International Journal of Medical and Health Research
ISSN: 2454-9142
Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 4; Issue 7; July 2018; Page No. 149-154

To study the efficacy of Heart Failure Reversal Therapy (HFRT) program in elderly male patients with reduced ejection fraction

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Abstract
Background and Aims: Some authors consider heart failure (HF) to be a pandemic now, since nearly 26 million people have been affected by it, globally. Out of these, India alone has around 8-10 million patients. Heart Failure Reversal Therapy (HFRT) combines Herbal *Panchakarma* therapy with Dietary management. This study was conducted to evaluate the effect of HFRT on VO2peak, 6 Minute Walk Test (6MWT), systolic blood pressure (SBP), and diastolic blood pressure (DBP), BMI, weight, abdominal girth, and heart rate.
Setting and Design: This observational study was conducted from January 2015 to December 2017, wherein the data of elderly male patients with HF (NYHA class II and III) with reduced ejection fraction (<40%) who attended *Madhavbaug hospital, Khopoli, Maharashtra,* India were identified.
Materials and Methods: 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: 50 elderly males with HF and EF < 40% were enrolled in the study for analysis. There was significant improvement in VO2peak, from 12.71 ± 2.47 at baseline to 14.89 ± 2.05 at day 90 ($p<0.001$). 6MWT also showed significant improvement from 339.42 ± 106.85 at day 1 to 432.4 ± 89.27 at day 90 ($p<0.001$). Also, BMI, abdominal girth, weight showed similar statistically significant improvements. Improvements in SBP, DBP and HR were not statistically significant.
Conclusion: From the findings of our study, HFRT has been found to be a potent and viable therapeutic alternative for elderly male patients with HF with reduced ejection fraction.

Keywords: heart failure reversal therapy, HFRT, Panchakarma, heart failure, blood pressure, systolic, diastolic, VO2peak, 6MWT, NYHA

1. Introduction

Reduced capacity of the heart to function optimally leading to insufficient amount of blood pumped for routine metabolic activities, resulting in increased resting pressure within the heart is known as Heart Failure (HF) [1, 2]. Some authors consider HF to be a pandemic now, since nearly 26 million people have been affected by it, globally. Out of these, India alone has around 8-10 million patients. Even the mortality rates in India due to HF are as high as 0.16 million per year [3]. In past few decades, urbanization and industrialization has boomed significantly in India, which has greatly contributed to increased sedentary lifestyle and other risk factors of HF. Due to improved healthcare, population in age group>60 years have escalated by more than 1.7 times in a short span of 20 years [4]. Since advancing age is a major risk factor for HF, it is logical to anticipate that prevalence and burden of HF in India is rising [5]. Apart from age, Hypertension (HTN) is other major risk factor for HF patient. Cases of HTN are consistently increasing with every passing year, thus increasing the likelihood of HF cases [6, 7].

A variety of drugs are available for treatment of HF, like angiotensin 2 receptor blockers (ARBs), angiotensin converting enzyme inhibitors (ACEIs), beta blockers, diuretics, anti-platelet drugs, etc [8]. Despite availability of extensive list of conventional therapeutic options, HF carries poor prognosis. HF has dual effects on patients- firstly, direct effect of its symptoms, and secondly anxiety and dread associated with these symptoms. These dual effects adversely affect quality of life of patient. Also, it has been commonly observed that adherence to conventional therapies is less than 50% in such patients, attributed to high cost of therapy, adverse effects of drugs, etc [9]. Due to these drawbacks of conventional therapies, there is need of novel therapy which will maintain and preserve optimal heart function and raise the quality of life of the patient [10].

Therapeutic benefits of conventional therapies in HF like ACEIs, ARBs, beta blockers, diuretics are due to anti-inflammatory, hypolipidemic, antiplatelet, and antioxidant actions [11]. Similar actions have been found in various herbal drugs in clinical studies [12, 13, 14]. Thus, the quest for search of novel therapeutic agent for the management of HF can end up here. *Panchakarma* and diet therapy are combined under the umbrella of Heart Failure Reversal Therapy (HFRT). *Panchakarma* in HFRT is administered via *Snehana* (External Oleation Therapy), *Swedana* (Passive Heat Treatment), *Hrudaydhara* (Decoction Drip Therapy), and *Basti* (Per Rectal administration); which are established detoxifying procedures [15, 16].

Functional working capacity is reduced in HF, as measured by maximum aerobic capacity/VO2peak [17]. This reflects in reduced quality of life [18]. Keeping this in mind, we planned an observational study, to analyze the effect of HFRT on

VO2peak in elderly male of HF with reduced ejection fraction (EF<40%). We also analyzed the effect of HFRT on SBP, DBP, HR, weight, BMI, abdominal girth.

2. Materials and methods

a. Sample Size: 50
b. Study design: Observational.
c. Duration of study: January 2015 to December 2017
d. Study Site: *Madhavbaug Hospital, Khopoli, Maharashtra, India.*
e. Inclusion Criteria: We have observed the efficacy of HFRT program in:
   1. Elderly male patients = Age ≥ 60 years
   2. Ejection fraction = ≤ 40%
   3. NHYA Grade – II and III
f. Methodology
   1. We identified the data of male patients suffering from HF (New York Heart Association, NYHA Class II–III) of age >60 years, and who had attended the out-patient departments (OPDs) at *Madhavbaug hospital* located in *Khopoli, Maharashtra, India*. The data of patients who had been administered HFRT with minimum 7 sittings over a span of 7 days were considered for the study. Cases were identified, and data was assessed from the records of *Madhavbaug Hospital in Khopoli, Maharashtra*. The selection was based upon the availability of complete relevant baseline data (day 1 of HFRT) to final day data (day 90 of HFRT) of the patients. The information about comorbidities, if any, was also noted down.
   2. The Follow-up schedule is shown in figure 1.
g. Primary End-point: VO2peak
h. Secondary End-points: Weight, BMI, Abdominal Girth, Heart Rate, SBP and DBP.

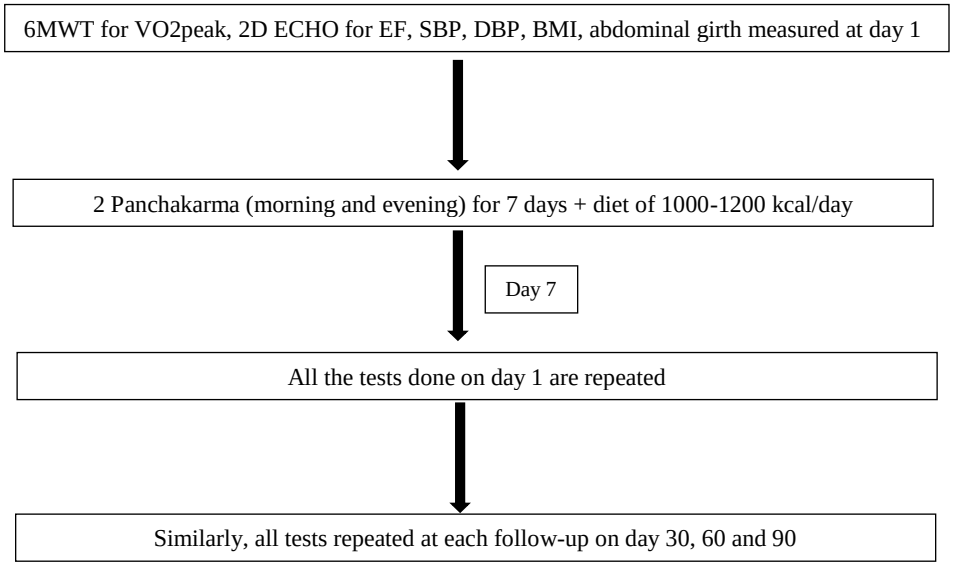

Fig 1: showing follow-up schedule.

The HFRT is a 4-step procedure, which was performed on the patients with HF after a light breakfast. One sitting of the procedure took 65-75 minutes, as described in table 1 [16, 19].

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 ≤ 40 degrees Celsius)	10-15 minutes + 3-4 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 ≥ 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

On day 1 of HFRT, the patients had undergone 6MWT, VO2peak, SBP, DBP as per international recommendations [20]. These readings were considered as baseline readings. This process was repeated as per figure 1. The patients followed a diet chart/plan of 1000-1200 kcal/day.

Statistical analysis

Repeated measured ANOVA was used to test statistical significance for Primary endpoint (Improvement in VO2peak) and secondary endpoint (reduction in Weight, BMI, abdominal Girth, Heart Rate, SBP and DBP as well as

reduction in dependency of conventional medicine) 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).

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 55 patients' data was screened for inclusion in the study. However, based on the availability of data (Day 1, day 7, day 30, 60 and Day 90) and the inclusion criteria, 50 patients were selected, and their data were considered for analysis. The baseline characteristics of these patients are shown in table 3.

Demographic characteristics of the subjects enrolled in the study was as shown in Table 2. The present involved a total of 50 HF patients. The mean age of the enrolled subjects was 67.84±5.71years. The mean ejection fraction in these patients was 30.78±5.54.

Table 3: Baseline characteristics of the study subjects (n= 30)

Variable	Mean ± SD
Gender (M)	50/0
Age (Years)	67.84±5.71
Height (cm)	165.45±5.93
LV Mass	241.22±61.08
EF	30.78±5.54
Past medical history Frequency (%)	
CAD	24 (48.00)
HTN	31 (62.00)
DM	21 (42.00)
IHD	33 (66.00)
MI	6 (12.00)
NYHA functional class Frequency (%)	
Class I	0 (0.00)
Class II	34 (68.00)
Class III	13 (26.00)
Class IV	1 (2.00)

Data were expressed in % and mean ± SD

The baseline characteristics of the study populations are shown in Table 3. In that 50 subjects, 24 (48%) have Coronary artery disease (CAD), 31 (62%) have Hypertension (HTN), 21 (42%) have Diabetic Mellitus (DM), 33 (66%) have ischemic heart disease (IHD), 6 (12%) have Myocardial infarction (MI). Most of the patients belongs Class II 34 (68%) and Class III 13 (26%) as per NYHA functional class. Only single respondent belongs 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	Conclusions from ANOVA
		DOA	DOD	1 f/u	2 f/u	3 f/u		
VO2 Peak	50	12.71± 2.47	13.96 ± 2.12	14.65 ±2.15	14.8 ± 2.19	14.89 ± 2.05	<0.001	Statistically significant
6 MWT (Meters)	50	339.42 ±106.85	391.98 ±91.97	422 ± 93.5	428.2 ±95.08	432.4 ±89.27	<0.001	Statistically significant
Weight	50	64.82 ± 12.01	62.91 ±11.67	62.31 ±11.26	62.37 ±10.89	62.48 ±10.94	<0.001	Statistically significant
BMI	50	23.56 ± 3.92	22.85 ± 3.73	22.64 ± 3.6	22.66 ± 3.47	22.7 ± 3.47	<0.001	Statistically significant
Abdominal Girth	50	91.66 ± 10.4	89.82 ±10.19	89.16 ± 9.94	88.2 ± 9.47	89.04 ± 9.43	<0.001	Statistically significant
Heart Rate	50	76.5 ± 12.77	78.3 ± 11.42	72.94 ±13.41	74.82 ±13.18	75.54 ±11.96	0.14	Statistically insignificant
SBP	50	114.04 ± 14.57	115.2 ±14.18	112.8 ±15.52	112.32 ±12.86	115.6 ±14.02	0.49	Statistically insignificant
DBP	50	73.6±8.75	74±8.08	72.4 ± 8.47	73.32 ±10.77	72.8 ± 8.34	0.79	Statistically insignificant

Effect of HFRT treatment on improvement of body parameter is summarized in Table 4. For all 50 cases, HFRT treatment showed significant improvement in weight, BMI, Abdominal Girth, 6MWT (meters) and VO2peak. HFRT treatment wasn't statistically significant for Heart rate, SBP and DBP.

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

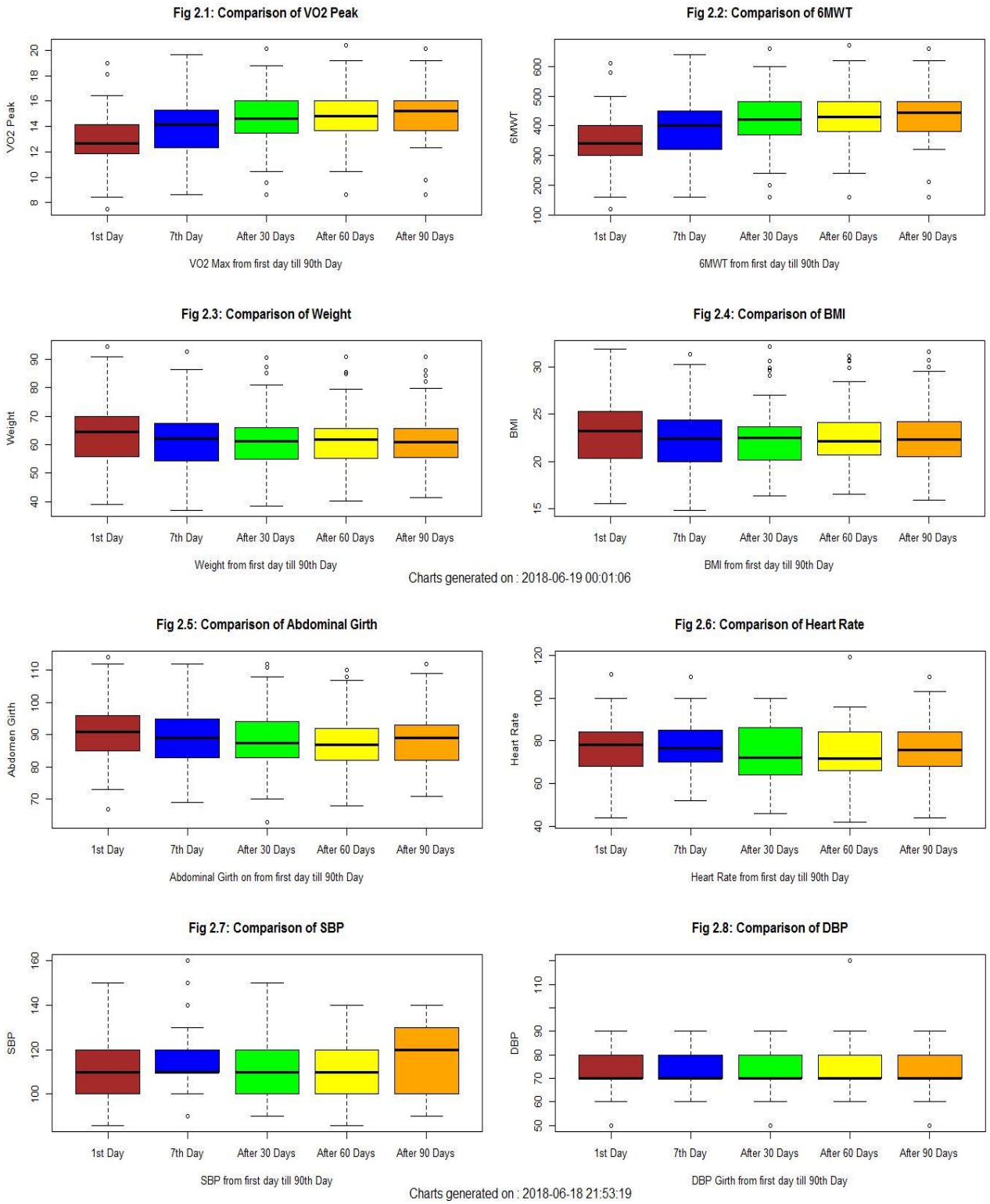

Fig 2: showing effect of HFRT on body parameters

Thus, HFRT treatment showed statistically significant results for the primary endpoint (Improvement in VO2peak) but partially significant in case of secondary endpoint (Reduction in Weight, BMI, abdominal Girth, Heart Rate, SBP and DBP). Heart rate, SBP and DBP were statistically insignificant amongst secondary endpoint.

4. Discussion

The present observational study analyzed the effect of HFRT in elderly males of HF, found that there was significant improvement in 6MWT and VO2peak from day1 to day 7 of HFRT. It was fascinating to observe that these improvements were sustained even on day 90 of follow-up. Even secondary

endpoints like BMI, weight, abdominal girth showed substantial improvement after HFRT. Oxygen uptake is drastically reduced in patients of HF due to weakened heart. This is reflected by reducing VO2peak [21]. Thus, significant improvement in VO2peak in the present study carries a favourable prognosis in patients with HF. This was corroborated by the findings of other such studies, although treatments used in those studies were different [22]. Around 14-16% reduction in risk of mortality with increase in VO2peak by 1ml/kg/min was seen in one clinical study in patients with ischemic heart disease [23]. Thus, significant improvement in VO2peak in the present study signifies favourable prognosis in patients of HF. VO2peak increased in the present study by hefty margin of around 50% from baseline to day 90 of follow-up. This indicates a reduction in death risk in patients with HF.

Despite availability of wide range of conventional allopathic drugs and extensively designed guidelines to combat the havoc of HF, morbidity and mortality of HF is rising continuously. *Panchakarma* is administered in HFRT as 4-step process, which includes *Snehana, Swedana, Hrudaydhara* and *Basti* [24]. Plausible mechanism of HFRT might be:

1. *Snehana*- calms the patient through its anxiolytic effect
2. *Swedana*- reduces preload of the heart by reducing water and sodium load
3. *Hrudaydhara*- which is a type of *Shirodhara*; it calms the patient and helps in reduction of BP
4. *Basti- Terminalia arjuna* helps in reduction of BP, thus reducing afterload of heart [*terminalia*].

We studies the effect of HFRT in elderly male of HF with reduced EF and found significant improvement in VO2peak and 6MWT at the end of 3rd follow-up visit. Since the patients had EF< 40%, stress test was contraindicated. VO2peak is reduced in patients with HF due to the reduced pumping action of heart [25]. Reduced VO2peak in HF patients clinically as diminished capacity to work/exercise [26]. VO2peak is derived from Cahalin's formula, using the results of 6MWT, as stated below [25].

Mean Peak VO ml/kg/min = 4.948 + 0.023 x Mean 6 MWD (meters)

Where: 6MWD is 6 minute walk distance measured by 6 minute walk test (6MWT).

A 6MWT result >300 meter and VO2peak >12 has been found to be associated with better survival long term, in patients with HF [27]. In the present study we found that, both 6MWT was more than 400 meters and VO2peak more than 14 points, which signifies better prognosis, thus reducing risk of mortality in patients of HF. Increased BMI, and abdominal girth are associated with increased morbidity and mortality in HF patients. Significant reduction in BMI and abdominal girth after 90th day of HFRT, indicates favorable prognosis in terms of reduction of risk of mortality in patients of HF.[28] Although, significant positive findings were obtained in the present study, further such studies need to be done on a larger scale, probably a prospective head to head comparative clinical trial, so as to generalize the findings of present study to larger population.

6. Conclusions

We observed significant improvement in VO2peak, 6MWT coupled with reduction in body weight, BMI; HFRT offers a promising candidature for consideration as potent therapeutic option for treatment of elderly males of HF with reduced EF.

7. Acknowledgments

Author thanks to Dr Jagdish Hiremath, Chair Professor of Madhavbaug Institute of Preventive Cardiology, Chair of Maharashtra University of Health Science, Nashik for guiding us through this concept and data analysis.

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