Heart Rate Fluctuations and Late Ventricular Potentials in Depression Patients without Clinical Cardiovascular Disease

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ABSTRACT

Background: *Although there are a number of publications demonstrating how depression increases cardiovascular morbidity and mortality, there are few and contradictory publications regarding heart rate fluctuations and late potentials. In the present study, we aimed to investigate whether heart rate fluctuations (HRF) and late ventricular potential values are different in patients with depression compared to those in normal individuals.*

Methods: *Thirty two untreated depressive patients having no associated clinical cardiovascular disease and 29 healthy individuals were recruited in the study. Beck's depression inventory was used to determine patients with depression. Recordings were made with the Cardioscan digital ECG holter recorder. Heart rate fluctuations and late potential criteria were evaluated using a computer with Cardioscan software.*

Results: *There was a decrease in standard deviation of normal to normal intervals and its index (p= 0.001) and an increase in sympathetic tonus (p= 0.006) in depressive patients. No statistical significance in regard to the late ventricular potential values was determined between depressive patients and healthy individuals.*

Conclusions: *There was a decrease in some of the HRF parameters and an increase in sympathetic tonus in depressive patients, but late ventricular potentials were not different from those of healthy individuals.*

Key words: *Heart rate fluctuations, late ventricular potentials and depression.*

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INTRODUCTION

There has been contradictory results about association between major depression and cardiovascular diseases. Further research is needed to determine how depression increases risk for cardiac morbidity and mortality (1-3). Increased cardiovascular mortality and morbidity in depression patients was demonstrated in several studies and depression was defined as an independent risk factor (4-6). Various other studies in which depression was seen with decreased heart rate fluctuations were also reported (7-9), but some studies showed no difference between depressive and healthy individuals (10,11).

It is said that these fluctuations indicating an increased sympathetic and decreased parasympathetic effect in depression patients are concurrent with arrhythmic events and increased mortality particularly in patients with a known organic heart disease (8,12). However, there are no studies on late potential criteria and increase in the prevalence of arrhythmic events in untreated with antidepressant therapy depressive patients without an organic disorder. Therefore, we investigated parameters of heart rate fluctuations and late ventricular potentials changes in untreated with antidepressant therapy depressive patients without clinical cardiovascular disease in this study.

MATERIALS AND METHODS

Characteristics of the Patients and Control Groups

Patients were chosen from individuals who were not receiving any sorts of anti-depressants, but were diagnosed with depression by the psychiatry clinic and planned to begin drug treatment. Patients with hypertension, diabetes mellitus, coronary arterial disease, congestive heart failure, valvular heart disease, myocarditis, thyroid dysfunction, anemia, menstruation, chronic obstructive pulmonary disease were excluded from the study. Patients using drugs which might affect the autonomous system were also excluded from the study. Patients with previous arrhythmic event anamnesis were not included in the study. Consecutive 32 depression patients and 29 healthy individuals were included in the study. We recruited the healthy individuals according to physical and physicologycal examination by medical doctor (cardiologist and psychiatrist).

Patients were aged between 32 and 64 (mean: 41±14 years), and consisted of 18 male, 14 females. Healthy individuals were aged between 29 and 65 (mean: 39±15 years), consisting of 15 males, 14 females (Table 1).

Diagnosis of Major Depression

Beck's depression inventory was used under the supervision of a psychiatrist in order to determine depression patients. Patients who received 17 points or more defined as depressive. Beck's depression inventory was developed to determine the depression risk and to measure the level and intensity of depressive signs (13). This method is applicable both to psychiatric patients and healthy groups, and it has a self-assessment scale. It contains a total of 21 self-assessment sentences. Patients answer by marking on the scale and they fill out on their own. Each item is scored increasingly from 0 to 3, and the total score is obtained by adding these up. Total ranges in between 0-63 (13) and the validity and security cutting point of the scale is accepted to be 17 (14).

Heart Rate Fluctuations and Analysis of the Late Ventricular Potentials

Cardioscan 12 channel, 10 wire digital holter recorder was used to obtain 24-hour recordings of the

Table 1. Characteristics of the patient and control groups.

	Depression group	Control group	p value
Number of subjects (n)	32	29	0.277
Male	18	15	0.397
Female	14	14	0.729
Mean age	41±14	39±15	0.367
Depression score	26±7	9±5	0.001
Level of education (years)	7±4	5±6	0.039
BMI (kg/m²)	20±5	17±6	0.020
Number of smokers	21	12	0.049

BMI: Body mass index.

patients outside the hospital. The signal averaged electrocardiogram (SAECG) program of this device was also used with its 3 channel(orthogonal lead), 7 wire recorder, and late potential analyses were performed. Recordings that lasted 23 hours ± 35 minutes were used for Holter analyses. Recordings lasting 35±5 minutes were used in a quite setting for late potential analyses. Heart rate fluctuations and late potential criteria were evaluated using a computer with Cardioscan software. SDNN (standard deviation of normal to normal intervals, 24-Hour normal values < 50 ms), SDNN index(average of the standard deviation of normal to normal intervals, 24-Hour normal values < 30 ms), SDANN (the standard deviation of the 5-minute average NN intervals, 24-Hour normal values < 40 ms), pNN50 (the percent of R to R intervals differing > 50 ms from the preceding one, 24-Hour normal values < 0.75%) and rMSSD (the root mean squared of successive differences, 24-Hour normal values < 15) parameters were used for time-area parameter (15,16).

Ectopic beats or beats originating from outside the sinus were excluded from these analyses. We did not recruit indivudials and patients having frequent atrial and ventricular ectopic beat (> 10 beat/hour) in both groups. Each heart beat was marked as normal or abnormal. Distances from one normal beat to the other were calculated. In practice, measurements can be performed as short measurements ranging from 5 minutes to 1 hour, in addition to 24-hour measurements. However the frequently used method is the one that is 24 hours long. Long and short RR interval fluctuations were measured in the time-area method. Measurements of the frequency-area method were performed by calculating Power Spectral Density. It is calculated from High frequency (HF), low frequency (LF), very low frequency (VLF) and the LF/HF rate. While HF represents parasympathetic power, VLF and LF determines sympathetic activation. There is significant correlation between frequency-area and time-area parametersn (HF and rMSSD and pNN50 , LF and SDNN index, VLF and SDNN index , ULF and SDNN and SDANN) (15,16).

Late potential criteria were carried out again using the software found in the same device. QRS waves were filtrated at 40-250 Hz bi-directionally in this device. Total period of filtrated QRS, the period of terminal QRS below 40mVs, and the root of the mean squared voltage of QRS in the final 40 ms were studied. Recordings with noise values above 0.7 microvolts were excluded from the study. SAECG is a noninvasive technique detecting the high-frequency, low-amplitude signals found at the end of the QRS complex and called late potentials. It is accepted that these signals are recorded from the slow conduction sites of the ventricular myocardium and that these sites constitute a substrate for reentrant ventricular arrhythmias. As for criteria, duration of the filtrated QRS complex is significant if 1) longer than 114-120 ms 2) signals in the last 40 ms are below 20 microvolt (mV) 3) the period below 40mVs is longer than 38 ms (17), and the late potential is considered positive if 2 out of these 3 criteria are present.

Statistical Analysis

The unpaired t test was used in the comparison of the parametrical variables, and chi-square test was used when comparing the categorical variables of both groups. $p< 0.05$ was considered significant.

RESULTS

There were no statistical differences between the two groups in terms of age and sex. (Table 1). However the rate of smoking and the level of education and body mass index was significantly higher in the group of patients with depression (p= 0.049, p= 0.039, p= 0.020, respectively). Maximum, mean and minimum heart rate (beat/min) values were higher in the depression group. (p= 0.008; p= 0.002; p= 0.003, respectively) There were no statistical differences between the two groups in terms of systolic and diastolic blood pressure (p= 0.197, p= 0.661 respectively).

There were no significant differences in the QT and QTc values between the two groups,respectively (p= 0.16; p= 0.14, respectively). While two of the time-area parameters, the SDNN and SDNN index, showed a significant decrease (p= 0.001) in the depression group compared with the control group, the others, i.e. rMSSD (p= 0.662) and pNN50 (p= 0.205), showed no significant changes. Although VLF, LF, LF/HF tended to increase and HF tended to decrease in the depression group, no statistical difference was found between VLF (p= 0.181) and LF (p= 0.290) and HF (p= 0.195) and LF/HF (p= 0.679) values, which are the frequency-area parameters. The sympathetic activity increase was higher in the depression group (p= 0.006), but there was also a parasympathetic activity decrease (p= 0.001) (Table 2). There were no statistical differences between the late potential values of both groups (Table 3).

Table 2. Comparison of clinical parameters between depressive and healthy individuals.

	Depression group	Control group	p value
Max. heart rate(beats/min)	91±13	82±13	0.008
Mean heart rate (beats/min)	75±11	66±11	0.002
Min. heart rate (beats/min)	67±11	58±11	0.003
Systolic blood pressure(mmHg)	128±11	119±15	0.197
Diastolic blood pressure(mmHg)	76±8	71±7	0.661
Max. QT (ms)	419±22	405±19	0.16
Max. QTc (ms)	449±31	423±42	0.14
Total power	1028±830	1050±790	0.956
VLF	496±509	356±409	0.181
LF	281±233	211±196	0.290
HF	164±93	201±93	0.195
LF/HF	2.3±1.7	1.7±1.9	0.679
SDNN	32±11	112±11	0.001
SDNN index	22±12	39±17	0.001
rMSSD	21±9	23±7	0.662
pNN50	5±3.4	6±3	0.205
Parasympathetic %	69±20	86±16	0.001
Sympathetic %	31±21	14±21	0.006

Max: Maximum, Mean: mean, Min: minimum, Blood pressure: mmHg, QTc: Duration of QT adjusted according to the heart rate, Total Power: Total frequency power, VLF: Very low frequency , LF: Low frequency, HF: High frequency, LF/HF: Low frequency's proportion to high frequency, SDNN: standard deviation of normal to normal intervals, SDNN index: average of the standard deviation of normal to normal intervals, RMSSD :the root mean square of successive differences , pNN50: The percent of R to R intervals differing >50 ms from the preceding one.

Table 3. Comparison of late potential values between depressive and healthy subjects.

	Depression group	Control group	p value
Mean number of cycles	756±250	789±234	0.939
Standard QRS (ms)	89±11	91±12	0.951
Total QRS (ms)	99±8	96±8	0.840
LSTMS (ms)	34±10	32 ± 9	0.910
LAS40 (mV)	54±35	45 ± 28	0.985
Mean amount of noise (mV)	0.2±2	0.3 ± 2	0.955

LSTMS: Duration below 40 mV (ms), LAS40: Signals in the last 40 ms mV.

DISCUSSION

Increased sympathetic activity is associated with increased corticotrophin response to stress (18,19). Cortisone's synergy with hypertriglyceridemia, hypercholesterolemia and hypertension are known. There is also norepinephrine secretion in depression. Catecholamines increase the heart rate and blood pressure by increasing myocardial oxygen consumption. Serotonin also plays an important role in depression. Its effects on increasing thrombocyte activation

are known. Increase in thrombocyte aggregation was demonstrated in depression (20). And also major depressive disorder is associated with decreased nitric oxide production (21) and elevated plasma IL-6 level, a good predictor of future risk for both cardiovascular disease and osteoporosis (22).

Decreased heart rate fluctuation parameters mean a reduction in parasympathetic tonus and an increase in sympathetic tonus. It is known that major depressive diseases increase the prevalence of cardiovascular diseases (1-3). Increased cardiovascular mortality and morbidity in depression patients was demonstrated in several studies and depression was defined as an independent risk factor (1-5). In certain studies, it was stated that HRF of depressives is not different from those of healthy individuals (10,11). Similar to the above mentioned studies (4-6), significant changes in the values of heart rate fluctuations were determined in our results. It has been determined in several studies that reduced heart rate fluctuations indicate a bad prognosis, particularly when seen concurrent with organic heart disorders (4-6).

High heart rate fluctuations occur in people with a healthy heart. Heart rate fluctuations are decreased in coronary heart diseases and congestive heart failures (3). The rate of smoking in our study group was seen with a higher prevalence than the control group. It is known that smoking is a positive risk factor for coronary heart disease and that it leads to an increase in sympathetic tonus. Its effects on heart rate fluctuations were not evaluated in this study. Besides, body mass indexes were also higher than those of the control group. Our study has some confounding factors above mentioned such as smoking and body mass index.

There are no studies on late potential in untreated with antidepressant therapy depressive patients without an organic disorder (23). Further studies are required on this issue. According to our results, the late ventriculer potential positivity is not present in our depression patients without any clinical cardiovascular diseases. All patients with previous arrhythmic event anamnesis were excluded from this study. Thus, we did not consider depression to be a risk factor for arrhythmic events through this mechanism. However, some of the heart rate fluctiation parameters were reduced.

Consequently, we concluded that the use of heart rate fluctuation parameters useful in depression patients without any clinical cardiovascular disease and not receiving any sorts of antidepressants in clinical practice. Whereas, the use of late potentials has no practical benefit.

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