

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 II) 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=0.56) 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.~~ CVDs like heart failure (HF) and ischemic heart disease contribute to maximum deaths in women round the globe, accounting to nearly 4.5 lac deaths annually.^[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 like release of endothelial nitric oxide causing arterial vasodilation and reduction in afterload of heart and metabolism, menopause has been considered as major risk factor for CVDs. Interplay of variety metabolic changes due to menopause

27 induced oestrogen withdrawal like decreased glucose tolerance, abnormal plasma lipid levels,
28 increased sympathetic tone, vascular inflammation, endothelial dysfunction, abnormality in fat
29 distribution in the body, contribute to increase in cardiovascular risk.^[4]

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

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

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

61 2. MATERIALS AND METHODS:

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

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

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

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

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

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

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2.1 Follow-up flow is given as follows:

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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

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103 **3. RESULTS:**

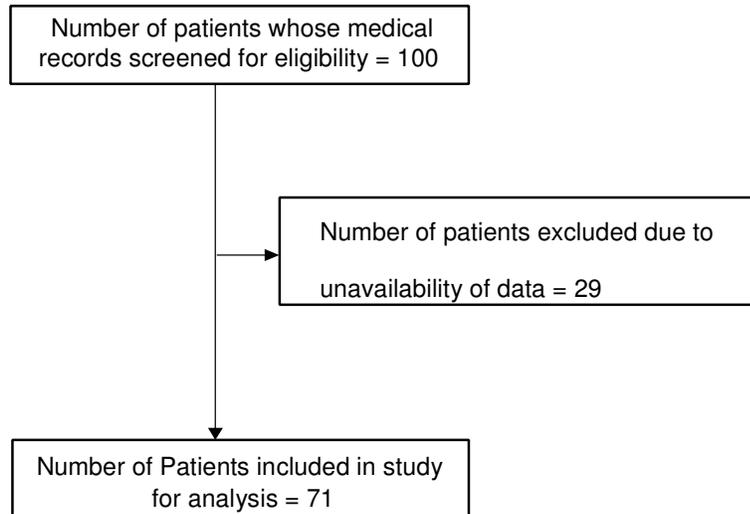
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105 **3.1 Study population:**

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

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111 **Figure 1. Patient Enrolment Flow Chart**

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

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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)

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

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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

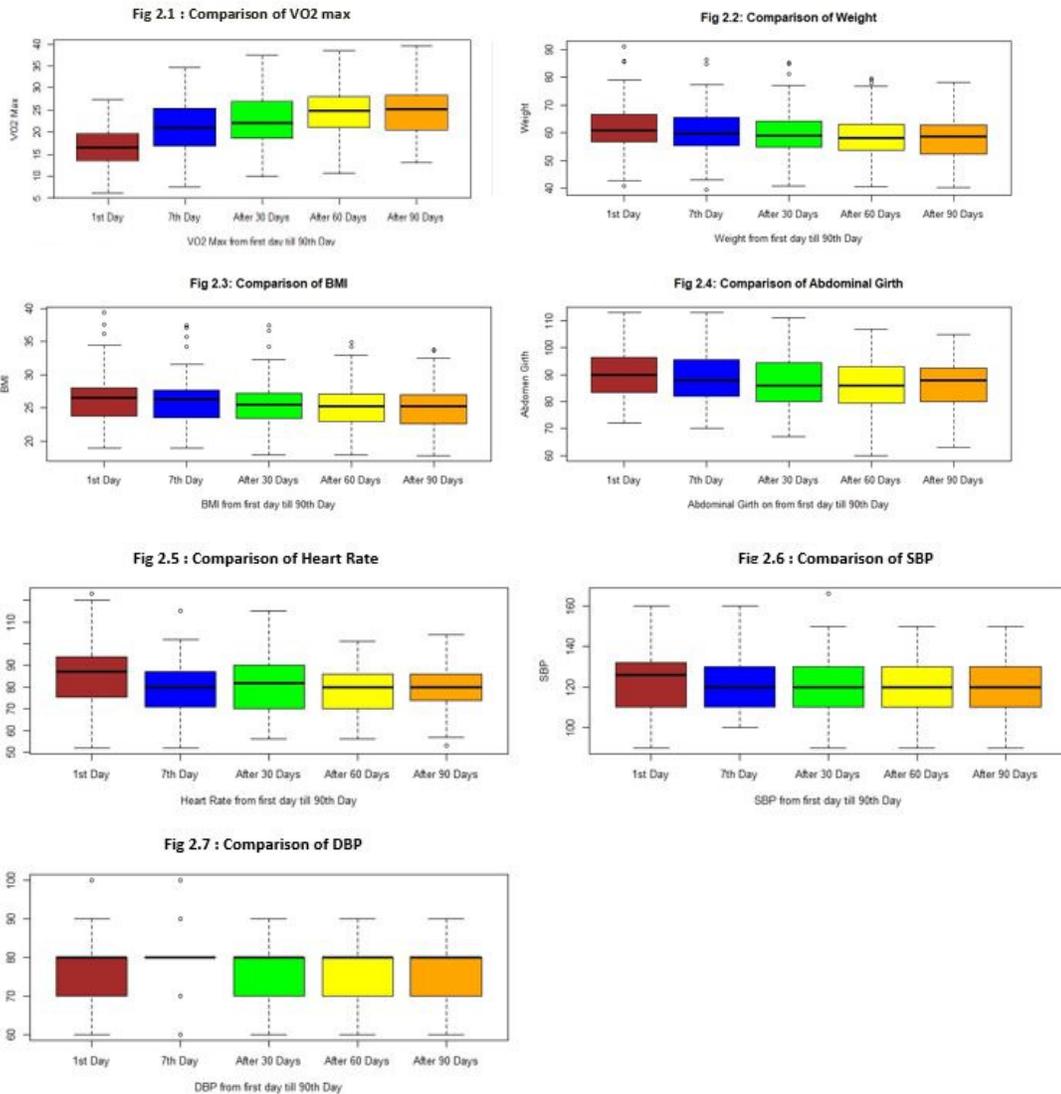
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Effect of HFRT treatment on improvement of body parameter is summarized in Table 4. For all 71 cases, HFRT treatment showed significant (high statistical significance) improvement in weight, BMI, Abdominal Girth, and VO2 Max, Heart Rate. HFRT treatment 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).

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Figure 2. Effect of HFRT on clinical parameters



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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.

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4. DISCUSSION:

Although, wide range of drugs are available for treatment of HF, it still remains one of the leading cause of mortality, especially in postmenopausal patients. Due to these drawbacks of conventional therapy, search for alternate therapeutic option has gained momentum in recent years. Ayurveda seems to be 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.^[19,20] Keeping these facts in mind, we analysed effect of HFRT on VO₂max in post-menopausal patients of HF with preserved EF. VO₂max was significantly improved consistently till 3rd follow up at 90th day after HFRT. BMI, abdominal girth, HR also showed 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 reduction in BP by Terminalia arjuna, antioxidant effect of Boerhaavia diffusa due to presence of flavonoid and dihydroxy anisole and antiinflammatory, antioxidant action of Ascorus calamus; all administered through basti.^[21,22,23] Also, HFRT leads to weight loss which might contribute to beneficial cardiovascular effects.

Heart rate is a critical factor in HF patients. Increased heart rate augments the work load on compromised heart i.e. it increases the demand while reducing the supply. Thus, it is very important to control the heart rate in patients of HF. In the present study heart rate increased in 1st follow up and then reduced in subsequent follow ups. The initial rise may be due to lack of adherence to low calorie diet and performing strenuous activities.

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.^[24] Significant improvement in VO₂max in the present study thus signifies better prognosis in patients of HF due to the fact that VO₂max is directly correlated with functional capacity and secondarily reduced VO₂max is mortality prognosticator in patients with HF, as is used in majority of clinical trials on CHF to study the efficacy of various interventions. 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 1 ml/kg/min.^[25] Thus, better prognosis can be anticipated with HFRT since it led to significant improvement in VO₂max.

There is limit in exertional capacity in patients with HF, due to which oxygen supply to muscular tissue is reduced. This has been linked to anaerobic formation of lactic acid in the muscle with limited activities. This is reflected in reduced VO₂ max in HF cases. VO₂ max has been accorded as important prognosticator in HF patients for further risk stratification, identifying heart transplant patients, etc.^[26]

Increased mortality is seen in patients of HF with increased BMI, which is marker of obesity.^[26] Apart from this, tachycardia/increased heart rate is considered to be 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.^[27,28] 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 large scale with prospective design, more duration of follow up, two arms to allow direct comparison with standard conventional therapy. The limitation of the study was that analysis of weight loss and improvement of VO₂ max was not studied.

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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Ethical Disclaimer: Yes, we considered the ethics, it's a retrospective data analysis

Consent Disclaimer:

We took a consent from all patients that they have no objection over publication of data by keeping confidentiality over their personal details

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