

COMPARISON OF HEART RATE VARIABILITY BETWEEN PATIENTS WITH MAJOR DEPRESSIVE DISORDER AND NORMAL SUBJECTS

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ABSTRACT: Major Depressive Disorder is one of the major mental health problems that affect the quality of life of the patients. The reduced heart rate variability (HRV) and elevated heart rate that associated with depression have been found as risk factors for cardiac mobility and mortality. These patients should be assessed regularly on HRV parameters and compare with those of normal subjects. This study aimed to compare heart rate variability between patients with the major depressive disorder and normal subjects. This study was conducted at a psychiatric department in Khon Kaen University, Srinagarind Hospital, Khon Kaen province, Thailand. A cross-sectional analytic study design was used. Forty patients diagnosed with the major depressive disorder (who had been treated with antidepressants) were matched according to age, gender with 40 normal subjects participated. They were assessed on HRV for time domain (standard deviation normal to normal: SDNN, and the root mean square of successive differences: RMSSD) and frequency domain (High frequency: HF, low frequency: LF, and LF/HF ratio) using SA 3000P Digital. The results showed that The HRV in the patients and in the normal subjects were found with SDNN 28.60, 31.44; RMSSD 23.78, 26.73; HF 4.70, 5.04; LF 4.46, 5.01; and LF/HF 1.16, 1.35 respectively. However, No significant difference in the HRV variables between MDD and normal subjects except LF. Findings of this study show that HRV in the treated patients with major depressive disorder seems to be a little lower than the normal subjects. This may be due to the effects of well treated with antidepressants. It is suggested that HRV may be one of the outcome measures for this patient population.

Keywords: Major depressive disorder, Heart rate variability, Time domain, Frequency domain

1. INTRODUCTION

Major depressive disorder (MDD) is the most common illness psychiatric problem and will be one of the most disabling medical conditions by 2020. It has a large prevalence worldwide, with an estimated 350 million people affected [1]. MDD has been found around 2.4% in Thai population from an epidemiological study of Mental Disorders National Survey in 2008 [2]. It could be one of the risk factors for developing ischemic heart disease and has been found to elevate mortality rate of cardiovascular diseases that sudden death can occur after cardiac infarction [3].

The cardiovascular system is a dynamic organ system that permits blood and nutrients to and from cells in the body. In normal physiology, heart rate responses to environmental stresses by the interaction between the sympathetic and parasympathetic activities of the autonomic nervous system (ANS). The normal heart rate is defined by the rate of sinus node depolarization. Sinus rhythm oscillates around the mean HR, which is dependent on continuous regulation by ANS. Heart rate

variability is a predictor that qualitative in charges of heart rate during normal beat to beat in physiological processes of the autonomic nervous system [4]. A number of techniques have been developed to quantify beat-to-beat variability in order to provide indices of cardiac autonomic regulation in both health and disease [5]. Depression and mental stress were initially associated with the sympathetic activities and then were found to correlate with parasympathetic activity [6]-[7]. Heart rate seems to be higher while heart rate variability (HRV) tend to be lower in depressed patients [8]. The reducing HRV and elevated heart rate were associated with depression [9] which have been known to be risk factors for cardiac mobility and mortality [10]. HRV components that are commonly affected by depression are the high-frequency power [11], and the SDNN [12-14]. Some evidence also suggests that depression is associated with altered brain function and elevated sympathetic activity, which may lead to cardiovascular dysregulation.

Interactions of the central nervous system increased sympathetic tone, decreased

parasympathetic tone to the heart will also reduce heart rate variability. However, the effects of sympathetic and parasympathetic activities on the interaction between stress and depression of the autonomic nervous system remains unclear [15]. HRV is an electrocardiograph-based technique developed to assess the relative influences of sympathetic and vagal branches over heart's beat-to-beat activity [16]. However, many factors that influence on depression have been associated with the decreased cardiac vagal control. It may be a trait marker for MDD [17] which can be used for evaluating and classifying the severity of symptoms in these patients. This study aimed to compare heart rate variability between patients with the major depressive disorder and normal subjects.

2. METHODS

2.1 Design and Setting

A cross-sectional analytical design was used in this study. The identification of cases and controls the diagram as shown in Fig 1.

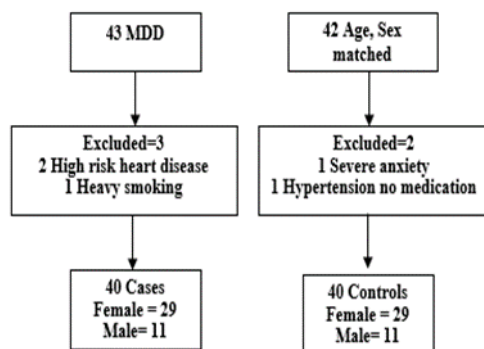


Fig. 1 Flow charts for the identification of cases and controls.

2.2 Participants

Forty patients, aged 18-64 years, who were diagnosed with MDD, were recruited at the psychiatry outpatient clinic of Srinagarind Hospital, Khon Kaen University, Khon Kaen province, Thailand.

2.3 Procedure

The study proposal was approved by the Khon Kaen University Ethics Committee for Human Research with reference number HE581192. The objective and design of the study were explained to all participants before they gave informed consent at the psychiatric clinic of Khon Kaen University, Srinagarind hospital. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) was conducted to ensure the diagnosis of MDD by a licensed psychiatrist.

The process of data collection consisted of three steps. The first step included demographic data (sex, age). The second step included physician

assessment measure were assessed by the Hamilton rating scale for depression and structured clinical interview for Mini International Neuropsychiatric Interview (MINI). It was used to determine depression and to rule out other similar psychiatric disorders such as bipolar disorder, schizophrenia, and psychotic disorder. The third step, all subjects were asked to have an early meal at least 2 hours prior to participating in the measurements.

They were also instructed to refrain from alcohol or caffeinated consumption 24 hours before participation. To control for diurnal variation, HRV was measured between 10.00 a.m. and 2 p.m. Subjects were asked to sit quietly for 20 minutes before recording. Each of the subjects was comfortably seated on a chair, then the probe was placed on his/her left index finger to measure HRV for 3 minutes. During HRV measurement the subject was guided to breathe naturally in order to obtain accurate HRV data. The process of data collection through interview and storage are shown in Figs.2-3.



Fig.2 Photo showing an interview with a psychiatrist

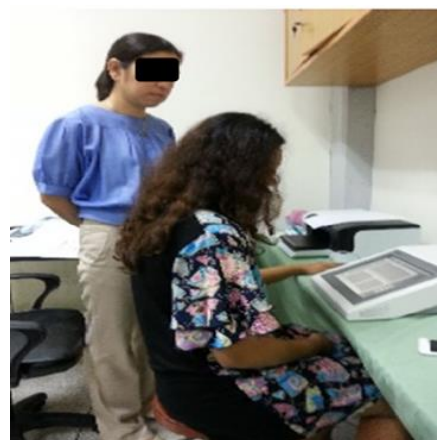


Fig.3 A SA3000 apparatus for analysis

2.4 Measurement Equipment

All variables were calculated as indicators of ANS function by using SA-3000P (Medicore Co., Ltd, Seoul, Korea). Time domain analysis reports the activity of circulation system and variables included: (1) the standard Deviation of all normal to normal intervals (SDNN) as an estimate of overall HRV, and (2) the Root Mean Square successive differences of normal to the normal interval (RMSSD) which indicate mostly parasympathetic activity.

Frequency domain analysis reflects the sympathovagal balance of ANS and variables included: (1) High-Frequency power expressed as normalized units (HF nu; 0.15-0.4 Hz); (2) Low-Frequency power expressed in normalized units (LF nu; 0.04-0.15 Hz). The LF- band is associated with both sympathetic and parasympathetic activity, while the HF band can be interpreted as a specific measure of parasympathetic control; and (3) LF/HF display for the sympathovagal balance of HRV.

3. STATISTICAL ANALYSES

Data were performed using IBM SPSS 19.0 software (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp) (Licensed from Khon Kaen University). Frequency (percent), mean, and standard deviation were presented for quantitative variables, respectively. The Shapiro-Wilk test was tested to verify normal distribution of the data. For analysis of HRV data that exhibit a non-normal distribution of the data, the median (with Quartile 1 and Quartile 3) was presented. All HRV variable were then compared between sex and age-matched groups.

4. RESULTS

The demographic variables based on age, sex were balanced between the case (MDD) group and the control group. Forty depression patients [11] males and 29 Female; Mean age (SD) = 43.35 (14.37) years participated. For the control group, age and sex-matched healthy volunteers were recruited from university students, teacher, hospital workers, and people in the community. They were chosen after excluding those with the psychiatric and physical disorder by a psychiatrist (Table 1). The comparison between the frequency domain and time domain of HRV in the two group was shown in Table 2. The Mean and standard deviation of HR, SDNN, RMSSD, LF, HF and LF/HF ratio in the depression patients were 79.40(12.62) beat/min, 28.60(15.84)ms², 23.78(15.87)ms², 4.46(1.50) ms², 4.70(1.37)ms², 1.16(1.01) and in the normal subjects were 79.32(13.79) beat/min, 31.44(16.58) ms², 26.73(15.28)ms², 5.01(1.10) ms², 5.04(0.91)ms², 1.35(1.09) respectively.

Table 1 Demographic data between patients with major depression and normal controls

Parameters	Depression Patients (n=40)	Normal Control (n=40)
Sex		
Male	11 (27.50%)	11 (27.50%)
Female	29 (72.50%)	29 (72.50%)
Age		
Mean	43.35	43.10
S.D.	14.37	14.50

No significant differences in the demographic variables (sex, age) between the control and depression groups were observed.

No significant difference in the HRV variables between MDD and normal subjects except LF. However, it was noted that mean of all variables in the MDD group seemed to be lower than those in normal group (Table 2).

Table 2. Comparison of HRV data between MDD and the control groups.

Parameters	MDD (n=40)	Control (n=40)	p-value
HR	79.40 (12.62)	79.32 (13.79)	0.98
SDNN	28.60 (15.84)	31.44 (16.58)	0.37
RMSSD	23.78 (15.87)	26.73 (15.28)	0.40
LF	4.46 (1.50)	5.01 (1.10)	0.01
HF	4.70 (1.37)	5.04 (0.91)	0.14
LF/HF	1.16 (1.01)	1.35 (1.09)	0.43

Present Mean (S.D.)

The HRV and HR data were also compared by mean of different medications for treatment. Furthermore, we found no difference in Serotonin and norepinephrine reuptake inhibitor (SNRI), Selective serotonin reuptake inhibitors (SSRIs) (Table 3).

Table 3. Comparison of HR, HRV, and difference of Drug

HRV	SNRI			SSRIs		
	Yes	No	p-value	Yes	No	p-value
	Median (IQR)	Median (IQR)		Median (IQR)	Median (IQR)	
HR	75.5 (15)	78 (20)	0.56	76 (20)	84.5 (18)	0.09
SDNN	23.04 (20.73)	26.33 (25.85)	0.91	26.33 (15.96)	18.42 (24.17)	0.10
RMSSD	19.03 (19.47)	19.47 (10.32)	0.82	20.02 (19.19)	16.57 (9.27)	0.09
LF	4.42 (1.85)	4.69 (2.20)	0.84	4.69 (1.92)	3.91 (2.93)	0.26
HF	4.49 (2.95)	4.74 (1.31)	0.93	4.81 (1.47)	3.65 (2.16)	0.06
LF/HF	0.82 (1.50)	0.84 (1.35)	0.69	0.64 (1.38)	1.34 (1.41)	0.20

SNRI: Serotonin and norepinephrine reuptake inhibitor
SSRIs: Selective serotonin reuptake inhibitors

The HRV variables in patients with different degree of depression were also compared. No statistically significant difference in median HR, frequency domain and time domain (Fig 4).

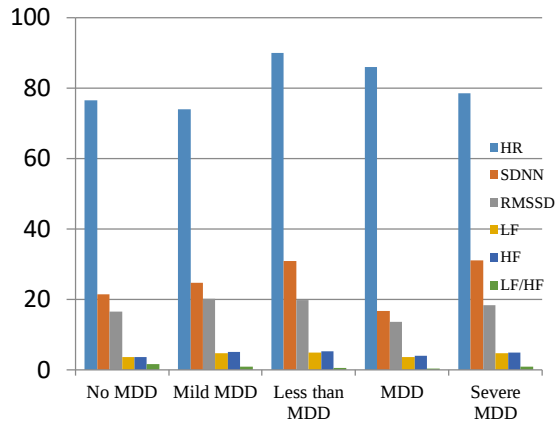
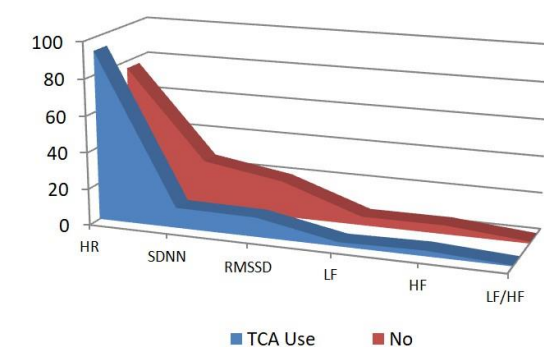


Fig 4. HR, HRV in patients with depression Level

Kruskal-Wallis equality-of-population rank test
No sign of depression (0-7), Mild (8-12), Less than MDD (13-17)
MDD (18-29) and severe (30+)

There was significant increase on HR and decrease HRV associated with Tricyclic antidepressants (TCA) (p -value 0.003), SDNN (p -value 0.0009), RMSSD (p -value 0.008), LF (p -value 0.0009), HF (p -value 0.008) and LF/HF (p -value 0.02). According to for the results on antidepressants, patients treated with TCA has relatively low HRV as compared with other antidepressants (Fig. 5).



TCA: Tricyclic antidepressants

Fig. 5 TCA relatively low HRV

5. DISCUSSION

Depression is an affective disorder of patients who are suffering to daily life. Prolonged depression they may lead to the risk of have heart diseases.

Previous studies, MDD patients were found to have a decrease in HRV as compared to the non-depressed group [14]-[15]. Conversely, our findings did not find a significant difference in HRV between MDD and normal subjects except Low frequency (LF). Some studies on antidepressants show dose-related increase the risk of sudden cardiac death [18] and have a greater likelihood of drug-induced long QT syndrome and torsade de points [19]. Physical treatment should be considered for older Tricyclic antidepressants (TCAs) when first-line drug treatment has failed. [20] This could be due to a small sample size of the current study. With a trend of having lower HRV in the MDD as compare to the normal indicate that a large sample size may show a larger power for statistical analysis. Another reason may be that the patients in the MDD group of this study have been on medication for a while where their conditions may be getting near normal. Therefore, the only small difference in HRV between the two groups was observed. Further study on a new case of MDD that have not started any medication may provide a clearer result.

6. CONCLUSION

With the aim to compare HRV between patients with the major depressive disorder and normal subjects, we had 40 patients and 40 normal subjects underwent HRV measurement at rest in quiet sitting position. Based on the results of the study, HRV variables in the treated patients with MDD seemed to be a little lower than those in the normal subjects but no statistical significance. This may be due to the effects of well treated with antidepressants and small sample size of the study. Further study with a larger sample size is needed to explore the differences in HRV between the MDD and normal subjects.

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