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ORIGINAL RESEARCH

Negative Predictors of Heart Rate Variability and Quality of Life in Patients with Heart Failure and Mid-Range Ejection Fraction:A Cross-Sectional and Descriptive Study

Predictores negativos de variabilidad en la frecuencia cardiaca y calidad de vida entre pacientes con insuficiencia cardiaca y fracción de eyección media: un estudio transversal descriptivo

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Abstract

Introduction. Heart Rate Variability (HRV) is a health indicator and a predictor for sudden cardiac death among patients with Heart Failure with mid-range Ejection fraction (HFmrEF). Many factors have a negative influence on HRV. This study aims to assess the prevalence of known factors associated with low HRV and the correlation between HRV and Quality of life (QoL)among HFmrEF patients. **Methods.** A cross-sectional descriptive study took place at a tertiary cardiac care center in Kannur district, Kerala, from February to June 2023. The study involved 250 participants with HFmrEF. The researchers collected data using a consecutive sampling technique. They utilized the Minnesota Living with Heart Failure Questionnaire to assess quality of life, and a checklist to identify negative predictors of HRV. They used an HRV finger sensor to assess HRV and performed the analysis using Spearman's rank correlation coefficient and descriptive statistics. **Results.**The significant study findings show the prevalence of known negative predictors among HFmrEF patients such as stress (83.6%), male gender (78.8%), poor sleep habits (58.4%), unhealthy eating behavior (55.6%), physical inactivity (53.2%), being overweight (40.8%), age over 60 years(39.2%), smoking (36.8%), diabetes (33.6%), alcoholism (23.6%), and chronic noise exposure (20.4%).The quality of life for patients with HFmrEF was reported as poor in 59% of cases, moderate in 27%, and good in 14%. A moderate negative correlation was identified between the quality of life and HRV score ($r = -0.43$, $p < 0.001$).**Conclusion.** The moderate inverse relationship between HRV and QoL score emphasizes the importance of improving HRV in patients with HF.Stress emerged as the primary adverse predictor, and acknowledging these negative factors can shed light on their management, ultimately contributing to a more favorable prognosis.

Keywords: Heart Rate Variability; Factors influencing HRV; Heart Failure with mid-range ejection fraction; Predictors of HRV; Quality of life.

Resumen

Introducción. La variabilidad de la frecuencia cardiaca (VFC) es un indicador de salud y un predictor de muerte súbita entre pacientes con insuficiencia cardiaca y fracción de eyección media (Ic-fEM), son muchos los factores que influyen negativamente sobre la VFC. El objetivo de este estudio es valorar la prevalencia de factores conocidos asociados a una VFC baja y la correlación entre la VFC y la calidad de vida (CdV) entre los pacientes con Ic-fEM. **Métodos.** Se realizóun estudio descriptivo transversal en un centro de atención cardiaca terciaria en el distrito de Kannur, Kerala, de febrero a junio de 2023, participaron 250 personas con Ic-fEM. Las y los investigadores recabaron datos mediante una técnica de muestreo consecutivo, utilizando el Cuestionario de Minnesota para Personas con Insuficiencia Cardiaca, con el fin de evaluar su calidad de vida y una lista de verificación para identificar predictores negativos para la VFC. Se utilizó un sensor dactilar para evaluar la VFC y se llevó a cabo un análisis mediante el coeficiente de correlación de rangos de Spearman y estadística descriptiva. **Resultados.** Los hallazgos significativos del estudio muestran la prevalencia de predictores negativos conocidos entre los pacientes con Ic-fEM, como estrés (83.6%), género masculino (78.8%), malos hábitos de sueño (58.4%), comportamientos alimenticios poco saludables (55.6%), inactividad física (53.2%), sobrepeso (40.8%), edad superior a 60 años (39.2%), tabaquismo (36.8%), diabetes (33.6%), alcoholismo (23.6%) y exposición crónica al ruido (20.4%). La calidad de vida de los pacientes con Ic-fEM fue mala en 59% de los casos, moderada en 27% y buena en 14%. Se identificó una correlación negativa moderada entre la calidad de vida y la puntuación de la VFC ($r = -0.43$; $p < 0.001$). **Conclusiones.** La moderada relación inversa entre la VFC y la calidad de vida enfatiza la importancia de mejorar la calidad de vida de pacientes con Ic-fEM, el estrés se revelócomo el principal factor predictivo adverso. La identificación de estos factores negativos puede arrojar luz sobre su tratamiento, contribuyendo, en última instancia, a un pronóstico más favorable.

Palabras clave. Variabilidad de la frecuencia cardiaca; factores que influyen en la VFC; insuficiencia cardiaca con fracción de eyección media; predictores para la VFC; calidad de vida.

Introduction

Heart failure (HF) poses a substantial challenge to patients and healthcare systems in both developed and developing nations, presenting a significant public health issue. Heart Failure with mid-range Ejection Fraction is a recently added type in the HF classification, where the ejection fraction falls between 40-49%. This type receives relatively less attention from healthcare professionals when compared to other types. As per a longitudinal study by Trivandrum Heart Failure Registry (THFR), out of 1205 participants, heart failure with reduced ejection fraction(HFrEF) was the most common group (62%), followed by heart failure with preserved ejection fraction (HFpEF) (20%) and HFmrEF (18%). They identified an unadjusted 5-year mortality rate of 59% among HF patients (61.3%, 60.5%, and 46.8% in HFrEF, HFmrEF, and HFpEF groups, respectively.[1]

Patients with heart failure commonly face limitations in performing everyday tasks and often endure a decline in their quality of life. Gastelurrutia et al. identified that QOL scores were similar in HFmrEF (30.1±18.3) and HFrEF (30.8±18.5).[2]

Heart Rate Variability (HRV) is a fundamental element that plays a major role in maintaining the general health status and Quality of life.Heart Rate Variability is a widely used index of health that corresponds to the adaptation of the heart to any stimulus or changing circumstances. Many studies have demonstrated that HRV is a strong predictor of cardiovascular mortality. Depressed HRV was associated with increased mortality.[3]

In patients with cardiac failure, reduced HRV was noticed and interpreted as a result of predominantly sympathetic and reduced vagal modulation of the sinus node.[4]Hassan et al. identified disturbed cardiac autonomic function in heart failure patients with reduced ejection fraction, and also HRV parameters had a strong positive correlation with the New York Heart Association (NYHA) functional class and with six minute walk test (6MWT) distance in patients with HF.[5]

Other than cardiac diseases, a positive and a negative influence on HRV has been observed in connection with non-influenceable physiological factors, many acute and chronic diseases, numerous lifestyle factors, and environmental factors.[6] The presence of negative predictors of HRV in HF patients can be a reason for poor prognosis of the disease. On the other hand, assessing and identifying negative predictors of HRV among these patients and controlling such modifiable factors will support them for a better outcome.

Studies identified that advancing age, gender, and ethnicity as non-modifiable influencing factors and lack of exercise, diet, alcoholism, smoking, disturbed sleep pattern, stress, negative emotions, and chronic exposure to environmental factors such as noise, air pollution, electromagnetic field as modifiable negative predictors of HRV.[7]

This cross-sectional survey intended to assess the prevalence of known factors associated with low HRV and the correlation between HRV and Quality of life among HFmrEF patients.

Materials and Methods

This cross-sectional descriptive study was carried out at the inpatient and outpatient Cardiology department of Government Medical College Kannur(GMCK) from February to June 2023.The researchers selected the study sample using consecutive sampling technique. The sample size was defined based on the estimated prevalence of HFmrEF in patients with HF as 18% with a precision of 5% and value at 1.96.[1] Thus, the calculated sample size was 250.Two hundred seventy-two individuals underwent eligibility screening, and 250 were included in the study.

Heart failure patients with a mid-range ejection fraction between the age of 20 and 80 years diagnosed with Ischemic Heart Disease and were included in this study. Subjects with comorbid non-cardiac diseases affecting the quality of life, implant of Automatic Implantable Cardioverter Defibrillator (AICD), ventricular dysrhythmias, atrial flutter, or fibrillation were excluded from the study.

The sample characteristics were collected using the sociodemographic and clinical data form. The presence of factors contributing to low HRV, including non-influenceable physiological factors, acute and chronic diseases, stress, lifestyle factors, and environmental factors, were assessed with a checklist, International Physical Activity Questionnaire, and Perceived Stress Scale. The quality of life assessment was done using the Minnesota Living with Heart Failure Questionnaire, which encompasses questions on physical, emotional, social, and mental dimensions. The Heart Rate Variability assessment was performed with an Elite HRV Finger sensor, where HRV is assessed by Photoplethysmography using the Peak-to-Peak Interval series (PPI).Here, the HRV score is calculated from the RMSSD(root-mean square difference of successive R-R intervals) and represents the strength of autonomic nervous system.

The tools achieved satisfactory content validity and were consistent, as the alpha value was more than 0.7 (PSS: Cronbach's Alpha: 0.899, MLHFQ: Cronbach's Alpha: 0.956).Since the Holter monitor is the gold standard for measuring HRV, the bland-Altman plot was used to determine the agreement between Holter and HRV Finger Sensor, and the difference between the two methods was -0.97, which was clinically acceptable. After translating the tools into the local language, i.e., Malayalam, we established the language validity. A total of 272 subjects were screened for eligibility, of which 250 were included in the study. (Fig. 1.)

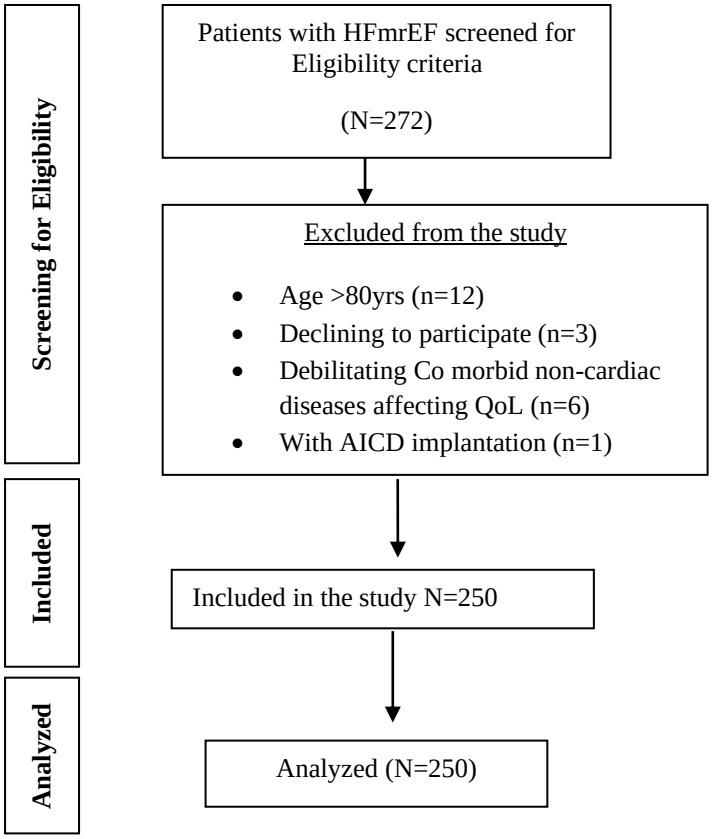


Figure 1:- Flow diagram of the study sample

Table 1. Frequency and percentage distribution of sample characteristics (N = 250).

Sample characteristics	f (%)
Age in years	
20-39	7 (2.8%)
40-59	145 (58%)
60-80	98 (39.2%)
Gender	
Male	197(78.8%)
Female	53(21.2%)
Marital status	
Married	222(88.8%)
Unmarried	12 (4.8%)
Widow	10 (04%)
Widower	06 (02.4%)
Occupation	
Managers/ Professionals	20 (08%)
Associate professionals	13 (05.2%)
Clerical support workers	24 (09.6%)
Services and sales workers	27 (10.8%)
Skilled workers	26 (10.4%)
Craft and trade workers	05 (02%)
Plant and machine operators	18 (07.2%)
Elementary occupations	55 (22%)
Unemployed	62 (24.8%)
Socio Economic Status	
Upper class	05 (02%)
Upper middle class	89(35.6%)
Lower middle class	61 (24.4%)
Upper lower class	88 (35.2%)
Lower class	07 (2.8%)
Type of family	
Nuclear family	201 (80.4%)
Joint family	49 (19.6%)
Duration of illness	
<6 months	125(50%)
Six months to 1 yr	67 (26.8%)
1 -3yrs	43 (17.2%)
>3yrs	15 (6%)

Source: All tables use primary data

Ethical approval

The study was consented by the Institutional Ethics Committee of Government Medical College Kannur and the Central Ethics Committee of Nitte Deemed to be University [NU/CEC/2021/195]. A subject information sheet explained the purpose of the study, and informed consent was obtained from all participants. The study followed the principles of the Declaration of Helsinki.

Statistical analysis

We used SPSS 16 software to perform the data analyses. All the categorical variables were summarized using frequency and percentage. Quantitative variables were summarized using mean and SD if the data followed the normality assumption. The researchers conducted the Kruskal-Wallis and Mann-Whitney U tests to determine the association of HRV with selected variables, as the data violated the normality assumption. They considered $p<0.05$ to be statistically significant.

Results

Sample characteristics

The study outlined the demographic profile of the sample, including age, gender, marital status, family type, socio-economic status, and duration of illness (Table 1). The majority of the sample, 58%, were aged between 40 and 59, and 78.8% were male. A large proportion, 88.8%, were married, and 80.4% belonged to nuclear families. Half of the sample, 50%, had been ill for less than six months.

Prevalence of known factors contributing to low HRV among patients with HFmrEF

The research examined the occurrence of non-modifiable physiological factors such as male gender and being over 60 years old. It also considered various lifestyle factors like lack of physical activity, obesity, unhealthy eating habits, smoking, alcohol abuse, poor sleep patterns, and stress. Additionally, it looked into diseases such as diabetes, kidney diseases, obstructive sleep apnea, migraine, epilepsy, asthma, COPD, depression, anxiety disorders, and brain injuries. Environmental factors like prolonged exposure to noise, air pollution, electromagnetic fields, and the use of vibrating tools were also taken into account (Table 2). The study revealed that stress-moderate to high (83.6%), male gender (78.8%), unhealthy sleep habits (58.4%), unhealthy eating behavior (55.6%), and physical inactivity (53.2%) were the main factors contributing to low HRV present among patients with HFmrEF.

Table 2. Frequency and percentage distribution of Negative Predictors of HRV among patients with HFmrEF(N=250)

Factors contributing to Low HRV		F (%)
Physiological Factors		
Age	20-39	7 (2.8)
	40-59	145 (58)
	60-80	98 (39.2)
Gender	Male	197(78.8%)
	Female	53(21.2%)
Life style Factors		
BMI	Underweight	6 (2.4)
	Normal	142 (56.8)
	Over weight	78 (31.2)
	Obese	24 (9.6)
Physical activity	Low	133 (53.2)
	Moderate	98 (39.2)
	High	19 (7.6)
Stress	Low	41 (16.4)
	Moderate	183 (73.2)
	High	26 (10.4)
Smoking		92 (36.8)
Alcoholism		59 (23.6)
Unhealthy sleep habits		146 (58.4)
Unhealthy eating behaviour		139 (55.6)
Diseases		
Depression		12 (4.8)
Anxiety disorders		10 (4)
COPD		15 (6)
Obstructive sleep apnea		20 (8)
Bronchial Asthma		18 (7.2)
Kidney Diseases		23 (9.2)
DM		84 (33.6)
Epilepsy		19 (7.6)
Migraine head ache		48 (19.2)
Brain Injuries		8 (3.2)
Environmental factors		
Noise		51 (20.4)
EMF		27 (10.8)
Air pollution		47 (18.8)
Vibrating tools		21 (8.4)

Assessment of Quality of Life of Patients withHFmrEF

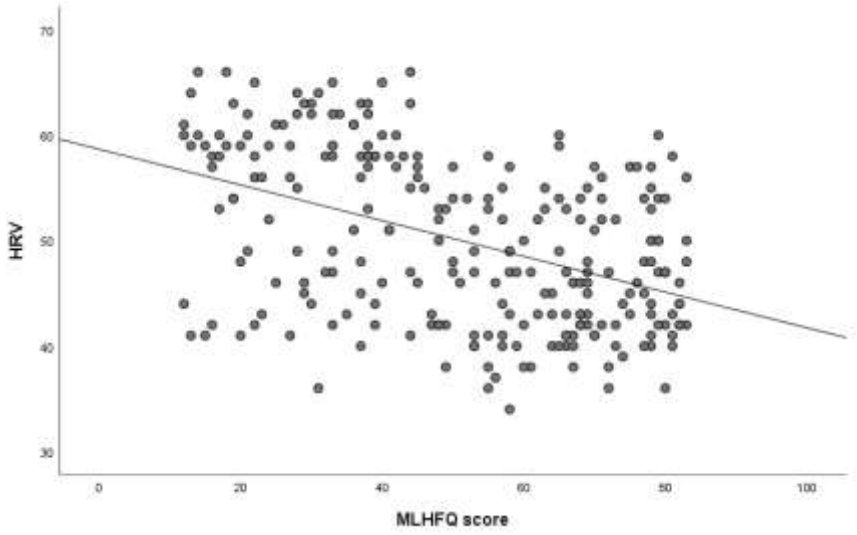
Percentages have summarized the quality of life. (Table 3). A higher percentage of subjects with HFmrEF had poor quality of life(59%), followed by moderate(27%) and good(14%).

Table 3. Percentage distribution of subjects based on Quality of LifeScore(N=250

Quality of Life	**MLHFQ* Score**	**Percentage**
Poor	46 - 105	59
Moderate	45 - 25	27
Good	0 - 24	14

*Minnesota Living with Heart Failure Questionnaire

Fig. 2. Scatter plot depicting the correlation betweenHRVscore and MLHFQ score of patientswithHFmrEF (N=250)



Correlation between HRVscore and QoL Score among patients with HFmrEF

The study assessed the correlation between the HRV and the Quality of Life scores of HFmrEF patients. The Spearman's rank correlation coefficient value between QoL score and HRV score was-0.43, indicating a moderate negative correlation. It was found to be statistically significant (p-value<0.001). (Fig.2)

Association Between HRV score and Selected Variables of patients with HFmrEF

Kruskal-Wallis Test and Mann-Whitney U test were done to determine the association of HRV score with selected variables as data violate the normality assumption. The study observed a significant association between HRV score and variables such as occupation (27.843, p<0.001), duration of illness (53.153, p<0.001), and BMI (50.55, p<0.001). (Table.4)

Discussion

The present study estimated the factors capable of reducing HRV among HFmrEF patients, providing practical insights for patient care. Most of the sample had stress, sleep-related problems, unhealthy eating behavior, and poor physical activity. Similarly, a comprehensive literature overview on factors affecting HRV enlisted physiological and pathological factors, environmental factors, lifestyle factors, and non-modifiable factors.[6] A systematic review identified environmental factors (18%), Obesity (9%), stress (3%), and eating behavior (3%) as negative influencers of HRV.[7]

An experimental study by Wu Y et al. revealed that HRV improves with amusement and decreases with fear, stress and, anger.[8]Another study identified that disturbed sleep pattern is inversely related to heart rate variability during the working day (P = 0.022), independently of demographic and behavioral confounders.[9]

The present study identified the median Quality of life score of patients with HFmrEF as 53 (IQR 33-63). In contrast, a study conducted at University Hospital Germans Trias I Pujol identified it as 30.1 ($\pm$18.3)[2]. Another study conducted in Switzerland reveals a 17 % prevalence of HFmrEF with a QOL of 40.2 ($\pm$20.3).[10]

Table 4.Association between Heart Rate Variability score and selected variables (N=250)

Variables		HRV score				Test statistic(P value)
		Count	Median	Q_1	Q_3	
Age in years	20 -39	7	50.00	43.00	54.00	4.91§
	40 - 59	145	51.00	43.00	58.00	(0.178)
	60 - 80	98	47.50	42.00	56.00	
Gender	Male	197	50.00	43.00	58.00	4339‖
	Female	53	47.00	42.00	54.00	(0.059)
Marital status	Married	222	49.00	43.00	57.00	0.43§
	Unmarried	12	49.00	42.00	57.50	(0.933)
	Widow	10	47.00	44.00	54.00	
	Widower	6	45.00	43.00	56.00	
Occupation	Managers/ Professionals	20	46.50	43.00	52.50	
	Technicians and associate professionals	13	47.00	42.00	54.00	
	Clerical support workers	24	58.00	48.00	61.50	27.84§ (0.001*)
	Services and sales workers	27	46.00	41.00	57.00	
	Skilled workers	26	46.50	41.00	52.00	
	Craft and related trade workers	5	42.00	40.00	42.00	
	Plant and machine operators	18	45.00	42.00	48.00	
	Elementary occupations	55	53.00	45.00	58.00	
	Unemployed	62	50.50	44.00	58.00	
SEC†	Upper class	5	42.00	40.00	46.00	5.28§ (0.260)
	Upper middle class	89	49.00	43.00	57.00	
	Lower middle class	61	47.00	42.00	57.00	
	Upper lower class	88	51.00	44.00	57.00	
	Lower class	7	47.00	41.00	59.00	
Type of family	Nuclear family	201	49.00	43.00	57.00	4936‖
	Joint family	49	48.00	43.00	58.00	(0.979)
Duration of illness	<6 months	125	45.00	41.00	52.00	53.15§
	Six months to 1 yr	67	54.00	47.00	58.00	(<0.001*)
	1 -3yrs	43	56.00	47.00	60.00	
	>3yrs	15	58.00	48.00	60.00	
BMI‡	Under weight	6	44.00	43.00	50.00	50.55§
	Normal	142	55.00	46.00	59.00	(<0.001*)
	Over weight	78	44.00	41.00	50.00	
	Obese	24	46.00	41.00	52.00	

†Socio Economic Class, ‡Body Mass Index, §Kruskal-Wallis Test, ‖U test, * Significant at p<0.05

A review on HRV in Myocardial Infarction and HF reports HRV as a strong predictor for cardiovascular mortality and identified several studies showing depressed HRV levels among MI and HF patients.[3]

The present study identified an association between HRV and variables such as occupation, duration of illness, and BMI. A cohort study in the Netherlands identified that age and sex were the most critical determinants of HRV. In contrast, the contribution of lifestyle and psychosocial factors was negligible.[11]Molfino A et al. states that an elevated BMI corresponds to raised sympathetic and reduced parasympathetic activities.[12]Lindholm H et al. identified an attenuated HRV level among media workers with irregular shift work.[13]

The present study demonstrated a moderate negative correlation between HRV and Quality of life. A correlation study conducted in Taiwan highlights the independent role of low HRQOL physical in contributing to reduced HRV in healthy adults.[14]

The study was of a cross-sectional design, and thus the association that has been demonstrated may not imply a causal relationship. The study was restricted to patients from inpatient and outpatient departments of a tertiary care hospital in the Kannur district, which may limit the generalizability of the findings. This information is crucial for future research and clinical practice.

Conclusion

HRV is an emerging concept in medical treatment. The moderate inverse relationship between HRV and QoL score emphasizes the significance of improving HRV in patients with HF. Stress emerged as the primary adverse predictor, and acknowledging these negative factors can shed light on their management, ultimately contributing to a more favorable prognosis. The results of this study aim to assist healthcare providers in supporting low HRV risk groups, particularly heart failure patients. These findings can also be used as a foundation for future research focusing on interventions to enhance HRV among patients with heart failure.

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Declaration of competing interest

All authors have reviewed the article and agree with its contents, and there are no conflicts of interest.

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