in patients with TIA. Our study may help to increase quality of life (QOL) in patients with TIA and provide potential novel predictor for prognosis of patients with TIA.

2. Subjects and methods

2.1. Subjects

From November 2015 to December 2017, all available patients during the enrollment period were enrolled. A total of 120 patients diagnosed with TIA by magnetic resonance imaging were enrolled. All TIA patients met the TIA diagnostic criteria proposed by American Heart Association/American Stroke Association in 2008.[6] Patients with other neurological diseases, such as intracranial hemorrhage, infection, etc., or coexist with heart disease, cardiomyopathy, and severe liver and kidney dysfunction, thyroid dysfunction, malignant tumors, acute or chronic infectious disease, were excluded. A total of 120 healthy people were also enrolled as health controls.

2.2. HRQOL measurement

All patients enrolled were asked to fill in the Short Form 36 Health Survey (SF-36). All of the subjects finished the questionnaires in a quiet room without any disruption. They could get help from professional staff if they had problem in understanding the questions. The SF-36 is a brief self-administered HRQOL instrument commonly used in various diseased populations.[18,19] It includes 8 items: physical functioning, role limitations due to physical problems (RP), bodily pain, general health (GH), vitality (VT), social functioning, role limitations due to emotional problems (RE), and mental health. The tool's validity and screening ability have been shown in various samples in China.[18,19]

2.3. HRR measurement

Baseline electrocardiogram (ECG) was assessed in all TIA patients and healthy controls. The ECG was continuously recorded during the exercise test. At the end of the exercise test, the heart rate was recorded for 5 minutes after exercise in a supine position. The HRR index was calculated by subtracting the heart rate of the first (HRR1), the second (HRR2), the third (HRR3), the fourth (HRR4), and the fifth (HRR5) minutes during HRR from the peak heart rate at exercise. The HRR index was calculated as follows: HRR 1, 2, 3, and 5 = heart rate at peak exercise − heart rate at 1, 2, 3 and 5 minutes.

Table 1

Characteristics of patients in transient ischemic attack group and control group.

Characteristics	TIA group N = 120	Control group N = 120	P
Gender			.695
Male	71	68	
Female	49	52	
Age, years	37.84 ± 8.57	35.47 ± 7.92	.199
BMI	24.2 ± 2.2	23.7 ± 1.8	.419
Fasting glucose, mg/dL	93 ± 16	94 ± 9	.551
Triglycerides, mg/dL	122 ± 53	119 ± 62	.687
LDL cholesterol, mg/dL	98 ± 31	89 ± 29	.606
HDL cholesterol, mg/dL	41 ± 9	40 ± 6	.312
Creatinine, mg/dL	0.8 ± 0.3	0.7 ± 0.2	.122

BMI = body mass index, HDL = high-density lipoprotein, LDL = low-density lipoprotein, TIA = transient ischemic attack.

2.4. Statistical analysis

Continuous variables were expressed as mean and standard deviation, and categorical variables were expressed as percentages. The Chi-squared test and *t* test were applied to determine whether the results were statistically different. Univariate and multivariate analyses were used to explore the factors associated with outcomes. The statistical significance of all tests was set as $P < .05$ by two-tailed tests. Data analyses and quality control procedures were performed using SPSS for Windows, version 13.0 (SPSS Inc, Chicago, IL).

3. Results

3.1. Clinical features of TIA patients and controls

The baseline clinical variables of the TIA patients and controls were shown in Table 1. The TIA and control groups were similar with respect to gender, age, body mass index (BMI), and levels of triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, fasting glucose, and creatinine.

3.2. Exercise test results of TIA patients and controls

All patients underwent exercise test. The results showed that TIA patients and controls were similar in terms of duration of exercise (Table 2). The maximum heart rate of TIA patients was significantly higher than that of controls (166 ± 11 vs. 162 ±

Table 2

Exercise test results between transient ischemic attack group and controls.

Characteristics	TIA group N = 120	Control group N = 120	P
Duration of exercise, min	12.2 ± 2	11.8 ± 2	.123
Maximum heart rate, beats/min	166 ± 11	162 ± 14	.015
Maximum systolic BP, mm Hg	172 ± 15	165 ± 14	<.001
Maximal diastolic BP, mm Hg	102 ± 12	93 ± 16	<.001

BP = blood pressure, TIA = transient ischemic attack.

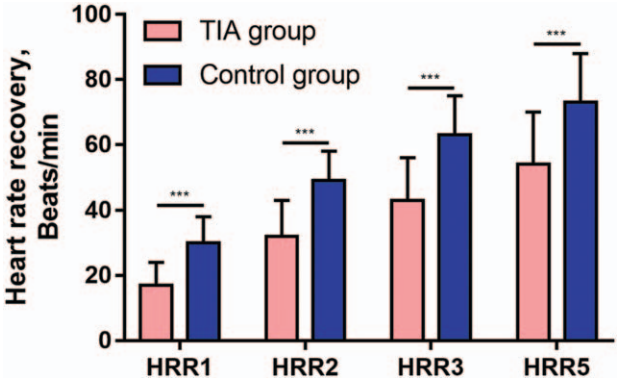

Figure 1. The HRR indices of the TIA group and the control group. The HRR indices were significantly lower in the TIA group as compared with the control group (TIA vs. controls, HRR1: 17 ± 7 vs. 30 ± 8 beats/min, HRR2: 32 ± 11 vs. 49 ± 9 beats/min, HRR3: 43 ± 13 vs. 63 ± 12 beats/min, HRR5: 54 ± 16 vs. 73 ± 15 beats/min, $P < .001$). HRR = heart rate recovery, TIA = transient ischemic attack.

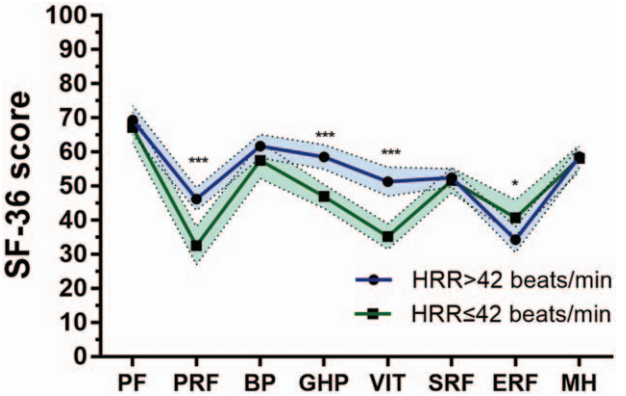

Figure 2. The HRQOL of the TIA patients with or without normal HRR. RP, GH, VT, and RE were significantly lower in TIA patients with abnormal HRR compared with patients with normal HRR (TIA patients with normal HRR vs. without normal HRR, PF: 69.4 ± 18.6 vs. 67.1 ± 15.16, RP: 46.2 ± 14.6 vs. 32.5 ± 18.8, BP: 61.7 ± 15.1 vs. 57.5 ± 17.9, GH: 58.5 ± 15.7 vs. 46.9 ± 11.8, VT: 51.3 ± 18.7 vs. 35.1 ± 12.6, SF: 52.5 ± 11.8 vs. 51.6 ± 12.3, RE: 34.3 ± 16.4 vs. 40.7 ± 17.5, MH: 58.6 ± 13.4 vs. 58.1 ± 12.7). *, $P < .05$; ***, $P < .001$. BP = bodily pain, GH = general health, HRQOL = health-related quality of life, HRR = heart rate recovery, MH = mental health, PF = physical functioning, RE = role limitations due to emotional problems, RP = role limitations due to physical problems, SF = social functioning, TIA = transient ischemic attack, VT = vitality.

Table 3

Characteristics of transient ischemic attack patients with normal and abnormal heart rate recovery at 2 minutes.

Characteristics	HRR2 ≥42 beats/min	HRR2 <42 beats/min	*P*
Gender			.811
Male	45	26	
Female	30	19	
Age, years	35.52 ± 7.16	38.92 ± 9.28	.026
BMI	23.5 ± 1.8	24.7 ± 2.6	.003
Fasting glucose, mg/dL	92 ± 18	95 ± 15	.349
Triglycerides, mg/dL	121 ± 51	123 ± 54	.839
LDL cholesterol, mg/dL	97 ± 33	98 ± 29	.867
HDL cholesterol, mg/dL	41 ± 10	40 ± 9	.583
Creatinine, mg/dL	0.7 ± 0.3	0.8 ± 0.3	.08

BMI = body mass index, HDL = high-density lipoprotein, HRR2 = heart rate recovery at 2 minutes, LDL = low-density lipoprotein, TIA = transient ischemic attack.

14 beats/min, $P = .015$). Similarly, maximum systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly different between TIA patients and healthy controls (SBP: 172 ± 15 vs. 165 ± 14 mm Hg, $P < .001$; DBP: 102 ± 12 vs. 93 ± 16 mm Hg, $P < .001$).

The HRR indices of the TIA group and the control group were shown in Figure 1. The HRR indices were significantly lower in the TIA group as compared with the control group (TIA vs. controls, HRR1: 17 ± 7 vs. 30 ± 8 beats/min, HRR2: 32 ± 11 vs. 49 ± 9 beats/min, HRR3: 43 ± 13 vs. 63 ± 12 beats/min, HRR5: 54 ± 16 vs. 73 ± 15 beats/min, $P < .001$).

3.3. Factors associated with abnormal HRR in patients with TIA

HRR2 ≥42 beats/minutes was defined normal (n = 75). The characteristics of TIA patients with normal and abnormal HRR were shown in Table 3. To further explore the relationship between characteristics and HRR, the multivariate logistic regression analysis was conducted (Table 4). The results showed that older age ($P = .03$) and high BMI ($P = .04$) were risk factors associated with abnormal HRR in patients with TIA.

3.4. Relationship between HRR and HRQOL in TIA patients

The HRQOL of the TIA patients was investigated. RP, GH, VT, and RE were significantly lower in TIA patients with abnormal HRR compared with patients with normal HRR (Fig. 2).

Table 4

Factors associated with abnormal heart rate recovery at 2 minutes among patients with transient ischemic attack.

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
Gender	0.59	0.20–1.91	.46			
Age	1.88	1.14–1.94	.02	1.54	1.05–1.57	.03
BMI	1.17	1.06–1.95	.03	1.12	1.01–1.42	.04
Fasting glucose	0.85	0.21–1.05	.09			
Triglycerides	0.64	0.49–1.65	.57			
LDL cholesterol	1.54	0.89–1.71	.63			
HDL cholesterol	0.84	0.47–2.01	.58			
Creatinine	1.59	0.46–1.92	.44			

BMI = body mass index, CI = confidence interval, HDL = high-density lipoprotein, HRR2 = heart rate recovery at 2 minutes, LDL = low-density lipoprotein, OR = odd ratio, TIA = transient ischemic attack.

Table 5

Social Characteristics of transient ischemic attack patients with normal and abnormal heart rate recovery at 2 minutes.

Characteristics	HRR2 ≥42 beats/min	HRR2 <42 beats/min	P
Marital status			.800
Single	12	8	
Married	63	37	
Level of education			.688
Primary	15	11	
Secondary	52	31	
Tertiary	8	3	
Income			.674
Low	8	3	
Middle	55	36	
High	12	6	

HRR2 = heart rate recovery at 2 minutes.

Table 6

Factors associated with health-related quality of life among patients with transient ischemic attack.

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P	OR	95% CI	P
Gender	1.07	0.72–1.96	.48			
Age	1.21	1.12–1.68	.02	1.11	1.01–1.53	.04
Marital status	1.11	0.71–1.18	.41			
Level of education	0.94	0.48–2.49	.55			
Income	0.72	0.76–1.49	.79			
HRR	1.34	1.09–2.18	.01	1.14	1.05–1.98	.03

CI = confidence interval, HRQOL = health-related quality of life, HRR = heart rate recovery, OR = odd ratio.

Similarly, TIA patients with abnormal HRR suffered from a significantly poorer HRQOL.

3.5. Factors associated with HRQOL in patients with TIA

To further validate the relationship between HRR and HRQOL in TIA patients, the social characteristics of TIA patients were compared and shown in Table 5. There were no significant differences of marital status, level of education, and level of income in TIA patients with normal or abnormal HRR. Multivariate analysis showed that older age ($P = .04$) and abnormal HRR ($P = .03$) were the predictors for the poor HRQOL in TIA patients (Table 6).

4. Discussion

TIA is an important early warning symptom of recurrent vascular events and management of TIA is critical for preventing disabling and fatal vascular events. In this study, we found that HRR was significantly reduced in TIA patients and was closely related to HRQOL. This suggests that early screening of TIA is important for preventing the occurrence of adverse vascular events, especially for those with abnormal HRR. Moreover, it is necessary to improve the HRQOL of this population.

HRR have been reported associated with poor HRQOL in some diseases.[20–22] HRR is an indicator of autonomic nervous system function and parasympathetic activity level.[23,24] At the end of exercise, parasympathetic reactivation plays a leading role in heart rate regulation. Pierpont et al[25,26] showed that HRR is closely related to cardiovascular death and all-cause mortality. Ardic et al[27] demonstrated impaired HRR index in patients with sarcoidosis. Compared to healthy controls, TIA was also closely related to cardiovascular diseases. Prospective studies are warranted to validate that TIA patients with abnormal HRR are more likely to have adverse cardiovascular events.[28,29]

Despite remarkable progression have been reached for the treatment of TIA, the life quality of TIA patients received limited attentions. As the evolvement of modern medical pattern has been transformed from the traditional biomedical model into biology-psychology-social medical model, HRQOL was emerging as important components of care in patients with chronic diseases.

Here, we first tested HRR in patients with TIA and assessed the relationship between HRR and HRQOL. We found that HRR impairment in TIA patients was closely related to poor HRQOL. Old age and abnormal HRR were independent factors related to poor HRQOL. This suggests that for patients with TIA, monitoring HRR is an effective method of assessing HRQOL. By this means, patients with high risk of poor HRQOL can be effectively screened and targeted for intervention.

This article has some limits. First, the sample size of this study was relative small, which may cause a certain bias. All patients were enrolled in a medical center. To explore the relationship between HRR and QOL in TIA patients, a prospective multicenter randomized study is warranted.

Author contributions

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Writing – original draft: Yongmei Liang, Xuanmin Li, Zhaona Qiao.
Writing – review & editing: Yongmei Liang.

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