

ORIGINAL ARTICLE

Association between Depression and Heart Rate Variability in Rehabilitation Ward Patients with Musculoskeletal Dysfunction: A Pilot Study

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Objectives: The purpose of this study was to determine the relationship between depression and heart rate variability (HRV) in rehabilitation ward inpatients. **Methods:** Depression was assessed using the Self-Rating Depression Scale (SDS) in 10 inpatients in a convalescent rehabilitation ward. We also measured R–R intervals during nighttime rest, evaluated HRV by frequency analysis, and confirmed the association between autonomic activity and depression by calculation of Spearman’s rank correlation coefficient. **Results:** A negative correlation was found between depression and the very low-frequency (VLF) band of HRV ($\rho=-0.70$, $P<0.05$). SDS showed no significant correlation with low-frequency (LF) band ($\rho=-0.32$, $P=0.36$) or high-frequency (HF) band ($\rho=-0.21$, $P=0.46$). **Conclusions:** The results of this study suggest that the VLF band of HRV may be an effective indicator of autonomic activity in the evaluation of depression. Further studies are needed to verify the usefulness of the VLF band of HRV as an indicator for detecting depression.

Key Words: depressive symptoms; autonomic activity; convalescent rehabilitation

INTRODUCTION

Previous studies have shown that depression negatively affects patients’ adherence to treatment and the effectiveness of rehabilitation program interventions.¹⁾ Therefore, it is important to screen patients for depression before they undergo rehabilitation.²⁾

To date, subjective assessments of depression have been mainly conducted via self-report methods,³⁾ whereas endocrine/immunological evaluations have been used to obtain objective assessments.⁴⁾ The majority of physiotherapists assess depression with self-report methods, because it is seldom practical to evaluate endocrine/immunological parameters in the clinical setting. However, existing evidence suggests that subjective assessments should not be performed for patients with significant cognitive impairments; the identification of depressive symptoms is especially problematic in patients

with dementia or those with difficulties in verbal communication.⁵⁾

Previous studies have suggested an association between depression and autonomic activity.⁶⁾ Autonomic activity has been systematically investigated by monitoring heart rate variability (HRV), which is simple non-invasive technique.^{5,7)} High-frequency (HF), low-frequency (LF), and very low-frequency (VLF) bands can be extracted from HRV data.⁸⁾ The HF band indicates vagal activity, whereas the LF/HF ratio reflects sympathetic activity. The VLF band represents the balance between sympathetic and vagal activity⁹⁾ and has also been linked to the renin–angiotensin system and chronic inflammation.^{10,11)}

A recent meta-analysis investigating the association between depression and HRV found that depressed older adults may have lower HRV, particularly LF-HRV, but HRV in the

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VLF band was not considered in the analysis because of insufficient data.¹²⁾ Patients admitted to rehabilitation wards tend to be older and present with some disease because they are inpatients recovering from the acute phase of an emergency illness.¹³⁾ Previous studies have shown that the level of chronic inflammation tends to be higher in inpatients presenting with disease,¹⁴⁾ and that chronic inflammation is associated with the VLF band of HRV.^{10,11)} Aging also increases chronic inflammation.¹⁵⁾ Furthermore, depressive symptoms and chronic inflammation are associated with each other.¹⁶⁾

Therefore, we hypothesized that higher levels of depression would be associated with lower variability in the VLF band. The objective of this study was to determine the relationship between depression and the VLF band of HRV in patients admitted to a rehabilitation ward.

MATERIALS AND METHODS

Research Period and Patient Recruitment

The research period for the study was from July to October 2018. The inclusion criteria were as follows: 1) undergoing rehabilitation for musculoskeletal disease or disuse syndrome; 2) available for evaluation within 30 days of hospitalization; and 3) received the lowest gait monitoring level in the ward [Functional Independence Measure (FIM) score ≥ 5 for mobility items]. The FIM is an evaluation chart for activities of daily living with 18 items, each rated on a 7-point scale. Of the 18 motor items, 6 items are for self-care, 2 items are for elimination control, 5 items are for transfer, and 5 items are for mobility. The FIM score ranges from 18 to 126, with higher scores indicating a greater ability to perform activities of daily living.¹⁷⁾ The following exclusion criteria were used for our study: inability to provide written informed consent; difficulties communicating because of cognitive decline; arrhythmia; history of atrial fibrillation or cerebrovascular disease; New York Heart Association class III heart failure; or a postoperative diagnosis of malignant tumor. During the study period, 10 of 30 patients admitted to the convalescent rehabilitation ward met all of the inclusion criteria and were included in the study. Five patients of the 30 patients did not give consent to participate in the study and 15 patients were excluded because of communication difficulties (**Fig. 1**).

Patient Characteristics

The following patient characteristics, laboratory parameters, and assessment results were extracted from the electronic health records: sex, age, diagnosis, body mass

index, medical history, serum albumin, serum hemoglobin, C-reactive protein, Geriatric Nutritional Risk Index (GNRI), Berg Balance Scale (BBS), Short Physical Performance Battery (SPPB), and Hasegawa's Dementia Scale (HDS-R).

The GNRI assesses nutritional status with the following three objective parameters: weight, height, and serum albumin. Patients with a GNRI higher than 98 are classified as having a normal nutritional status. Mild, moderate, and severe malnutrition are indicated by GNRI scores of 92–98, 82–91, and less than 82, respectively.¹⁸⁾ The BBS evaluates balancing ability in elderly individuals. It consists of 14 items and is rated on a scale of 0 to 4; the maximum total score is 56.¹⁹⁾ The SPPB assesses balance, gait, strength, and endurance. The summary score ranges from 0 to 12, with higher scores indicating a better function.²⁰⁾ HDS-R, first proposed in 1991, is a screening test for age-related dementia.²¹⁾ It consists of nine simple questions, with a maximum total score of 30 points.

Depression

Depression was assessed using the Self-Rating Depression Scale (SDS) questionnaire. Items are categorized into depressive main emotions (2 items), physical symptoms (8 items), and psychological symptoms (10 items).²²⁾ The assessment was conducted by the ward physiotherapist or occupational therapist in the speech and hearing room between 8:40 and 10:00 a.m., before the start of the rehabilitation intervention.

HRV

HRV was measured within 30 days of admission using an active tracer (AC-301, GMS, Tokyo, Japan). A physical therapist from the ward visited each patient's room at 7:00 p.m. Electrodes were attached at the bedside and connected to the active tracer. The active tracer was fixed with a belt at the level of the umbilicus; this was worn for 12 h during the night. The ward physiotherapist visited the patient's room the next morning at 7:00 a.m. and removed the active tracer and electrodes at the bedside. The R–R interval (time between R waves) was calculated by dividing the time series data from 9:00 p.m. to 5:00 a.m. on the next day into 5-min segments using Mem Calc (a GMS spectral analysis software) and determining the power spectral density in each segment using the maximum entropy method. The integrated power values of the VLF (0.003–0.04 Hz), LF (0.04–0.15 Hz), and HF (0.15–0.4 Hz) bands were determined, and the LF/HF ratio was subsequently calculated.⁸⁾ The frequency domain indices were log-transformed to normalize the distribution before performing statistical analysis. Previous reports have

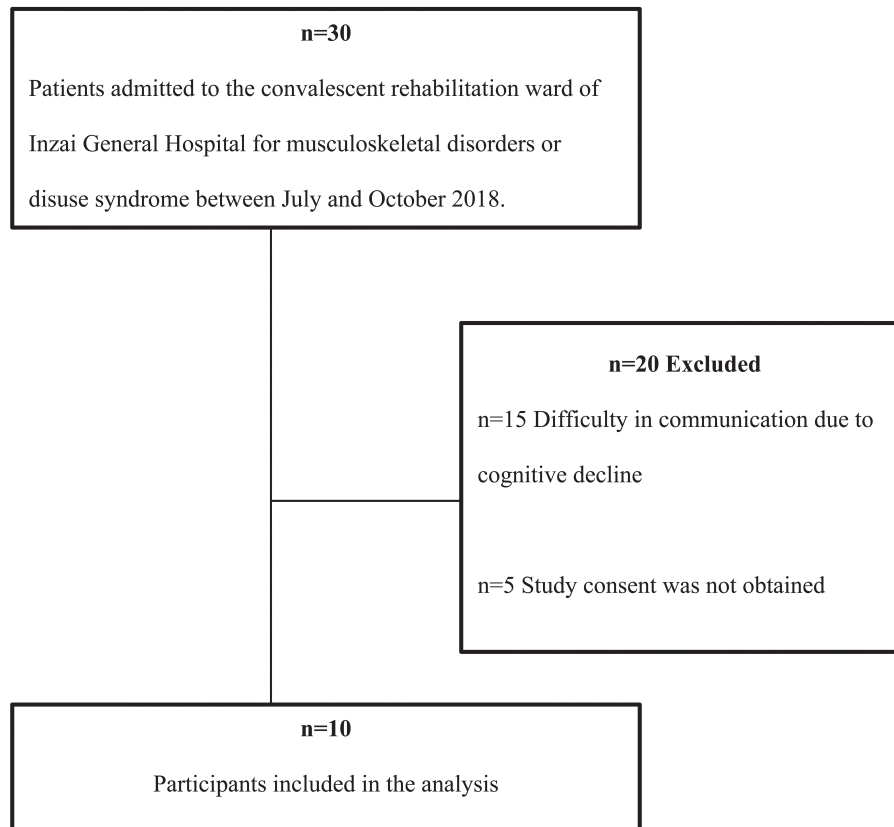


Fig. 1. Derivation of the study cohort.

suggested that data collected at night are more stable than data collected at other times because the effects of factors such as mental stress, exercise, and diet are eliminated.^{23,24} As a result, we investigated HRV during nighttime rest.

Statistical Analysis

The normality of the measurements was confirmed by the Shapiro–Wilk test. Representative values of the measured indices are presented as mean \pm standard deviation. The associations between depression and HRV, HDS-R, BBS, SPPB, and GNRI were assessed using Spearman’s rank correlation coefficient. Statistical analysis was performed with IBM SPSS Statistics Ver. 23. (SPSS, Chicago, IL, USA). The level of statistical significance was set at $P < 0.05$.

Ethical Considerations

This study was conducted with the approval of the Ethics Review Committee of the International University of Health and Welfare (Approval No. 18-10-3) and the Ethics Review Committee of Inzai General Hospital (Approval No. 3). Written informed consent was obtained from all patients.

RESULTS

Patient Characteristics

Patient characteristics, laboratory parameters, and assessment results are shown in **Tables 1 and 2**. The mean age of the 10 patients was 84.6 years. Six and four patients were undergoing rehabilitation for musculoskeletal diseases and disuse syndrome, respectively. The mean SDS, GNRI, SPPB, and BBS scores were 40.0, 89.9, 9.4, and 43.2, respectively. The mean HDS-R score was 25.5. Frequency analysis of HRV showed that the mean of \ln VLF was 6.77, the mean of \ln LF was 5.31, the mean of \ln HF was 4.69, and the LF/HF ratio was 1.14.

Relationship between Depression and Autonomic Activity

The association between depression and each indicator is shown in **Table 3**. In addition, scatter plots of the association between depression and HRV are shown in **Figs. 2 to 4**. A significant negative correlation was found between the VLF band and SDS ($\rho = -0.70$, $P < 0.05$). However, SDS showed

Table 1. Representative patient attributes and metrics

Item	All patients (n=10)
Male/female	4/6
Age (years)	84.6 ± 4.5
Height (cm)	152.5 ± 9.8
Weight (kg)	46.5 ± 9.2
BMI (kg/m ²)	19.9 ± 3.1
Alb (g/ml)	3.77 ± 0.43
Hb (g/dL)	11.3 ± 1.6
CRP (mg/dL)	0.25 ± 0.26
GNRI score	89.9 ± 21.5
HDS-R score	25.5 ± 2.6
FIM mobility items score	5.8 ± 0.4
SPPB score	9.4 ± 1.5
BBS score	43.2 ± 9.0
SDS score	40.0 ± 6.7
ln VLF	6.77 ± 0.74
ln LF	5.31 ± 0.80
ln HF	4.69 ± 0.93
LF/HF	1.14 ± 0.11

Data are presented as mean ± standard deviation. BMI, body mass index; Alb, serum albumin; Hb, serum hemoglobin; CRP, C-reactive protein.

no significant correlation with ln LF ($\rho=-0.32$, $P=0.36$), ln HF ($\rho=-0.26$, $P=0.46$), HDS-R ($\rho=-0.43$, $P=0.20$), BBS ($\rho=-0.43$, $P=0.20$), SPPB ($\rho=-0.10$, $P=0.77$), or GNRI ($\rho=-0.53$, $P=0.11$).

DISCUSSION

In this study, we investigated the relationship between depression and HRV in rehabilitation ward inpatients. The results showed that there was a significant negative correlation between SDS and the VLF band. However, SDS showed no significant correlation with LF band, HF band, HDS-R, BBS, SPPB, or GNRI.

The negative correlation between the VLF band and SDS scores suggests an association between depression and autonomic activity. In addition, patients with higher SDS scores had lower VLF variability, which reflected a higher sympathetic activity. These results may be attributed to the effects of mental and physical stress stimuli on the limbic system and hypothalamus, which lead to an increase in sympathetic function through the activation of the sympathetic nuclei, adrenal cortex, and medulla.²⁵⁾ In addition, stress-induced activation of the hypothalamic–pituitary–adrenal axis is

considered to be a central nervous system mechanism that leads to depressive symptoms.¹²⁾ The VLF band, which is strongly associated with depression, is known to be an indicator of renin–angiotensin–aldosterone system activity.²⁶⁾ The negative correlation between SDS and the VLF band suggests that higher severity of depression leads to lower parasympathetic nervous system activity and higher activities of the sympathetic nervous system, renin–angiotensin–aldosterone system, and hypothalamic–pituitary–adrenal axis, which are reflected in the lower VLF. Decreased VLF bands are associated with chronic inflammation in many studies,^{10,11)} and chronic inflammation is known to increase with age.¹⁵⁾ In addition, levels of chronic inflammation tend to be higher in hospitalized patients who present with disease,¹⁴⁾ and depressive symptoms and chronic inflammation are known to be associated with each other.¹⁶⁾ In other words, the results of the present study, which showed a significant negative correlation between SDS and VLF, suggest that the level of chronic inflammation may be higher in patients admitted to rehabilitation wards.

Previous studies have used LF and HF variabilities and LF/HF ratio as objective measures of changes in autonomic function associated with depression.²⁷⁾ Other studies have also found that HF variability is decreased in depressed adults and depressed children.^{6,28)} In a studies of patients aged over 60 years, LF band was found to be decreased when depression was present.^{12,29)} In comparison to the previous studies described above, the subjects of the current study were recovering from the acute phase of an emergency illness, were in the rehabilitation ward, and very old. In addition, each of them was in a convalescent but diseased state, suggesting that chronic inflammation may have been increased. This characteristic of patients admitted to the rehabilitation ward may have affected the depressive symptoms of the subjects in this study and may have been associated with the VLF band.

The results the present study suggest that the VLF band may be one of the indicators of autonomic activity that captures depression in inpatients in rehabilitation wards because VLF variability showed a significant association with depression when compared with LF and HF variabilities, which have been associated with depression in previous studies. In the past, assessment of depression in hospitalized patients has been conducted mainly by self-report methods.³⁾ However, self-report methods have been found to be problematic in identifying depressive symptoms in patients with dementia or those that have difficulty with verbal communication.⁵⁾ In the present study, HRV analysis suggested that the VLF band and depression are interrelated and that VLF may be a use-

Table 2. Patient assessment outcomes

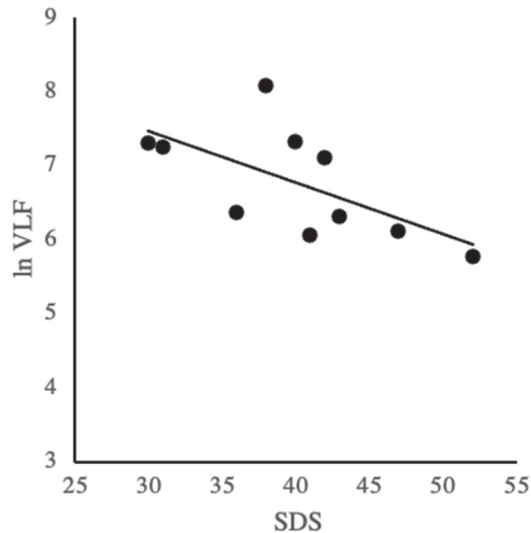
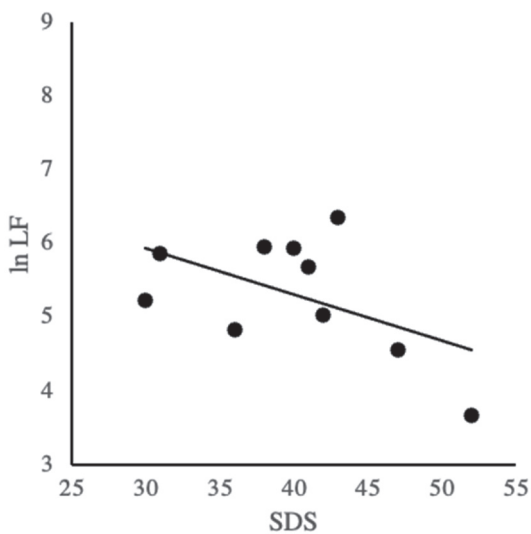
Case	Sex	Age (years)	Diagnosis	Height (cm)	Weight (kg)	BMI (kg/m ²)	Alb (g/ml)	Hb (g/dL)	CRP (mg/dL)	GNRI	HDS-R score	FIM mobility items score	SPPB score	BBS score	SDS score	ln VLF	ln LF	ln HF	LF/HF
1	Female	81	Right femoral neck fracture	145	34.3	16.1	3.8	10.1	0.25	88.6	27	6	9	46	41	6.05	5.69	5.01	1.14
2	Female	78	Post-pneumonia disuse syndrome	140	42.8	21.8	4.0	13.9	0.09	101.1	28	6	8	38	40	7.33	5.93	5.46	1.09
3	Female	84	Lumbar compression fractures	148	36.9	16.9	3.6	9.1	0.10	89.1	29	6	10	48	31	7.25	5.86	4.99	1.17
4	Male	84	Post-pneumonia disuse syndrome	158	37.2	14.9	2.9	10.9	0.90	78.9	24	6	10	53	47	6.11	4.56	3.53	1.29
5	Female	94	Post-pneumonia disuse syndrome	155	44.7	18.6	3.8	13.7	0.46	35.3	27	6	8	48	52	5.77	3.67	2.79	1.32
6	Female	84	Lumbar compression fractures	149	47.9	21.6	4.0	11.8	0.08	100.5	24	5	9	37	36	6.37	4.83	4.09	1.18
7	Female	85	Lumbar compression fractures	143	50	24.5	3.8	12.0	0.05	108.7	24	6	10	43	42	7.11	5.04	5.13	0.98
8	Male	81	Fracture of right femoral tilt	172	62	21	4.5	10.5	0.09	96.3	21	6	12	48	38	8.08	5.96	4.93	1.20
9	Male	86	Left femoral neck fracture	163	58.4	22	4.0	11.7	0.36	110.2	28	5	7	22	43	6.32	6.35	5.83	1.01
10	Male	89	Post-pneumonia disuse syndrome	151	50.6	22.1	3.3	9.6	0.15	90.8	23	6	11	49	30	7.30	5.24	5.21	1.21

BMI, body mass index; Alb, serum albumin; Hb, serum hemoglobin; CRP, C-reactive protein.

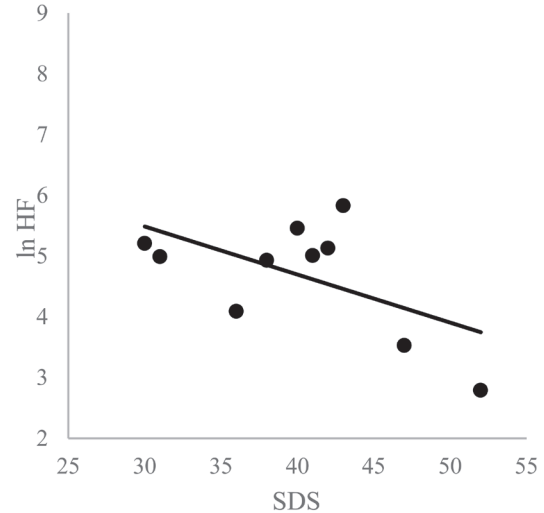
Table 3. Spearman's rank correlation coefficients for association between SDS and each indicator (n=10)

	ln VLF	ln LF	ln HF	LF/HF	HDS-R	BBS	SPPB	GNRI
SDS	-0.70*	-0.32	-0.26	0.36	-0.43	-0.43	-0.10	-0.53

*P<0.05.

**Fig. 2.** Relation between ln VLF and SDS (n=10).**Fig. 3.** Relation between ln LF and SDS (n=10).

ful indicator of autonomic activity to capture depression in inpatients in rehabilitation wards. HRV is easy to monitor in clinical settings because it is based on a simple non-invasive measurement. The results of this study may contribute to future research to validate objective assessment of depressive symptoms for patients with dementia and those that have

**Fig. 4.** Relation between ln HF and SDS (n=9).

difficulty with verbal communication.

Some limitations are acknowledged in the present study. First, the sample size was relatively small and included a wide variety of disease, so the results may change with an increased number of subjects. There has been no analysis comparing HRV with other predictive parameters. Second, given that a cross-sectional design was used, we were unable to confirm a causal relationship between depression and autonomic activity. Furthermore, considering that our study only included patients with more than 5 points for FIM mobility, our results may not be generalizable to patients who require mobility assistance. With regard to test-retest reliability, the diurnal variation in HRV may also compromise the reliability of single-day measurement. Therefore, future prospective studies utilizing larger sample sizes are required to confirm a causal relationship between depression and autonomic activity in patients admitted to convalescent rehabilitation wards. Such studies should also consider whether the assessment of autonomic activity can be used as a clinical indicator of depression.

CONCLUSION

The results of the current study suggest that depression is associated with the VLF band of HRV in rehabilitation ward inpatients and may reflect a state of heightened sympathetic

activity. Therefore, the VLF band of HRV has potential for use as a valid indicator of autonomic activity for the assessment of depression in rehabilitative settings. However, to validate the usefulness of the VLF band of HRV as an indicator for detecting depression, further research is needed. Future studies should continue to examine the reliability and validity of the measurement method of HRV in patients admitted to rehabilitation wards.

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CONFLICTS OF INTEREST

The authors report no conflicts of interest.

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