

ORIGINAL RESEARCH

**Depression and Heart Rate Variability in Physically Healthy subjects:
Implications for Cardiovascular Risk**

¹Dr. Harpreet Kaur, ²Dr. Karan Jindal, ³Dr. Akash, ⁴Dr. Akshay Sharma,
⁵Dr. Karanbir Singh Dhillon, ⁶Dr. Gurleen Kaur Garry

¹Medical Officer, CHC, Bara Pind, Punjab, India

²Medical Officer, PHC Nanowal, Fatehgarh Sahib, DHFW, Punjab, India

³Senior Resident, Department of Ophthalmology, GMC & Rajindra Hospital, Patiala, Punjab, India

⁴Medical Officer, State Health Agency, DHFW, Punjab, India

⁵Medical Officer, Park Hospital, Patiala, Punjab, India

⁶Senior Resident, Department of Surgery, GMC & Rajindra Hospital, Patiala, Punjab, India

Corresponding author

Dr. Karan Jindal

Medical Officer, PHC Nanowal, Fatehgarh Sahib, DHFW, Punjab, India

Received: 06 September, 2022

Accepted: 11 October, 2022

Abstract

Background: To study depression and heart rate variability in physically healthy subjects.

Materials & methods: A total of 60 patients were enrolled. The subjects were divided into 2 groups as control group and depression group. The age of patients was between 20 – 50 years. HRV recording was done. Chi-square test was employed to compare categorical variables. The data was analysed using SPSS software.

Results: A total of 60 patients were enrolled. In the comparison of HRV measures in between the two groups, values of LF (nu) ($p < 0.001$), LF:HF Ratio ($p < 0.001$) were significantly higher and HF (nu) ($p < 0.001$) parameter was significantly lower in depression group compared to controls.

Conclusion: HRV recordings showed significant changes in the patients suffering from depression.

Keywords: depression, Heart rate variability.

Introduction

Depression is assuming an importance globally, as it will become the second leading cause of disability worldwide by 2020. ¹The implications of depression is not only limited to an impaired quality of life or occupational functioning but now it extends to various unfavourable health outcomes it may result in. ²Most studies have now identified depression as a strong and independent risk factor for cardiovascular disease even in physically healthy individuals and also for adverse cardiovascular outcomes such as mortality.^{3,4} Although the underlying pathophysiological mechanism is yet to be elucidated, autonomic imbalance has been projected as one of the underlying mechanism.⁵ Heart Rate Variability (HRV) is a useful non-invasive measure for assessing cardiac autonomic modulations. Autonomic nervous system acts through dynamic nature of the interplay between the sympathetic and parasympathetic branches and HRV reflects a balance between sympathetic and parasympathetic inputs to the cardiac pacemaker.⁶ HRV is the variation over time of period

between consecutive heart beats. Low HRV signifies increase in cardiac sympathetic modulation or relative decrease in cardiac parasympathetic modulation or both of heart rate.⁷ Depressive symptoms and fitness are critically linked, and physical fitness is known to be lower in healthy individuals diagnosed with depression.⁸ Cardiorespiratory fitness, and not obesity or higher weight, predicted onset of depressive symptoms in a large, diverse sample.⁹ Additionally, maintenance of cardiorespiratory fitness appears to be protective against incidence of depression complaints to physicians, and higher cardiorespiratory fitness was associated with a lower risk of incidence of depressive symptoms in a longitudinal study.^{10,11} Thus, fitness is clearly associated with depression and may be mechanistic in the association between depression and HRV, particularly in HF patients. In HF, depression is associated with reduced physical activity, which likely leads to reduced physical fitness.¹² Physical fitness may be especially important in HF patients given the severe decompensation of the cardiovascular system. In patients with coronary artery disease, poorer cardiopulmonary fitness was associated with more depressive symptoms.¹³ Further, another study demonstrated that improvements in cardiopulmonary fitness during cardiac rehab were associated with a reduction in depressive symptoms.¹⁴ Hence, this study was conducted to study depression and heart rate variability in physically healthy subjects.

Materials & methods

A total of 60 patients were enrolled. The subjects were divided into 2 groups as control group and depression group. The age of patients was between 20 – 50 years. HRV recording was done. Five minutes recording was taken after 15 minutes of supine rest using lead II ECG. Comparisons between depressed and control groups were made, using unpaired students t-test for normally distributed data. Chi-square test was employed to compare categorical variables. The data was analysed using SPSS software.

Results

A total of 60 patients were enrolled. In the comparison of HRV measures in between the two groups, values of LF (nu) ($p < 0.001$), LF:HF Ratio ($p < 0.001$) were significantly higher and HF (nu) ($p < 0.001$) parameter was significantly lower in depression group compared to controls. While no significant difference was obtained in SDNN and RMSSD parameters.

Table: Comparison of HRV measures low frequency (LF), High frequency (HF), LF: HF Ratio, SDNN and RMSSD.

Parameters	Control group	Depression patients	p- value
LF	69.20	76.33	0.001*
HF	30.15	23.88	0.001*
LF: HF ratio	2.02	3.20	0.001*
SDNN (ms)	53.26	60.45	0.4
RMSSD (ms)	35.96	35.96	0.1

*: significant

LF (nu): Low frequency; reflects both sympathetic and parasympathetic modulations of heart rate.

HF(nu): high frequency; primarily reflects parasympathetic activity of heart rate.

LF:HF Ratio: Signifies sympathovagal balance and thus sympathetic modulations.

SDNN: Standard deviation of all N-N intervals-reflects both sympathetic and parasympathetic influences.

RMSSD: Root mean square of successive differences of NN intervals-primarily reflects parasympathetic influences on heart rate.

Discussion

Lower HRV is related to depression in both cardiac and healthy samples.^{15,16} Abnormal HRV scores were associated with depression in a review including patients with acute coronary syndromes.¹⁷ In other samples of patients with stable coronary artery disease, those with moderate to severe depression demonstrated significantly reduced HRV when compared to their non depressed counterparts, and all time-domain measures of HRV, including root mean square of the successive differences (RMSSD), were lower in patients with major depression.^{18,19} Finally, in a sample of physically healthy, unmedicated patients, RMSSD was significantly reduced in those with major depressive disorder (MDD) versus a control group.¹⁵ Hence, this study was conducted to study depression and heart rate variability in physically healthy subjects.

In the present study, a total of 60 patients were enrolled. In the comparison of HRV measures in between the two groups, values of LF (nu) ($p < 0.001$), LF:HF Ratio ($p < 0.001$) were significantly higher. A study by Walter FA et al, studied the sample consisted of HF patients (N = 125) aged 68.55 ± 8.92 years, 68.8% male, and 83.2% Caucasian. Controlling for sex, age, β -blocker use, hypertension, and diabetes, higher BDI-II scores significantly predicted lower HRV, $\beta = -.29$, $t(92) = -2.79$, $p < .01$. Adding 2MST did not attenuate the relationship in a follow-up regression. Depressive symptoms were associated with lower HRV in HF patients, independent of physical fitness. Given the prevalence of depression and suppressed HRV common among HF patients, interventions addressing depressive symptoms and other predictors of poor outcomes may be warranted.²⁰

In the present study, HF (nu) ($p < 0.001$) parameter was significantly lower in depression group compared to controls. While no significant difference was obtained in SDNN and RMSSD parameters. Another study by Kemp AH et al, studied seventy-three MDD and 94 healthy age- and sex-matched control participants were recruited from the general community. Participants had no history of drug addiction, alcoholism, brain injury, loss of consciousness, stroke, neurological disorder, or serious medical conditions. There were no significant differences between the four groups in age, gender, BMI, or alcohol use. HRV was reduced in MDD relative to controls, an effect associated with a medium effect size. MDD participants with comorbid generalized anxiety disorder displayed the greatest reductions in HRV relative to controls, an effect associated with a large effect size.²¹ Udupa et al., who studied drug naïve Major Depressive Disorder (MDD) patients without any comorbidity and reported significantly higher LF:HF ratio and lower HF (nu) in MDD group compared to control. However LF, SDNN and RMSSD showed no significant difference between two groups.²² A meta-analysis done by Kemp et al., in depression patients without cardiovascular diseases also reported the association between reduced HRV and depression and was found to be more in severely depressed individuals.²³ In addition, Agelink et al., showed the inverse correlation of parasympathetic HRV values with the severity of depression.²⁴ In a recent study Wang et al., also observed higher LF, LF:HF Ratio and lower SDNN, RMSSD and HF values in depression group compared to control group.²⁵ In the present study we did not find any significant differences in RMSSD and SDNN parameters in between the two groups. Similar findings were reported by Sayar et al., as no significant differences in any of the time-domain measures in between major depressive and healthy control group could be ascertained.²⁶

Conclusion

HRV recordings showed significant changes in the patients suffering from depression.

References

1. Lopez AD, Mathers CD, Ezzati M, Jannison DT, Murray CJ. Global burden of disease and risk factors. Washington: The World Bank; 2006.
2. Penninx B WJH, Milaneschi Y, Lamers F, Vogelzangs N. Understanding the somatic consequences of depression: biological mechanisms and the role of depression symptom profile. *BMC Medicine*. 2013;11:129.
3. Gan Y, Gong Y, Tong X, Sun H, Cong Y, Dong X, et al. Depression and the risk of coronary heart disease: a meta-analysis of prospective cohort studies. *BMC Psychiatry*. 2014;14:371.
4. Freedland KE, Carney RM. Depression as a risk factor for adverse outcomes in coronary heart disease. *BMC Medicine*. 2013;11:131.
5. Huffman JC, Celano CM, Beach SR, Motiwala SR, Januzzi JL. Depression and cardiac disease: Epidemiology, mechanisms and diagnosis. *Cardiovascular Psych and Neuro*. 2013:1–14.
6. Acharya UR, Joseph KP, Kannathal N, Lim CM, Suri JS. Heart rate variability: a review. *Med Biol Eng Comput*. 2006;44:1031–51.
7. Kleiger RE, Stein PK, Bigger JT. Heart rate variability: measurement and clinical utility. *Ann Non-invasive Electrocardiol*. 2005;10:88–101.
8. Boettger S, Wetzig F, Puta C, et al.. Physical fitness and heart rate recovery are decreased in major depressive disorder. *Psychosom Med*. 2009;71:519–523.
9. Becofsky KM, Sui X, Lee DC, Wilcox S, Zhang J, Blair SN. A prospective study of fitness, fatness, and depressive symptoms. *Am J Epidemiol*. 2015;181:311–320.
10. Dishman RK, Sui X, Church TS, Hand GA, Trivedi MH, Blair SN. Decline in cardiorespiratory fitness and odds of incident depression. *Am J Prev Med*. 2012;43:361–368.
11. Sui X, Laditka JN, Church TS, et al.. Prospective study of cardiorespiratory fitness and depressive symptoms in women and men. *J Psychiatr Res*. 2009;43:546–552.
12. Alosco ML, Spitznagel MB, Miller L, et al.. Depression is associated with reduced physical activity in persons with heart failure. *Health Psychol*. 2012;31:754–762.
13. Swardfager W, Herrmann N, Dowlati Y, Oh P, Kiss A, Lanctôt KL. Relationship between cardiopulmonary fitness and depressive symptoms in cardiac rehabilitation patients with coronary artery disease. *J Rehabil Med*. 2008;40:213–218.
14. Milani RV, Lavie CJ. Impact of cardiac rehabilitation on depression and its associated mortality. *Am J Med*. 2007;120:799–806.
15. Kemp AH, Quintana DS, Felmingham KL, Matthews S, Jelinek HF. Depression, comorbid anxiety disorders, and heart rate variability in physically healthy, unmedicated patients: Implications for cardiovascular risk. *PLoS One*. 2012;7:e30777.
16. Carney RM, Blumenthal JA, Stein PK, et al.. Depression, heart rate variability, and acute myocardial infarction. *Circulation*. 2001;104:2024–2028.
17. Harris PR, Sommargren CE, Stein PK, Fung GL, Drew BJ. Heart rate variability measurement and clinical depression in acute coronary syndrome patients: Narrative review of recent literature. *Neuropsychiatr Dis Treat*. 2014;10:1335–1347.
18. Stein PK, Carney RM, Freedland KE, et al.. Severe depression is associated with markedly reduced heart rate variability in patients with stable coronary heart disease. *J Psychosom Res*. 2000;48:493–500.
19. Aydin Sunbul E, Sunbul M, Gulec H. The impact of major depression on heart rate variability and endothelial dysfunction in patients with stable coronary artery disease. *Gen Hosp Psychiatry*. 2017;44:4–9.

20. Walter FA, Gathright E, Redle JD, Gunstad J, Hughes JW. Depressive Symptoms are Associated with Heart Rate Variability Independently of Fitness: A Cross-Sectional Study of Patients with Heart Failure. *Ann Behav Med.* 2019 Oct 7;53(11):955-963.
21. Kemp AH, Quintana DS, Felmingham KL, Matthews S, Jelinek HF. Depression, comorbid anxiety disorders, and heart rate variability in physically healthy, unmedicated patients: implications for cardiovascular risk. *PLoS One.* 2012;7(2):e30777.
22. Udupa K, Sathyaprabha TN, Thirthalli J, Kishore KR, Lavekar GS, Raju TR, et al. Alteration of cardiac autonomic functions in patients with major depression: A study using heart rate variability measures. *J Affect Disord.* 2007;100:137–41.
23. Kemp AH, Quintana DS, Gray MA, Felmingham KL, Brown K, Gatt JM. Impact of depression and antidepressant treatment on heart rate variability: A review and meta-analysis. *Biol Psychiatry.* 2010;67:1067–74.
24. Agelink MW, Majewski T, Wurthmann C, Postert T, Linka T, Rotterdam S, et al. Autonomic neurocardiac function in patients with major depression and effects of antidepressive treatment with nefazodone. *J Affect Disord.* 2001;62:187–98.
25. Wang Y, Zhao X, O’Neil A, Turner A, Liu X, Berk M. Altered cardiac autonomic nervous function in depression. *BMC Psych.* 2013;13:187.
26. Sayar K, Gulec H, Gokce M, Ak I. Heart rate variability in depressed patients. *Bull Clin Psychopharmacol.* 2002;12:130–33.