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Original Article

The assessment of heart rate recovery index in patients with essential tremor

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Abstract

Aim: In this study, it was aimed to investigate whether heart rate recovery index(HRRI), which is marker of cardiovascular mortality, was affected in patients with essential tremor(ET).

Materials and Method: The study was conducted as retrospective and it consisted of 30 patients with ET and 30 healthy controls which were similar in terms of age and gender. During admission blood pressure and heart rate, fasting blood tests, hemogram, transthoracic echocardiography and exercise stress test results were recorded.

Results: The groups were similar in point of age, gender, smoking(p>0.05). Diastolic and systolic blood pressure of the groups were similar, whereas patients with ET had higher heart rate during admission. When exercise stress test results were assessed, 1st minute heart rate recovery, 2nd minute HRRI, 5th minute HRRI were lower in ET group and these differences were statistically significant(respectively p=0.017; 0.033; 0.019). However both groups were similiar with regards to 3rd minute HRRI(p=0.063)

Conclusion: According to this study results it might be thought that cardiovascular and total mortality may be higher in ET patients than healthy controls due to lower HRRI. Furthermore, it can be speculated that this disease may have an autonomous component since HRRI might be marker of an abnormal autonomic nervous system response.

Keywords: Autonom nervous system; cardiovascular mortality; essential tremor; heart rate recovery index

INTRODUCTION

Heart rate which is determined as heart beats per minute is affected by multiple factors such as exercise, sleeping, eating, mental activations. Regulation of the heart rate is a balance which is controlled by autonomic nervous system (ANS). The ANS consists of sympathetic and parasympathetic arm (1). We can show this balance most clearly in exercise test by calculating heart rate recovery index (HRRI) and heart rate variability via rhythm holter monitorization. The changes in heart rate during and/ or after exercise are related to the balance between sympathetic system and vagal activity. While sympathetic system is dominant in exercise period; parasympathetic activity is dominant in recovery period (2-4). Several variables may influence HRRI, including activity (e.g., complete cessation of exercise or cool down) and position (supine, sitting or standing). Suggested thresholds for normal responses are ≥12 bpm at 1 min for upright position, ≥18 bpm at 1 min for supine position and ≥22 bpm at 2 min for sitting position (2). The decrease in HRRI has been related to increase in sympathetic activity. Some studies showed that this situation is related with an increased cardiovascular mortality (5,6) .

Essential tremor (ET) that is characterized by postural and/ or kinetic tremor is the most common movement disorder around the world. The prevalence of ET increases with age and it affects nearly 4% percent of adults(7). There has not been any confirmed certain cause therefore ET has thought to be a syndrome which consisting of several causes (7). Although ET is a motor neuron disease, its relationship with the autonomic nervous system is not clear. However, recent studies revealed that patients with ET had significant cognitive dysfunctions and neuropsychiatric problems which include depression, autonomic symptoms and sleep problems (8-10).

The aim of this study was to investigate whether ET has any relationship with heart rate recovery index which is one of the independent predictors of cardiovascular mortality.

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MATERIALS and METHODS

Study Group

The study was single centred and retrospective. It consisted of total 60 cases who applied to our cardiology and neurology outpatient clinic between January 2016 and December 2018 because of chest pain, dyspnea and/or tremor were examined. There were 2 groups in the study. While 30 cases were patients with ET, the rest of the participants were healthy controls. The diagnosis of ET was made based on clinical and physical examination findings after excluding other possible diseases. The patients with ET were chosen among patients who were newly diagnosed and who were not treated with any medication, because any medication could affect heart rate and exercise stress test results. The age range was determined as 18-45 years. The exclusion criterias were any cardiovascular disease, hypertension, diabetes mellitus, liver or renal failure, any other chronic disease, active infection, endocrinologic diseases and pregnancy. The study was approved by local ethic committee.

Assesment of Blood Sample Tests, Arterial Pressure and Heart Rate

The blood sample tests results were obtained from patients' hospital records. Afterwards, fasting blood glucose, total cholestrol, low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides worked with colorimetric method (Cobas 8000, Roche, Germany), and hemogram parameters (BS-200, Mindray, Shenzhen, China) were recorded. The arterial blood pressure and heart rate of all participants, which was measured after 5 minutes rest at the outpatient clinic, was recorded.

Echocardiographic Evaluation

The left and right heart chambers diameters, ejection fraction(%EF) were measured from apical and parasternal views by using 2,5 MHZ transducer of Vivid 5 echocardiography(GE Medical Systems, Hortan, Norway).

The Evaluation of Exercise Stress Test

Before the exercise stress test electrocardiography (ECG) of cases is assessed. If there are no significant changes in ECG, the patients in whom ischemia are investigated are oriented for exercise stress test routinely. In our center, exercise stress test is performed according to Bruce protocol via Kardiosis TM Pro 2200. The ECG is recorded continuously during the test. When the exercise ends, recovery periods start and 1st minute heart rate recovery(HRRI1), 2nd minute HRRI(HRRI2), 3rd minute HRRI(HRRI3) and 5th minute HRRI(HRRI5) are recorded. The cases who achieved 85% percent of maximum heart rate were included in the study. The maximum heart rate was calculated according to that formula: 220 – age. Then heart rate recovery indices were calculated according to that formula:

HRRI 1,2,3,5: Heart rate at peak exercise –Heart rate in 1.,2.,3.,5. minute of recovery period.

Also, peak exercise heart rate, exercise duration and exercise capacity were recorded.

Statistical Analysis

In this study, Statistical Package for Social Sciences(SPSS) 20.0 for Windows, USA, Armonk New York program was used for statistical analysis. The descriptive statistical methods (mean, standard deviation) were used to evaluate the datas. It was shown by being calculated with Skewness Kurtosis test whether variables distributed normal. Non-normal distributed variables, such as smoking, fasting blood glucose, ejection fraction (EF%), exercise capacity and peak exercise heart rate were assessed with Mann Whitney U test, while normal distrubited variables were assessed with Independent Sample Student t Test. Correlation analysis was used to explore the relationship between HRRI2 and HRRI 1, HRRI 3, HRRI 5, total cholesterol, LDL, HDL, triglycerides. Also, the relationships between HRRI2 and HRRI 1, total cholesterol, LDL were calculated by using multivariate regression analysis. When p<0,05 was reached, result was accepted meaningful.

RESULTS

The study included total 60 cases (30 of controls and 30 of ET patients). In the study, 13 (43,3%) of the control group and fourteen (46.6%) of the ET group were female. The mean age of controls was 34.55±10.75 year, while in group of ET was 32.82±10.24 year and there was no significant difference between the groups (p=0.542).

Table 1. General charateristics of the groups

	Essential Tremor Patients	Controls	p
Gender	Male, 16 (53.4%)	Male, 17, (56.7%)	
Age (year)	32.82±10.24	34.55±10.75	0.542
Heart rate (per minute)	97±33.6	81.7±9.5	0.044
Diastolic arterial pressure (mmHg)	74.34±12.73	69.41±8.94	0.107**
Systolic arterial pressure (mmHg)	117.26±16.95	114.29±13.8	0.490
Smoking*	19 (%63)	22(%73)	
Smoking (box/year)	2.5±9.4	5.4±10	0.124**

p:Independent sample student; p*,Chi square test; p**: Mann Whitney u; mmHg: milimeter mercury

Twenty two (73%) of controls and 19 (63%) of patients' group were smoking. All of the cases were in sinus rhythm. The participants were compared in point of resting arterial pressure and heart rate. There was no discrepancy in terms of systolic and diastolic arterial pressure between the groups(respectively p=0.490, 0.107). However heart rate was higher in ET groups (p=0.044). The general characteristics were presented in Table 1. The groups were compared in terms of fasting blood tests such as fasting blood glucose, total cholesterol, LDL, HDL, triglycerides. The results of fasting blood glucose, total cholesterol, LDL and triglycerides were found similar (respectively p= 0.883; 0.589; 0,877; 0.385) but there was significant difference with regard to HDL between groups (p= 0.004). HDL was higher in ET patients than controls. Hemogram parameters levels were similar(p>0.05). The groups were assessed in point of diameters of heart chambers. The left ventricle end-diastolic diameter, left ventricle end-systolic diameter, left atrium diameter, right atrium and ventricle, EF were statistically similarity in both groups(p>0.05). The blood sample test and echocardiography results were seen in Table 2.

The groups were compared in terms of exercise stress test results. According to statistical analysis while a meaningful difference in terms of HRRI1, HRRI2, HRRI5 (respectively p=0.017; 0.033; 0.019) was found, there was no statistical difference with regard to HRRI3, peak exercise heart rate, exercise capacity and duration of exercise (respectively, p=0.063; 0.052; 0.441; 0.190). The HRRI1, HRRI2, HRRI5 were higher in controls than patients with ET. The results of exercise stress test were shown in Table 3. Correlation analysis revealed that there was a strong positive correlation between HRRI2 and HRRI1. However there was a negative correlation between HRRI2 and total cholesterol, LDL. The results were summed in Table 4. When relationship between HRRI2 and HRRI1, LDL, total colesterol was assessed by using multiple regression analysis in ET group there was relationship among variables. The results were summarized in Table 5 and 6.

Table 2. Blood sample tests and transthoracic echocardiography results

	Essential Tremor Patients	Controls	p
Total cholesterol (mg/dL)	183.95±40.87	178.58±28.79	0.589
LDL (mg/dL)	106.43±36.31	107.79±25.44	0.877
HDL (mg/dL)	52.78±9.31	43.79±12.33	0.004
Triglycerides (mg/dL)	119.56±55.64	134.11±55.64	0.385
Fasting blood glucose (mg/dL)	89.92±19.26	93.0±8.65	0.883*
Hemoglobin (g/dL)	13.74±1.37	14.15±1.56	0.304
Platelet (109/L)	272.21±58.08	257.88±46.47	0.329
EF (%)	65	64.47±1.5	0.098*
LVEDD (cm)	4.55±0.29	4.49±0.41	0.517
LVESD (cm)	3.54±0.29	3.71±0.49	0.111
LA (cm)	3.17±0.39	3.32±0.28	0.151
RA (cm)	2.96±0.29	2.92±0.29	0.698
RV (cm)	2.23±0.25	2.2±0.23	0.9679

p:Independent sample t test; p*: Mann Whitney U; cm: centimeter; EF: Ejection fraction; HDL: High density lipoprotein; mg/dL: miligram/deciliter;LDL: Low density lipoprotein; LA:Left atrium; LVEDD: Left ventricle end-diastolic diameter; LVESD: Left ventricle end-systolic diameter; RA: Right atrium; RV: Right ventricle

Table 3. Exercise stress test results of the groups

	Essential Tremor Patients	Controls	p
Peak exercise heart rate (beats/min)	173.86±13.43	168.82±11.38	0.052*
Exercise capacity (METs)	12.02±1.23	11.69±1.84	0.441*
Duration of exercise, sec	597.3±152.3	547.32±115.58	0.190
HRRI 1st min,beats/min	25.91±6.72	31.73±11.1	0.017
HRRI 2nd min,beats/min	44.78±10.87	51.32±11.3	0.033
HRRI 3rd min,beats/min	53.73±13.07	60.14±11.37	0.063
HRRI 5th min,beats/min	57.82±13.09	66.17±12.24	0.019

HRRI: Heart rate recovery index; METs: Metabolic equivalent units; min: minute; sec:Second; p: Independent sample t test , When it is <0,05 , it was associated meaningful; p*: Mann Whithney U testi

Table 4. Corelation analysis of the some variables

No	Variable	1	2	3	4	5	6	7	8	9
1	HRRI 1st min,beats/min	1								
2	HRRI 2nd min,beats/min	r:0.686**	1							
		p:0.000								
3	HRRI 3rd min,beats/min	r:-0.042	r:0.230	1						
		p:0.425	p:0.146							
4	HRRI 5th min,beats/min	r: -0.126	r :0.116	r:0.899**	1					
		p:284	p:0.299	p:0.000						
5	Heart rate(per minute)	r:-0.326	r:-0.232	r:-0.122	r:-0.212	1				
		p:0.065	p:0.144	p:0.234	p:0.234					
6	Total choletsterol	r:-0.248	r:-0.463*	r:-0.535*	r:-0.487	r:-0.197	1			
		p:0.127	p:0.013	p:0.004	p:0.009	p:0.184				
7	LDL	r:-0.248	r:0.427*	r:-0.578*	r:0.551	r:0.219	r:0.953**	1		
		p:0.21	p:0.021	p:0.002	p:0.005	p:0.157	p:0.000			
8	HDL	r:-0.32	r:-0.15	r:-0.111	r:0.183	r:0.113	r:0.208	r:0.043	1	
		p:0.068	p:0.247	p:0.307	p:0.202	p:0.304	p:0.171	p:0.423		
9	Triglycerides	r:-0.031	r:-0.205	r:-0.018	r:0.119	r:0.1	r:0.399*	r:0.246	r:0.306	1
		p:0.444	p:0.174	p:0.467	p:0.294	p:0.324	p:0.03	p:0.129	p:0.078	

HDL: High density lipoprotein; HRRI: Heart rate recovery index, min: minute., LDL: Low density lipoprotein
*: Correlation is significant at the 0.05 level. **: Correlation is significant at the 0.01 level

Table 5. Linear regression analysis between HRRI2 and Total cholesterol, LDL, HDL, Triglycerides, HRRI1, HRRI3 and HRRI5

Variables	Unadjusted		
	B(CI%)	p	R2
Total colesterol	-0.463 ([-0.23]-[-0.016])	0.026	0.215
LDL	-0.427 ([-0.251]-[-0.005])	0.042	0.182
HDL	-0.15 ([-0.639]-0.318)	0.494	0.023
Triglycerides	-0.205 ([-0.127]-0.047])	0.042	0.348
HRRI 1st min	0.686 (0.575-1.642)	0.000	0.47
HRRI 3th min	0.23 ([-0.176]-0.558)	0.292	0.053
HRRI 5th min	0.116 ([-0.278]-0.47)	0.598	0.013
Heart rate (per min)	0.232 ([-0.068]-0.218)	0.287	0.054

HDL: High density lipoprotein; HRRI: Heart rate recovery index, min: minute., LDL: Low density lipoprotein

Table 6. Multivariate regression analysis between HRRI2 and Total cholesterol, LDL, HRRI1 (R^2: 0.499; p:0.001)

Variables	B(CI%)	p
Total colesterol	-0.073 ([-0.306]-[-0.267])	0.888
LDL	-0.247 ([-0.391]-0.243)	0.631
HRRI 1st min	0.624 (0.471-1.546)	0.001

HDL: High density lipoprotein; HRRI: Heart rate recovery index, min: minute., LDL: Low density lipoprotein

DISCUSSION

Essential tremor is one of the most common neurological disorder. There is growing evidence to suggest that ET is a multiple-system disorder because it involves a wide spectrum of motor and autonom nervous system features (8). In this study, we investigated that whether ET has an autonomic component by using exercise stress test. It was shown that HRRI was lower in ET group than controls. It might be suggested that ET has an autonomic component. This study is a unique research investigating the relationship between ET and HRRI.

In the literature, there are few studies which investigated autonomic dysfunction in ET patients. In the study by Habipoğlu et al., the autonomic nervous system function was evaluated sympathetic skin response (SSR) and R–R interval variation (RRIV) by using electrophysiological evaluations. The mean latency of SSR in ET patients was significantly delayed compared with the controls (p = 0.01) (11). Kim et al. used Tilting test, ambulatory 24-h blood pressure monitoring and 24-h Holter monitoring values in their study. The frequencies of orthostatic hypotension, supine hypertension, nocturnal hypertension and non-dipping were similar in the ET patients and the controls, although ET patients had more episodes of orthostatic intolerance. Also, there was no significant discrepancy between the ET group and controls in terms of heart rate variations for all the time-domains. In the study by Lee at all., they assessed nonmotor symptoms in essential tremor with Parkinson's disease (PD) and normal control by using the Nonmotor Symptoms Scale. They found that there were significant differences in the Nonmotor Symptoms Scale total scores of the ET with PD, and control groups (ET: 25.500 ± 2.346; PD: 27.960 ± 3.267; controls 3.328 ± 3.796) (12). Similar to these studies, HRRI1, HRRI2 and HRRI5 were lower in patients with ET in this study. According to these studies, it might be assumed that ET has an ANS dysfunction.

Coronary artery disease is one of the foremost death reasons (13). Hence, there are a lot of tests for diagnosis of coronary atherosclerosis. The exercise stress test is one of them. The exercise stress test allows not only assessment of ST segment change but also functional aerobic capacity, chronotropic response and heart rate recovery. The HRRI is an important prognostic factor in cardiovascular and total mortality (14). The impaired HRRI was diagnosed in patients with obstructive sleep apnea syndrome, silent myocardial ischemia, heart failure with preserved ejection fraction and type 2 diabetes mellitus (15-19). In a study, it was found that HRRI is a prognostic factor in primary prevention. In our study HRRI1, HRRI2, HRRI5 was lower in ET. According to this study, patients with ET should be assessed in terms of cardiovascular risk factors because of prognostic feature of HRRI. In this study, it was found that HRRI 1,2,5 were impaired in patients with ET. The withdrawal in sympathetic nervous system is dominant in the late phase of recovery while parasympathetic nervous system is active in early phase of recovery. Rapid reduction can be prevented with atropine in the early period indicates that reduction occurs due to the vagal effect; a decrease in heart rate observed at 30th second and 2nd minute after resting was weakened with atropine and with dual blockade. Therefore late-phase sympathetic nervous system modulation plays a more important role on the improvement in heart rate (20). Because of this change it was thought that there was no difference between groups in point of HRRI 3 in our study.

LIMITATIONS

One of the limitations of study were small sample size. Additionally, the study was retrospective. Also, these results could not be compared another as an indicator of autonomic dysfunction.

CONCLUSION

HRRI is one of the markers of cardiovascular, non-cardiovascular and total mortality, and it proves information about abnormal ANS. According to results of this study, it might be speculated that in patients with ET may be increased in cardiovascular mortality. Also, it might be a clue of abnormality of ANS.

Competing interests: The authors declare that they have no competing interest.

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