Original Article

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Impact of Heart Rate Variability Enhancement Programme on Functional Outcomes and Quality of Life of Patients with Heart Failure with Mid-range Ejection Fraction: A Quasi-experimental Study

Nursing Section

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ABSTRACT

Introduction: Low Heart Rate Variability (HRV), an indicator of autonomic imbalance, is correlated with an elevated risk of Heart Failure (HF). Nonetheless, its association with HF with mid-range Ejection Fraction (HFmrEF) has not been previously investigated.

Aim: To evaluate the effect of the HRV Enhancement Programme (HRV-EP) on functional outcomes and QoL of patients with HFmrEF.

Materials and Methods: This quasi-experimental study was conducted at the Department of Cardiology, Government Medical College Kannur, Pariyaram, Kannur, Kerala, India from February 2024 to December 2024. involving patients with HFmrEF. Utilising a consecutive sampling technique, the study was completed with 60 participants in each group. The intervention group engaged in the HRV-EP in conjunction with Guideline-directed Medical Treatment (GDMT) daily for 16 weeks, while the control group received only GDMT. The study assessed functional outcomes such as Resting Heart Rate (RHR), Blood Pressure (BP), HRV, Six Minute Walking Distance, (6MWD) and Ejection Fraction (EF) and the Quality of Life (QoL). Data were collected at baseline and following the interventions at the 10th and 16th weeks using a semi-structured interview schedule, biophysiological measures, and the Minnesota Living with HF Questionnaire for QoL.

Results: The comparison between groups with two way repeated measure mixed Analysis of Variance (ANOVA) revealed significant differences across various time points. Specifically, Systolic Blood Pressure (SBP) ($p<0.001$) and Diastolic Blood Pressure (DBP) ($p=0.008$) were significantly lower in the intervention group compared to the control group. Additionally, HRV ($p<0.001$), 6MWD ($p<0.001$), and EF ($p<0.001$) were significantly higher in the intervention group relative to controls. However, RHR did not exhibit a significant difference between the groups ($p=0.550$). The intervention group also demonstrated significant improvements in overall QoL ($p<0.001$), as well as in the physical ($p<0.001$) and emotional domains ($p=0.007$).

Conclusion: The HRV-EP is a safe, effective home intervention for enhancing vagal tone and improving outcomes among HFmrEF patients. Community-based cardiac rehabilitation can implement HRV-EP.

Keywords: Cardiac rehabilitation Physical exercises, Resting heart rate, Slow breathing exercises

INTRODUCTION

The HF is a clinical condition marked by the heart's inability to efficiently circulate blood due to structural or functional deficiencies [1]. Affecting 64 million individuals worldwide [2], and 9% in India [3], chronic HF leads to increased healthcare expenses, diminished functional abilities, and impacts QoL.

The HFmrEF is often called the 'middle child' within the HF family, receiving less attention than HFrEF and HF with preserved EF (HFpEF) [4]. HFmrEF is characterised by a Left Ventricular Ejection Fraction (LVEF) of 40-49%, first identified as a new HF category in the 2016 European Society of Cardiology guidelines [5]. However, evidence regarding long-term follow-up care remains deficient for this category. While exercise training strategies exist for HFrEF and HFpEF patients, data for HFmrEF remain limited [6]. In 2020, the Trivandrum HF Registry (THFR) reported a 5-year mortality rate of 59% among HF patients, with rates of 61.3% for HFrEF, 60.5% for HFmrEF, and 46.8% for HFpEF [7]. This highlights the importance of considering HFmrEF patients in this context.

A key contributor to the deterioration in HF is an unbalanced autonomic regulatory system. HRV serves as a non invasive diagnostic tool for evaluating the autonomic regulation of the heart and its responsiveness to diverse stimuli [8]. Greater HRV complexity correlates with improved functional outcomes in cardiac patients [9]. HRV shows strong correlation with New York Heart Association (NYHA) functional class and 6MWD in HF patients [10]. HFmrEF is associated with autonomic instability, leading to psychological distress, reduced social functioning, and diminished QoL [11]. While medical therapy improves HRV, patients with HFmrEF will benefit from a structured programme for autonomic stability, which is currently unavailable. The hypothesis of present study was that the patients with HFmrEF who engage in four months of HRV-EP in conjunction with conventional management exhibit a significantly greater improvement in functional outcomes and QoL compared to those who adhere solely to conventional management. The HRV-EP is a practice guideline for HFmrEF patients and this study aimed to investigate the effects of the HRV-EP on functional outcomes and QoL of HFmrEF patients.

MATERIALS AND METHODS

This quasi-experimental research was conducted in the Department of Cardiology, Government Medical College, Pariyaram, Kannur, Kerala, India from February 2024 to December 2024 among HFmrEF patients. The study was approved by the Institutional review board of Government Medical College Kannur (B1/3245/07/

CON/2019) and Nitte University Ethics Committee (NU/CEC/2021/195). The trial was registered with Clinical Trial Registry of India (CTRI/2021/09/036682). Copy right obtained for HRV-EP (L-155074/2024). The permission to collect the data was obtained from the hospital authority. Participants provided written informed consent after receiving information sheets. The study followed Declaration of Helsinki principles.

Inclusion criteria: HFmrEF patients aged 40 to 60 years and with ischaemic heart disease.

Exclusion criteria: HFmrEF patients with recurrent angina, recent surgeries (within three months), orthopaedic impairment, implant of pacemaker/automated implantable cardioverter-defibrillator, primary angioplasty, ventricular arrhythmias, atrial flutter or fibrillation, severe co-morbid non cardiac diseases/debilitated patients, and those who routinely practiced yoga, meditation, or walking exercises.

Sample size calculation: The sample size was determined using the sample size equation for a two-way repeated measure ANOVA, specifically for the outcome measure of QoL, which yielded the highest value.

$$n=\frac{2\,(Z_{1-}\alpha_{/2}+Z_{1-}\beta)^2\,\sigma^2\,[1+(m-1)\,\rho]}{m\,(d)^2}$$

Here,

$Z_{1-}\alpha_{/2}$=1.96 {at 5% level of significance}

$Z_{1-}\beta$=0.84 {at 80% power}

From the pilot study result:

σ=9.5 (SD)

d=5 (significant difference)

m=2 (number of repetitions)

ρ=0.3 (Intra-class correlation coefficient)

n=42

Sample size adjustment for dropout rate of 30%

$$n^*=\frac{n}{1\text{-dropout rate}}$$

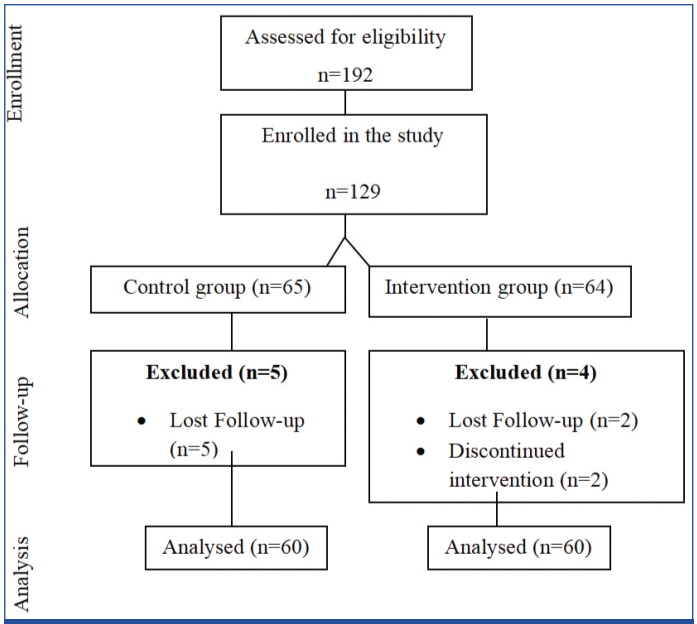
=42/0.7=60 in each group

Study Procedure

Sample selection was executed using a consecutive sampling method from admitted patients. During the pilot study, the investigator implemented random allocation of participants into the intervention and control groups. However, a challenge of sample contamination arose due to the inability to control the interaction among admitted patients. To mitigate this issue, the first 60 participants were assigned to the control group, followed by the allocation of the subsequent 60 participants to the intervention group [Table/Fig-1]. For the subjects with whom the follow-ups were lost, additional participants were recruited.

The outcome parameters were the functional outcomes and QoL:

- **Functional outcomes:** The parameters of functional outcomes including BP (SBP and DBP), RHR, and HRV score were measured using a digital sphygmomanometer (calibrated and validated-Mean D=0.87) and elite HRV finger sensor. The elite HRV finger sensor measured HRV score and HR. The Bland-Altman plot confirmed reliability between the Holter monitor and finger sensor in quantifying HRV variables. Subjects completed a 6MWD after their perceived exertion and fatigue was measured using the Borg scale [12]. Borg scale assessment is employed solely to determine the eligibility of participants for inclusion in the exercise program. A calibrated finger-type pulse oximeter was used to measure the SpO_2. EF% was noted from the medical record, which was measured by echocardiography.



[Table/Fig-1]: Flowchart.

- **Quality of Life (QoL):** A standardised tool, the Minnesota Living with HF Questionnaire (MLHFQ) [13], was found to be reliable (Cronbach's Alpha: 0.95) and was utilised to assess QoL. In MLHFQ, the participants were asked to utilise a six-point rating scale to assess the extent to which each of the 21 potential negative effects of HF has impacted their ability to live as they desire over the past month. The total MLHFQ score ranges from 0 to 105, with higher scores indicating a greater adverse impact of HF on the individuals' lives. Sub scores were also calculated for the physical domain, consisting of eight items with scores ranging from 0 to 40 (comprising responses to questions 2, 3, 4, 5, 6, 7, 12, and 13), and for the emotional domain, consisting of five items with scores ranging from 0 to 25 (comprising responses to questions 17 to 21). An educational license to use MLHFQ in both English and Malayalam version has been obtained through Mapi Research Trust.

As an effort to minimise missing data, the respondents were repeatedly instructed to put zero for the items that did not apply to them rather than leave them blank.

Intervention:

- **Heart Rate Variability Enhancement Programme (HRV-EP):** After conducting a systematic review [14] of factors influencing HRV, the investigator prepared a 30-min video-assisted educational programme, named HRV-EP, for patients with HFmrEF. It comprised patient education on predictors of HRV and a daily practice guideline on slow breathing and physical exercise [Table/Fig-2].

Exercise	Duration						
Breathing Exercise (Breathe in for five seconds, hold for two seconds, and continue breathing out for the next five seconds in a rhythmic manner, immediately after getting up and before bed)	Minimum 10 minutes and 10mts -30 minutes-Progressively from Wk.1 – Wk.16						
Physical Exercise	Wk-1	Wk-2	Wk-3	Wk-4	Wk-5	Wk-6	Wk-7-16
Warm up (Slow walk)	5mts	5mts	5mts	5mts	5mts	5mts	5mts
Aerobic exercises (Brisk walk)	3-5 mts	5 - 10 mts	10 -15 mts	15 - 20 mts	20 - 25 mts	25 - 30 mts	30 - 45 mts
Stretching (head, shoulder,elbow, hip,spine and calf muscle exercises)and strengthening exercises (semi sitting)	10 mts	10 mts	10 mts	10 mts	10 mts	10 mts	10 mts
Cool down(Slow walk)	5mts	5mts	5mts	5mts	5mts	5mts	5mts

[Table/Fig-2]: HRV-EP.

Slow breathing techniques with physical exercise influence heart-brain interactions and strengthen autonomic nervous system stability. Nine experts, including cardiologists, community medicine specialists, physiatrists, and cardiac nurses, validated the program. HRV-EP entails the daily practice of breathing exercises immediately upon waking and before bedtime, in addition to engaging in physical exercises 2-3 times weekly for six weeks, 3-5 times weekly for the subsequent four weeks, and five times per week thereafter.

- **Conventional management:** Is defined as the Guideline-directed Medical Therapy prescribed by the attending cardiologist, encompassing antiplatelets, lipid-lowering agents, beta-blockers, and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers/angiotensin receptor neprilysin inhibitors [1].

The control group was administered conventional GDMT, whereas the intervention group followed both HRV-EP and GDMT [Table/Fig-2].

The investigator individually demonstrated the exercises to the participants, either in their rooms or in the seminar hall adjacent to the cardiac unit. The researcher allocated 20 to 30 minutes for each participant to demonstrate the procedure. On the following day, the investigator conducted a return demonstration with the participants to reinforce and confirm the accuracy of the procedure. Subsequently, the intervention group received a video on HRV-EP via Quick Response code (QR code) for home guidance. Weekly telephone follow-ups were conducted for both groups, with post-test observations at the 10th and 16th weeks from the Outpatient Department (OPD), when they attended follow-up treatment [Table/Fig-3]. The investigator was responsible for sample selection, pre-testing, and intervention, while local assessors, who were blinded to treatment allocation, performed post-test measurements to minimise bias.

Group	Pre-test (Day-1)	Treatment (Day-2- Implementation Day-3- Return Demo)	Post-test 1 10th week	Post-test 2 16th wk
Intervention	O1*	X† with conventional management	O2‡	O3§
Control	O1	Only conventional management	O2	O3

[Table/Fig-3]: Schematic representation of the Quasi-experimental study.
*O1: Pre-test observation of functional outcomes and QoL; †X: Implementation of heart rate variability enhancement programme; ‡O2: Post-test observation; -1; § O3: Post-test observation- 2

STATISTICAL ANALYSIS

Categorical variables were described using frequencies and percentages. Quantitative variables were characterised by the mean and standard deviation for data exhibiting a normal distribution, and by the median and interquartile range (Q1, Q3) for data not conforming to a normal distribution. The assessment of normality was conducted using the Kolmogorov-Smirnov test [15] with Lilliefors correction for sample sizes exceeding 50. To evaluate demographic homogeneity between groups, either Fisher's-exact test or the Chi-square test was utilised. Baseline differences were assessed using the t-test for normally distributed data or the Mann-Whitney U test for non-normally distributed data, contingent upon the normality of the data.

A two-way repeated measures mixed Analysis of Variance (ANOVA) was performed to assess whether significant differences exist in the average QoL and Functional Outcomes across various time points, as well as between the experimental and control groups. This statistical methodology is particularly advantageous for analysing the effects of interventions over time or for comparing treatment responses between groups [16,17]. A p-value of less than 0.05 is regarded as statistically significant, and the entire analysis was conducted using SPSS version 16 software.

RESULTS

Socio-demographic and clinical characteristics: Socio-demographic and clinical characteristics were analysed using frequency and percentage [Table/Fig-4]. The majority of the subjects in the intervention and control groups were men 46 (76.67%), aged between 51 and 60 years {45 (75%) and 44 (73.33%)}, and married {52 (86.67%) and 54 (90%)}. Regarding their socio-economic status, 33 (55%) of the subjects from the intervention group and 31 (51.67%) from the control group belonged to the upper lower socio-economic class [18]. Most subjects were from nuclear families {50 (83.33%) and 49 (82.76%)}. Clinical characteristics such as duration of illness and Body Mass Index (BMI) showed that most had the disease for less than six months {39 (65%) and 43 (71.67%)} and had a normal BMI {35 (58.33%) and 40 (66.67%)} [19].

Variables		Intervention group		Control group		Chi-square/ Fisher's-exact statistics (p-value)
		f*	%	f	%	
Age	40-50 y	15	25.00	16	26.67	0.04§ (0.835)
	51-60 y	45	75.00	44	73.33	
Gender	Men	46	76.67	46	76.67	0.00§ (1.000)
	Women	14	23.33	14	23.33	
Marital status	Married	52	86.67	54	90.00	0.92¶, (0.918)
	Unmarried	2	3.33	1	1.67	
	Widow/Widower	4	6.67	4	6.67	
	Separated	2	3.33	1	1.67	
Socio-economic class†	Upper	1	1.67	2	3.33	1.33§ (0.856)
	Upper middle	8	13.33	10	16.67	
	Lower middle	12	20.00	9	15.00	
	Upper lower	33	55.00	31	51.67	
	Lower	6	10.00	8	13.33	
Type of family	Nuclear	50	83.33	49	81.67	0.007§ (0.934)
	Joint	10	16.67	11	18.33	
Duration of illness	<6 months	39	65.00	43	71.67	2.00§ (0.571)
	Six mnth- 1 y	5	8.33	7	11.67	
	1-3 y	7	11.67	5	8.33	
	>3 y	9	15.00	5	8.33	
BMI‡	Normal	35	58.33	40	66.67	2.00§ (0.368)
	Overweight	15	25.00	15	25.00	
	Obese	10	16.67	5	8.33	

[Table/Fig-4]: Sociodemographic and clinical characteristics at baseline in the intervention group (n=60) and control group (n=60).
*f: frequency; †Socio economic Class: as per Kuppuswami scale [18]; ‡BMI: Body mass index; (Normal-18.5-22.9 kg/m²; Overweight: 23.0-24.9 kg/m²; Obese ≥25 kg/m²) [19]; §Chi-square; ll: Fisher's-exact

Effect of HRV-EP on functional outcomes of patients with HFmrEF: The effect of HRV-EP on functional outcomes in HFmrEF patients was analysed using two-way repeated measures mixed ANOVA to determine differences in RHR score, BP, HRV, 6MWD, and EF score across time points and between groups [Table/Fig-5]. No significant difference existed in baseline RHR between groups (U=2045, p=0.195). Both groups showed a significant decrease in RHR across time points (p<0.001) with no significant between-group difference in RHR change over time (F=0.57, p=0.550). No significant difference existed in baseline SBP between groups (U=1988, p=0.601). SBP decreased significantly across time points in the intervention group (p<0.001) but not in controls (p=0.367). Between-group comparison showed a significant difference in SBP change over time (F=8.68, p<0.001). No baseline DBP difference existed between groups (U=1794, p=0.975). DBP declined significantly across time points in the intervention group (p<0.001), but not in controls (p=0.776). Between-group comparison showed DBP change differences over time (p=0.008).

Functional outcomes	Groups	Time points	Mean±SD‡	Within groups comparison: F-value (p-value)	Between groups comparison (F value (p-value) for change in values between pre-test and post-test 2)
RHR§ (bpm)	Intervention group	Pretest	77.77±7.23	10.94 (p<0.001)	0.57 (p=0.550)
		Post 1	75.93±5.06		
		Post 2	74.17±3.09		
	Control group	Pre-test	79.83±8.08	8.98 (p=0.001)	
		Post 1	77.23±5.55		
		Post 2	76.53±5.77		
SBP‖ (mmHg)	Intervention group	Pre-test	125.57±12.29	16.75 (p<0.001)	8.68 (p<0.001)
		Post 1	121.60±10.80		
		Post 2	119.03±10.17		
	Control group	Pre-test	126.50±11.34	1.01 (p=0.367)	
		Post 1	125.15±12.24		
		Post 2	125.77±12.33		
DBP¶ (mmHg)	Intervention group	Pre-test	78.73±7.46	9.44 (p<0.001)	5.17 (P=0.008)
		Post 1	77.17±5.95		
		Post 2	74.62±4.85		
	Control group	Pre-test	78.77±6.69	0.25 (p=0.776)	
		Post 1	78.27±7.12		
		Post 2	78.30±7.29		
HRV**	Intervention group	Pre-test	43.22±5.85	222.93 (p<0.001)	47.81 (p<0.001)
		Post 1	52.18±6.28		
		Post 2	55.20±5.49		
	Control group	Pre-test	44.33±6.52	39.21 (p<0.001)	
		Post 1	47.75±6.33		
		Post 2	49.47±7.43		
6 MWD†† (m)	Intervention group	Pre-test	273.17±66.37	203.11 (p<0.001)	18.14 (p<0.001)
		Post 1	408.45±92.21		
		Post 2	465.10±100.80		
	Control group	Pre-test	263.17±71.16	97.19 (p<0.001)	
		Post 1	333.93±94.25		
		Post 2	401.10±117.90		
EF%‡‡	Intervention group	Pre-test	45.92±1.87	267.84 (p<0.001)	31.76 (p<0.001)
		Post 1	53.87±4.36		
		Post 2	56.92±4.22		
	Control group	Pre-test	45.77±2.21	91.39 (p<0.001)	
		Post 1	51.08±4.00		
		Post 2	52.13±4.28		

[Table/Fig-5]: Two-way repeated measures mixed ANOVA on functional outcomes among HFmrEF† patients between intervention (n=60) and control groups (n=60).
†HFmrEF: Heart Failure with mid-range Ejection Fraction; ‡SD: standard deviation; §RHR: Resting heart rate; ‖SBP: Systolic blood pressure; ¶DBP: Diastolic blood pressure; **HRV: Heart rate variability; ††6MWD: six minute walking distance; ‡‡EF: Ejection fraction

No significant difference was found in HRV (t=0.98, p=0.325), 6MWD (U=1639, p=0.398), and EF (t=0.83, p=0.407) between groups at baseline. Both intervention and control groups showed significant increases in HRV, 6MWD, and EF (p<0.001) across time points. Between-group comparison revealed significant differences in the change of HRV (F=47.81, p<0.001), 6MWD (F=18.14, p<0.001), and Ejection Fraction (F=31.76, p<0.001). The improvement in ejection fraction observed in both groups surpassed the HFmrEF categorisation range (41-49%). In the intervention group, scores increased from a pre-test score of 45.92±1.87% to a post-test-2 score of 56.92±4.22%, while in the control group, scores rose from 45.77±2.21% to 52.13±4.28%. This highlights the importance of medical treatment and the additional impact of HRV-EP in managing HF patients.

Effect of HRV-EP on QoL of patients with HFmrEF: A Two-way repeated measures mixed ANOVA tested differences in average QoL scores across time points and between groups [Table/Fig-6]. No significant difference in QoL scores existed between groups at baseline (U=1963, p=0.393). Total QoL scores decreased significantly across time points in both intervention (F=182.23, p<0.001) and control groups (F=61.49, p<0.001). Between-group comparison showed significant differences in QoL score changes over time (F=27.61, p<0.001). QoL scores in the physical domain decreased significantly at various points in both intervention (F=224.02, p<0.001) and control groups (F=77.47, p<0.001), with significant between-group differences over time (F=31.94, p<0.001). QoL scores in the emotional domain showed significant reduction in both intervention (F=47.83, p<0.001) and control groups (F=18.32, p<0.001), with significant between-group differences over time (F=6.59, p=0.007) [Table/Fig-6]. While both management strategies improved functional outcomes and QoL, integrating HRV-EP with conventional management better enhanced BP, HRV, 6MWD, EF, and QoL in patients with HFmrEF.

On pair-wise comparison within each group, significant improvement was observed at post-test 2 in the intervention group for all the parameters. (p<0.001) improvement was also observed in control groups for all the parameters except SBP and DBP between pre-test and post-test-2 (p<0.001) [Table/Fig-7].

QoL	Groups	Time points	Mean±SD‡		Within groups comparison: F value (p-value)	Between groups comparison: {F value (p-value) for change in values between pre-test and post-test 2}
Total score (Max score-105)	Intervention group	Pre-test	47.03	15.94	182.23 (p<0.001)	27.61 (p<0.001)
		Post 1	23.25	10.08		
		Post 2	15.72	9.31		
	Control group	Pre-test	49.28	15.61	61.49 (p<0.001)	
		Post 1	35.60	12.67		
		Post 2	31.02	14.39		
Physical domain (Max score-40)	Intervention group	Pre-test	26.87	7.43	224.02 (p<0.001)	31.94 (p<0.001)
		Post 1	10.67	5.69		
		Post 2	6.43	5.50		
	Control group	Pre-test	27.93	7.06	77.47 (p<0.001)	
		Post 1	19.15	7.46		
		Post 2	15.78	8.57		
Emotional domain (Max score-25)	Intervention group	Pre-test	6.88	5.86	47.83 (p<0.001)	6.59 (p=0.007)
		Post 1	1.85	2.34		
		Post 2	0.98	1.27		
	Control group	Pre-test	7.45	5.71	18.32 (p<0.001)	
		Post 1	4.53	3.90		
		Post 2	3.77	3.94		

[Table/Fig-6]: Two-way repeated measures mixed ANOVA on QoL† among HFmrEF‡ patients between intervention (n=60) and control groups (n=60).
†QoL: Quality of Life; ‡HFmrEF: Heart failure with mid-range ejection fraction; §SD: Standard deviation

Pair-wise comparison	Bonferroni adjusted p-value	
	Intervention group	Control group
RHR		
Pre-test and post 1	0.054	0.003
Pre-test and post 2	<0.001*	<0.001*
Post 1 and post 2	0.014*	0.766
SBP		
Pre-test and post 1	0.001*	0.533
Pre-test and post 2	<0.001*	1.000
Post 1 and post 2	0.006*	1.000

DBP		
Pre-test and post 1	0.081	1.000
Pre-test and post 2	<0.001*	1.000
Post 1 and post 2	0.006	1.000
HRV		
Pre-test and post 1	<0.001*	<0.001*
Pre-test and post 2	<0.001*	<0.001*
Post 1 and post 2	<0.001*	0.001*
6MWD		
Pre-test and post 1	<0.001*	<0.001*
Pre-test and post 2	<0.001*	<0.001*
Post 1 and post 2	<0.001*	<0.001*
EF		
Pre-test and post 1	<0.001*	<0.001*
Pre-test and post 2	<0.001*	<0.001*
Post 1 and post 2	<0.001*	0.002*
Total QoL		
Pre-test and post 1	<0.001*	<0.001*
Pre-test and post 2	<0.001*	<0.001*
Post 1 and post 2	<0.001*	<0.001*
QoL- Physical Domain		
Pre-test and post 1	<0.001*	<0.001*
Pre-test and post 2	<0.001*	<0.001*
Post 1 and post 2	<0.001*	<0.001*
QoL- Emotional Domain		
Pre-test and post 1	<0.001*	<0.001*
Pre-test and post 2	<0.001*	<0.001*
Post 1 and post 2	0.002*	0.007*

[Table/Fig-7]: The Bonferroni adjusted pair-wise comparison.

DISCUSSION

The HF patients commonly exhibit reduced functional capacity and QoL due to neurocardiac incoherence, demonstrated by decreased HRV. In the present study, it was found that the intervention group who performed 16 weeks of HRV-EP, comprising slow breathing and physical exercises, had significantly enhanced functional outcomes such as HRV, BP, 6MWD, and EF as well as QoL, encompassing both physical and emotional domains, in comparison to the control group, thus accepting the hypothesis.

The HRV Score in the intervention group increased from (43.22±5.85) to (55.20±5.49), which was significantly higher than that of the control group (p<0.001). The mean post-test-2 values of SBP (119.03±10.17 mmHg) and DBP (74.62±4.85 mmHg) in the intervention group were lower than the pre-test values {SBP (125.57±12.29 mmHg) and DBP (78.73±7.46 mmHg)}, and that difference was significantly greater than that of the control group (p<0.001 and p=0.008). Slow breathing exercises of HRV-EP improve autonomic stability and enhance vagally mediated HRV and baroreflex sensitivity. This arises from temporal coherence between respiratory patterns, BP, and cardiac phases, known as respiratory sinus arrhythmia. Such practices can counteract elevated sympathetic activity associated with stress, anxiety, and sleep disturbances [20]. Similarly, with an experimental study, Sürücü CE et al., identified that slow and controlled breathing exercises over a period of six weeks enhance parasympathetic activity and HRV [21]. Ghati N et al., evaluated the effect of Bee-Humming Breathing (BHB) exercise and identified, marked improvement in HRV metrics [22]. Lin IM et al., conducted an experimental study and demonstrated that a 5:5 inhalation-to-exhalation ratio enhances HRV compared to four other slow breathing patterns [23].

Following the HRV-EP, the 6MWD in the intervention group increased from 273.17±66.37 m to 465.1±100.8 m. Additionally, the EF percentage improved from 45.92±1.87% to 56.92±4.22%, with these enhancements being more pronounced than those observed in the control group (p<0.001). Lu D-Y et al., reported that increased HRV indices were associated with prolonged exercise duration and improved HR recovery [24]. Furthermore, Shirole U and Joshi M identified a significant correlation between LF/HF (an HRV parameter) and LVEF [25]. Research has demonstrated that engaging in physical exercise training boosts vagal tone, reduces the expression of angiotensin-II, and enhances both endothelial function and the availability of nitric oxide [26].

Chronic HF has been identified as a neurological disorder [27] due to its association with autonomic imbalance, characterised by heightened sympathetic nerve activity, increased noradrenaline levels, and elevated N-terminal pro-brain natriuretic peptide. Besnier F et al., explain that a reduction in noradrenaline serves as a critical indicator of cardiac mortality risk in individuals with HF, a reduction that can be achieved through exercise [28]. Exercise training enhances the modified inhibitory pathway in the Paraventricular Nucleus (PVN) of HF patients through nitric oxide and gamma-aminobutyric acid mechanisms. It mitigates elevated sympathetic activity by normalising excitatory glutamatergic and angiotensinergic pathways within the PVN. Exercise training improves volume reflex function, facilitating fluid balance in HF [28].

In present study, the physical exercises, including aerobic, stretching, and strengthening exercises, which are deemed safe for patients with HFmrEF, were incorporated into the practice regimen. These exercises alleviate abnormal cardiac remodelling, improve myocardial perfusion, correct endothelial dysfunction, and modulate various stages of the inflammatory process by reducing major circulating pro-inflammatory cytokines, thereby enhancing ventricular function [29,30]. The study findings align with results from another observational study by Urvashi et al., on the Indigenous Exercise Protocol's effect on HF patients with NYHA class I and II, where QoL, 6MWD, LVEF, functional class of symptoms, and VO^2 max improved [31].

The study used the MLHFQ to measure QoL. Beyond clinical symptoms, it assesses an individual's physical and social activities, stress and anxiety levels, quality of sleep, and dietary issues as physical and emotional dimensions. Following the implementation of HRV-EP, the intervention group exhibited a significant improvement in QoL (from 47.03±15.94 to 15.72±9.31) compared to the control group (from 49.28±15.61 to 31.02±14.39) (p<0.001). It is important to note that a lower score indicates a higher QoL. Similarly, this difference was observed in both the physical (p<0.001) and emotional domains (p=0.007) of QoL. In a cross-sectional descriptive study, Kochupurayil RJ et al., identified that 59% of HFmrEF cases exhibited a poor QoL. Furthermore, a moderate negative correlation was observed between QoL and HRV score (r=-0.43, p<0.001) [32]. Usmanova N and Erkayev explain that regular physical activity enhances an individual's self-confidence, improves sleep quality, and contributes to overall well-being, thereby enhancing the QoL [33].

Overall, these findings indicate that a 16-week HRV exercise protocol significantly enhances autonomic function, exercise capacity, ejection fraction, and QoL in patients with HF, supporting its use as a safe and effective adjunctive therapy.

Limitation(s)

The study's limitations were that the MLHFQ was based on self-reports, and during repeated measurements, there was a chance of recall bias and dishonesty. The study could have been conducted in a cardiac rehabilitation centre under direct supervision to reduce sample dropout due to partial performance or discontinuation of the intervention. The allocation of subjects into experimental and control groups was not randomised to overcome the challenge of sample contamination. Generalising the findings is not possible, since it was conducted in a single setting.

CONCLUSION(S)

The HRV-EP is a safe, effective, home-based intervention for enhancing vagal tone and improving functional outcomes and QoL among HFmrEF patients. Community-based cardiac rehabilitation programmes can implement HRV-EP. Future studies may explore the effect of HRV enhancement on the prognosis of various disease conditions.

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