Original Research Article

Efficacy Of Heart Failure Reversal Therapy (HFRT) In Post-Menopausal Female Patients With Preserved Ejection Fraction (>40%).

ABSTRACT:

Purpose: Mortality in women round the world is attributed majorly to CVDs. Around 4.5 Lac women die annually due to plethora of CVDs like Heart Failure (HF) and Ischemic Heart Disease or their complications. Especially, postmenopausal women are majorly affected by CVDs. This study was conducted to evaluate the effect of Heart Failure Reversal Therapy (HFRT) on VO2max, 6 Minute Walk Test (6MWT), Blood Pressure (BP), Body Mass Index (BMI), abdominal Girth and Heart Rate.

Methods: This observational study was conducted from January 2015 to December 2017, wherein the data of post-menopausal CHF patients (New York Heart Association, NYHA Class I–IV) with preserved ejection fraction, who attended out-patient departments (OPDs) at *Madhavbaug clinics in Khopoli, Maharashtra, India* were identified. Data of patients who were administered HFRT (60-75 minutes) with minimum 7 sittings over 7 days were considered. Variables were compared between day 1, 7, 30, 60, and day 90 of HFRT.

Results: 71 postmenopausal women were finally enrolled in the study. HFRT showed significant improvement in VO2max from 16.53±4.86 to 24.8±6.25, p<0.001. SBP reduced significantly from 124.03±17.02 to 120.76±12.62 (p<0.001) at the end of 90th day. Heart rate reduced from 85.79±15.12 to 79.58±10.19 (p< 0.001).

Conclusion: HFRT can serve as potent and viable therapeutic option for management of HF in Post-menopausal women with Preserved Ejection Fraction.

Keywords: *Heart Failure Reversal Therapy, HFRT, Panchakarma, Heart Failure, VO2max, Menopause, BMI, BP.*

1. INTRODUCTION:

The prevalence of cardiovascular diseases (CVDs) is escalating on alarming scales on global geography. Mortality in women round the world is attributed majorly to CVDs. Around 4.5 Lac women die annually due to the plethora of CVDs like heart failure (HF) and ischemic heart disease or their complications.[1] Especially, postmenopausal women are majorly affected by CVDs. Lack of oestrogen due to menopause has been shown to be associated with increased cardiovascular morbidity and mortality.[2,3] Due to the protective effects of oestrogen on cardiovascular function and metabolism, menopause has been considered as a major risk factor for CVDs. Interplay of variety metabolic changes due to menopause induced oestrogen withdrawal like decreased glucose tolerance, abnormal plasma lipid levels, increased sympathetic tone, vascular inflammation, endothelial dysfunction, abnormality in fat distribution in the body, contribute to increase in cardiovascular risk.[4]

Despite the availability of extensively laid guidelines for treatment of HF, which suggest the use of pharmacological drugs like vasodilators, beta blockers, angiotensin converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARBs), in hospital mortality attributed to HF lies in the range of 30%, which is worrisome.[5] Optimal treatment of any disease is vastly dependent on patient adherence to treatment. This has been found to be only 30-50% in Indian HF patients, thus the suboptimal outcome of treatment, resulting in increased morbidity and mortality. Thus, it is dire need of the hour to explore novel therapeutic option which will have multifaceted actions of decreasing cardiovascular morbidity and mortality along with increasing the quality of life by reducing dread and apprehension associated with the diagnosis of disease.

Due to interplay of several components like concurrent numerous medications, old age, reduction in hepatic and renal function with advancing age, other co-existing diseases, etc.; the treatment of HF is intricate.[6] Major conventional drugs used in treatment of HF have beneficial effects through their anti-inflammatory and antioxidant actions.[7,8] Similar properties have been found in various herbal drugs in clinical studies, which makes them potent and viable nominees for treatment in patients of HF.[9,10,11,12] Ayurvedic practice of medicine idealizes the concept of administering *Panchakarma* i.e. 4-step internal body purification in chronic phase of disease, in addition to conventional drugs used in acute phase of disease.[13] A combination of *Panchakarma* and diet therapy is given under the span of Heart Failure Reversal Therapy (HFRT).[14] Four detoxifying techniques are used in *Panchakarma* of HFRT-*Snehana* (Oleation therapy), *Swedana* (Passive heat treatment), *Hrudaydhara* (Concoction dripping therapy) and *Basti* (Per rectal drug administration).[13,15]

Routine work capacity/exercise tolerance is drastically reduced in patients of HF, which is measured currently by VO2max, also known as maximum aerobic capacity/maximum exercise capacity.[16] Since this adversely affects performance of daily usual work, quality of life is also drastically reduced.[17] Hence, we planned an observational study with the objective of assessing the effect of HFRT in postmenopausal patients of HF with preserved ejection fraction. We also assessed the effect of HFRT on weight, body mass index (BMI), abdominal girth, systolic blood pressure (SBP), diastolic BP (DBP).

2. MATERIALS AND METHODS:

This was an observational study conducted between January 2015 to December 2017, wherein we identified the data of post-menopausal patients suffering from CHF (New York Heart Association, NYHA Class I–IV) with preserved ejection fraction (EF>40%), who had attended the out-patient departments (OPDs) at *Madhavbaug clinics in Khopoli, Maharashtra, India*.

The data of patients who had been administered HFRT with minimum 7 sittings over a span of 90 days (± 15 days) were considered for the study. Cases were identified, and data was assessed from the records of *Madhavbaug clinics in Khopoli, Maharashtra, India*.

The selection was based upon the availability of complete relevant baseline data (day 1 of HFRT) and final day data (day 90 of HFRT) of the patients. The information about prescribed concomitant medicines or comorbidities, if any, was also noted down.

The HFRT is a 4-step procedure which was performed on the patients with CHF after a light breakfast. One sitting of the procedure took 65-75 minutes, as described in table 1.[13,15]

Table 1. Study Treatment: Heart Failure Reversal Therapy (HFRT)

Step of HFRT	Type of Therapy	Herbs used for therapy	Duration of Therapy
Snehana	Massage or external oleation (centripetal upper strokes directed towards heart)	10 grams T. arjuna, 10 grams *Dashamoola* and 5 grams *V.negundo* [100 ml extract processed in *sesame oil*]	30-35 minutes
Swedana	Passive heat therapy	*Dashmoola* (group of ten herbal roots) with steam at $\leq$ 40 degrees Celsius)	10-15 minutes + 34 minutes of relaxation after procedure
Hrudaydhara	Decoction dripping therapy from a height of 7-8 cm	Luke-warm *dashmoola* decoction	15 minutes
Basti	Drug administered per rectal, should be in body for $\geq$ 15 minutes for maximum absorption	1.88 grams *T. arjuna*, 0.42 grams *B. diffusa* and 0.18 grams *A. calamus* [10 ml aqueous extract]	10 minutes

2.1 Follow-up flow is given as follows:

On day 1, the patients physical examinations (VO2max, SBP, DBP, weight, BMI and Abdominal Girth), 2D Echo (Ejection Fraction) were performed. Then, 2 *Panchakarma* therapy (morning and evening) is given to the patients. This pattern is followed for the next 7 days during the hospitalization with a diet plan of 1000-1200 kcals per day.

Then again on 7th day same tests were repeated. After discharge, the patients are called for follow-up, i.e. 30-days, 60-days and 90-days after 7 days of HFRT. Same Test were performed in every follow up. One way ANOVA (table 2) was used to test statistical significance for Primary endpoint (Improvement in VO2max) and secondary endpoint (Reduction in Weight, BMI, abdominal Girth, Heart Rate, SBP and DBP) for a washout period (DoA, DoD, 1st follow up, 2nd Follow up and 3rd Follow up). We used R (Version 3.5.0) software and excel to analyze the data.

Table 2. Hypothesis for ANOVA test

Null Hypothesis	Means are equal among all 5 different time periods i.e. DOA, DOD, 1 f/u, 2 f/u & 3 f/u
Alternative Hypothesis	Means of at least 2 groups are significantly different
Level of significance	0.05

3. RESULTS:

3.1 Study population:

A total of 100 patients' data was screened for inclusion in the study. However, based on the availability of data (Day 1, 7, 30, 60 and day 90) and the inclusion criteria, 71 patients were selected, and their data was considered for analysis (Figure 1). The baseline characteristics of these patients are shown in table 3.

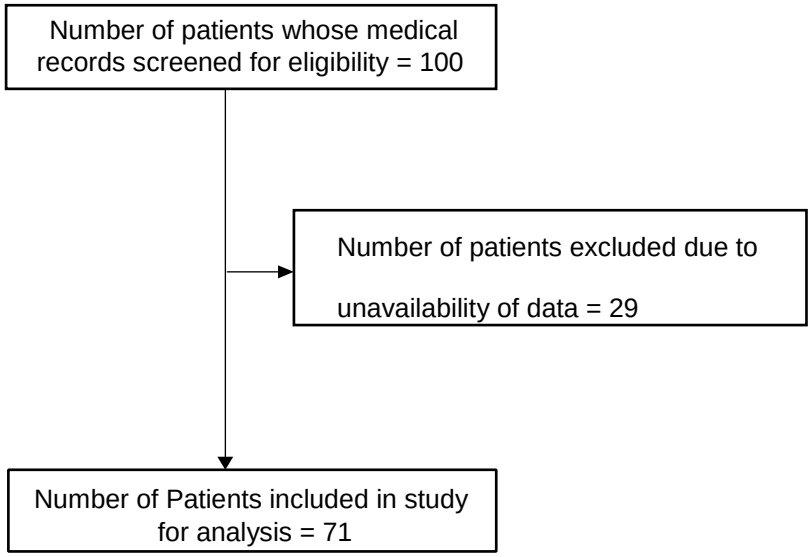


Figure 1. Patient Enrolment Flow Chart

HFRT program in post-menopausal female patients with preserved EF, there were 71 cases and baseline data included age, height, LV, EF, past medical history and NYHA Functional class variables. These baseline findings are depicted in table 3.

Table 3. Baseline characteristics of the study subjects (n= 71)

Variable	Mean ± SD
Gender (F)	71
Age (Years)	63.65±3.27
Height (cm)	152.54±6.14
EF	58.41±5.65
Past medical history Frequency (%)	
CAD	22 (30.99)
HTN	56 (78.87)
DM	33 (46.48)
ST.IHD	36 (50.7)
OBESITY	14 (19.72)
DYSLIPEDEMIA	14 (19.72)
CHF	11 (15.49)
THYROIDISM	3 (4.23)
PTCA	2 (2.82)
MI	5 (7.04)
UA	1 (1.41)
NYHA functional class Frequency (%)	
Class I	2 (2.82)
Class II	54 (76.06)
Class III	12 (16.9)
Class IV	1 (1.41)

Note: - Categorical data were expressed in terms of percentage and continuous data were expressed as Mean ± SD.

The baseline characteristics of the study populations are shown in Table 3. In that 71 subjects, 22 (30.99%) had Coronary artery disease (CAD), 56 (78.87%) had Hypertension (HTN), 33 (46.48%) had Diabetic Mellitus (DM), 36 (50.7%) had ischemic heart disease (IHD), 14 (19.72%) had Obesity, 14 (19.72%) had Dyslipedemia, 11 (15.49%) had Congestive Heart Failure, 3 (4.23%) had Thyroidism, 2 (2.82%) had PTCA, 5 (7.04%) had Myocardial infarction and 1 (1.41%) had UA. Most of the patients belonged to Class II i.e. 54 patients (76.06%) and Class III 12 (16.9%) as per NYHA functional class. Only single respondent belonged to class IV.

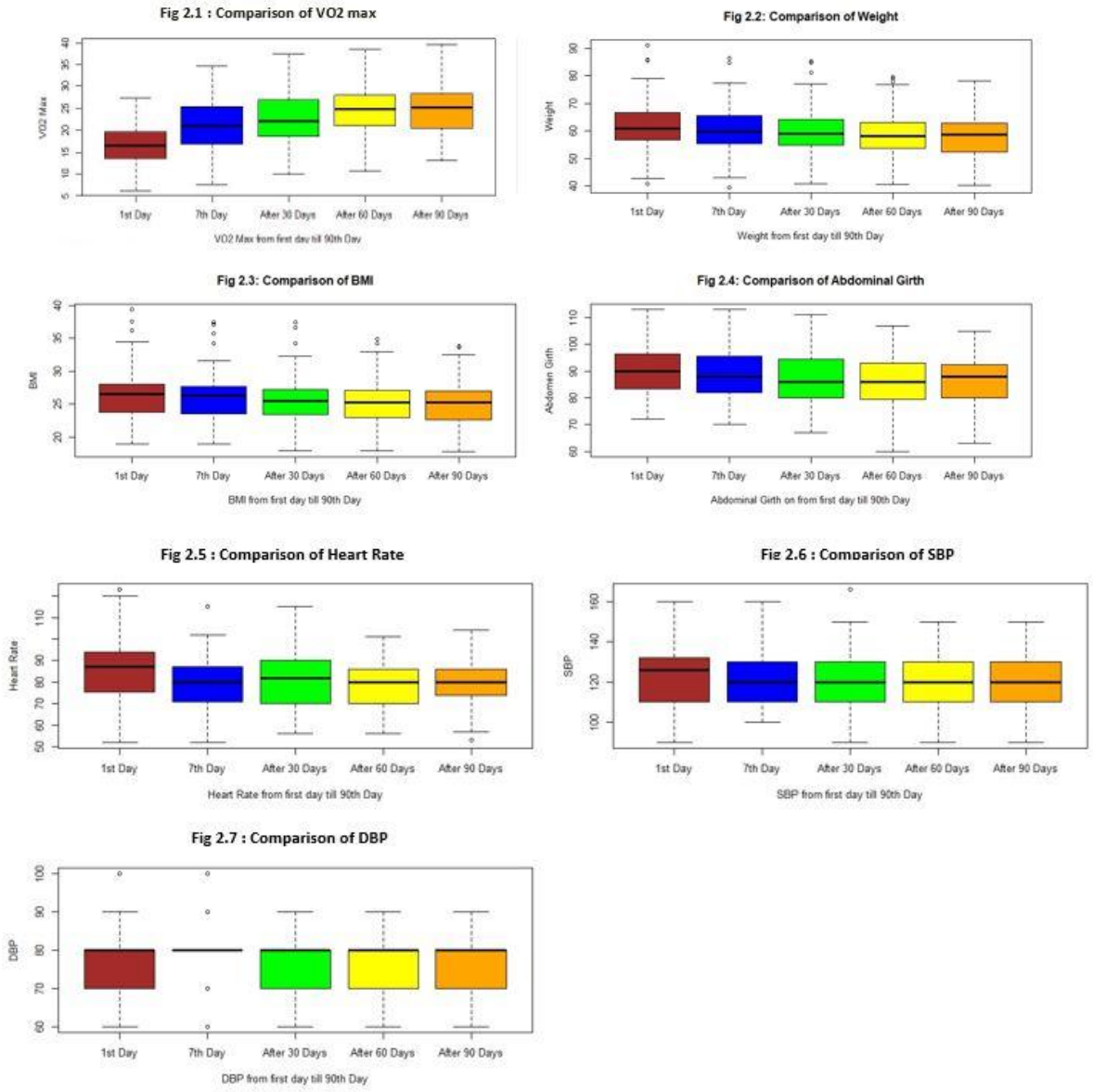
Table 4. Effect of HFRT treatment on improvement of various body parameters according to overall and NYHA subjects

Variable	Sample size	Mean ± SD					*P-value*
		DOA	DOD	1 f/u	2 f/u	3 f/u	
VO2 max	71	16.53±4.86	21.35±5.69	22.96±6.59	24.22±5.98	24.8±6.25	<0.001
Weight	71	62.16±9.93	60.92±9.57	59.78±9.5	58.98±9.11	58.64±8.97	<0.001
BMI	71	26.69±3.87	26.16±3.72	25.67±3.67	25.33±3.5	25.18±3.41	<0.001
Abdominal Girth	71	90.3±9.34	89.01±9.18	87.11±9.84	86.3±9.54	86.55±8.76	<0.001
Heart Rate	71	85.79±15.12	79±11.84	81.25±12.66	78.39±11.47	79.58±10.19	<0.001
SBP	71	124.03±17.02	123.52±12.66	121.18±14.54	121.41±13.55	120.76±12.62	0.56
DBP	71	76.56±9.77	79.3±6.83	77.04±8.18	77.18±8.97	77.32±7.74	0.12

Effect of HFRT treatment on improvement of body parameter is summarized in Table 4. For all 71 cases, HFRT treatment showed significant (high statistical significance) improvement in weight, BMI, Abdominal Girth, and VO2 Max, Heart Rate. HFRT treatment was not statistically significant for SBP, DBP.

Figure 2 shows us a comparison of endpoint among all time periods (DoA, DoD, 1st follow up, 2nd Follow up and 3rd Follow up).

Figure 2. Effect of HFRT on clinical parameters



Thus HFRT treatment was statistically significant for the primary endpoint (Improvement in VO2max) but partially significant in case of secondary endpoint (reduction in Weight, BMI, abdominal Girth, Heart Rate). SBP and DBP were statistically insignificant in secondary endpoint.

4. DISCUSSION:

Although, wide range of drugs are available for treatment of HF, it still remains one of the leading causes of mortality, especially in postmenopausal patients. Due to these drawbacks of conventional therapy, search for the alternate therapeutic option has gained momentum in recent years. Ayurveda seems to be a promising search candidate as an alternate therapeutic option, since many herbal drugs have been shown to possess anti-inflammatory and antioxidant properties which are beneficial in HF similar to traditional allopathic drugs like ACEIs, ARBs, etc. HFRT is administered by Ayurvedic physicians in the treatment of HF as a combination of Panchakarma and diet therapy.[18,19] Keeping these facts in mind, we analyzed effects of HFRT on VO2max in post-menopausal patients with HF with preserved EF. VO2max was significantly improved consistently till 3rd follow up at 90th day after HFRT. BMI, abdominal girth, HR also showed a significant reduction, as compared to baseline, after HFRT.

The possible mechanisms of HFRT might be reduction in HR via anxiolytic effects of *Snehana* and *Hrudaydhara*, reduction in sodium and water load by *Swedana* and a reduction in BP by *Terminalia arjuna*, the antioxidant effect of *Boerhaavia diffusa* and antinflammatory, antioxidant action of *Ascorus calamus*; all administered through *basti*.[20,21,22]

Cardiorespiratory capacity in an individual is measured by VO2max, which in turn is an indicator of work capacity. VO2max is reduced in all patients of HF and this reduction is directly proportional to severity of disease.[23] Significant improvement in VO2max in the present study thus signifies better prognosis in patients with HF due to the fact that VO2max is directly correlated with functional capacity and secondarily reduced VO2max is mortality prognosticator in patients with HF. This is corroborated by findings of clinical study done on patients with coronary artery disease, wherein it was found that 15% reduction in mortality was achieved by increasing VO2max by 1ml/kg/min. Thus, better prognosis can be anticipated with HFRT since it led to significant improvement in VO2max.

Increased mortality is seen in patients with HF with increased BMI, which is a marker of obesity.[24] Apart from this, tachycardia/increased heart rate is considered to be a major aggravating factor and also a poor prognostic indicator for HF. Therefore, it is commonly seen that each and every guideline on management of HF advocates sustained HR control.[25,26] In the present study, there was significant reduction in HR, which indicates that HFRT may improve prognosis in patients with HF. In order to generalize the findings of our study, it is recommended that similar studies be conducted on a large scale with prospective design, more duration of follow up, two arms to allow direct comparison with standard conventional therapy.

5. CONCLUSION:

VO2max was significantly corrected after treatment with HFRT. Thus, increased VO2max coupled with a significant reduction in HR, BMI, abdominal girth after HFRT signifies better prognosis in post-menopausal patients with HF with preserved ejection fraction >40%.

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