

## **EFFICACY OF HEART FAILURE REVERSAL THERAPY (HFRT) PROGRAM IN PATIENTS WITH PRESERVE EJECTION FRACTION: AN OBSERVATIONAL STUDY**

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### **ABSTRACT**

Heart failure with preserved ejection fraction (HFpEF) is a worldwide healthcare issue showing growing prevalence, with complex management algorithms. Heart failure reversal therapy (HFRT) is a combination of *Panchakarma* and allied therapies used by *Ayurveda* physicians for CHF patients. This observational study was done to evaluate HFRT in HFpEF patients. Study was conducted between January 2017 to December 2017. The data of HFpEF patients who had been administered HFRT with minimum 7 sittings over 90 days ( $\pm 15$  days) were considered. VO<sub>2</sub>max, metabolic equivalent (MET), body mass index (BMI), blood pressure (BP), dependency on conventional therapy were compared on day1 and 90. 28 patients were enrolled (21 males, 7 females) with a mean age of  $55.79 \pm 9.83$  years. On analysis, there was significant improvement in mean VO<sub>2</sub>max ( $18.16 \pm 5.71$  vs  $31.85 \pm 4.80$  ml/kg/min,  $p < 0.01$ ) and mean MET ( $5.19 \pm 1.63$  vs  $9.10 \pm 1.37$ ,  $p < 0.01$ ) of the patients on day 90, when compared to day 1. Mean BMI ( $27.01 \pm 3.98$  kg/m<sup>2</sup> vs  $25.69 \pm 3.21$  kg/m<sup>2</sup>,  $p < 0.01$ ) and mean SBP ( $129.64 \pm 15.36$  vs  $118.79 \pm 9.69$  mm Hg,  $p < 0.01$ ) were decreased after 90-day HFRT therapy. Dependency on medications was also reduced.

To conclude, HFRT is effective in managing HFpEF patients and also decreases the dependency on allopathic medications.

**KEYWORDS:** Heart Failure Reversal Therapy, HFRT, *Panchakarma*, Chronic Heart Failure, Preserved Ejection Fraction, *Ayurveda*, Alternative medicine

### **INTRODUCTION**

According to the World Health Organization, cardiovascular diseases (CVDs) have become the leading cause of mortality and morbidity worldwide, and amongst all ethnic population, it is assumed that Indians are majorly affected.<sup>1</sup> CVD affects Indian

population in their most productive midlife years and at least a decade earlier as compared with the people of European ancestry.<sup>2</sup> In India, 52% of CVD deaths occur prior to the age of 70 years; in Western population it is as low as 23%. There is an increase in the occurrence of CVD cases worldwide, and it shows an

annual increase rate of 0.5-1.8 million in India. Amongst the many CVDs affecting the population, chronic heart failure (CHF) is a major health concern due to the enormous number of people being affected by it. Prolonged life expectancy and progressive aging of the population have led to the rising prevalence of CHF.<sup>3</sup> 26 million people are estimated to be affected by CHF worldwide.<sup>4</sup> In India, it is estimated that 1.3 and 4.6 million people are affected by CHF, which roughly means a prevalence of 0.12–0.44 %, although this may be an underestimated number.<sup>5</sup> CHF is classified into two major types based on the functional status of the heart: heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF).<sup>6</sup> Dunlay et al. have stated that approximately 50% of patients with CHF have HFpEF.<sup>7</sup> The prevalence of HFpEF was greater than that of HFrEF with the former being more prevalent in women, while the latter being higher in men. HFpEF could be dominant in driving the overall CHF prevalence as the incidence of HFpEF is increasing at a higher frequency, and it is expected that by 2020, 65% of patients hospitalized for CHF will have HFpEF.<sup>8</sup> The condition is challenging to tackle because of multiple mechanisms being proposed which are hypothetical. Experimental models mimicking the disease are lacking and patients of HFpEF also suffer from other co-morbidities like hypertension and metabolic syndrome.<sup>9</sup> Campbell et al. have compared outcomes in HFpEF with patients of similar sex distribution, co-

morbidities and age that were enrolled in trials of diabetes mellitus, angina pectoris, hypertension and atrial fibrillation, and concluded that patients in the HFpEF trials were at higher risk of death and at strikingly higher risk of HF hospitalizations.<sup>10</sup>

The standard management of CHF includes use of pharmacological agents like angiotensin receptor blockers (ARBs), beta blockers, angiotensin converting enzyme (ACE) inhibitors, antiplatelets, diuretics and vasodilators.<sup>11</sup> However, majority of CHF patients require elaborate management due to co-morbidities, multiple medications, growing age, reduced coping skills and depression.<sup>12</sup> CHF has poor prognosis despite improvement in therapeutic devices and drugs.

Considering these exigencies, there is a requirement and need for newer, cost-effective treatment modalities that will reduce the fear and anxiety of the patient and improve their quality of life. This search has brought researchers to the doorstep of alternative medicine.

Ayurvedic physicians recommend using conventional drugs in the acute disease phase while in the chronic stage of heart failure, use of *Panchakarma* therapy (a 5-step process for providing internal body purification) as an add-on for providing the best possible benefit to the patient.<sup>12</sup> Heart failure reversal therapy (HFRT), previously known as *Sampurna Hruday Shudhikaran* (SHS) therapy, is a combination of herbal treatment with *Panchakarma* and allied therapies. The

techniques used in *Panchakarma* are<sup>12</sup>: *Snehana* (External oleation), *Swedana* (Passive heat therapy), *Hridaydhara* (Concoction dripping treatment) and *Basti* (per rectal drug administration), which are known to get rid of toxins from the body. However, there is a lack of evidence which supports the use of this promising treatment modality, especially in patients suffering from HFpEF. Hence, we planned a study to evaluate the efficacy of HFRT program in a CHF patient having preserved ejection fraction. The efficacy of HFRT program was evaluated by using various variables like VO<sub>2</sub> max, metabolic equivalent (MET), systolic and diastolic blood pressure (SBP, DBP), body mass index (BMI), and reduction in concomitant medication intake.

### MATERIALS AND METHODS

This was an observational study conducted between January 2017 to December 2017.

We identified the data of patients who had visited the *Madhavbaug* clinics in Maharashtra, suffering from CHF but having an ejection fraction of more than 40 and the METS value of less than 8. The data of patients who had been administered HFRT with minimum 7 sittings over a span of 90 days ( $\pm$  15 days) were considered for the study. Cases were identified, and data was assessed from the medical records of *Madhavbaug* clinics in Maharashtra. 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 co-morbidities, if any, was also noted down.

The HFRT is a combination of *Panchakarma* and allied therapies. HFRT uses various decoctions and oils and constitutes of a 4-step procedure, as described below in table 1.

| 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>Dashamoola</i> and 5 grams <i>V.negundo</i><br>[100 ml extract processed in sesame oil] | 30-35 minutes   |
| <i>Swedana</i>     | Passive heat therapy  | <i>Dashmoola</i> (group of ten herbal roots) with steam at $\leq$ 40 degrees Celsius)   | 10-15 minutes + 3-4 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>       | Medicated enema administered per-rectal, should be in body for $\geq$           | 1.88 grams <i>T. arjuna</i> , 0.42 grams <i>B. diffusa</i> and 0.18 grams <i>A. calamus</i>                                     | 10 minutes  |

|                                   |                         |  |
|-----------------------------------|-------------------------|--|
| 15 minutes for maximum absorption | [10 ml aqueous extract] |  |
|-----------------------------------|-------------------------|--|

On day 1 of HFRT, the patients underwent Cardiac stress testing by Modified Bruce Protocol.<sup>19</sup> Their maximum work load was evaluated in terms of metabolic equivalents (METs) which represents a modest, practical, and easily understood technique for stating the energy cost of physical activities as a multiple of the resting metabolic rate.<sup>13</sup> This MET was multiplied by 3.5 to give peak VO<sub>2</sub> max, which is nothing but the maximal aerobic capacity (MAC). This process was repeated on day 90 of HFRT to calculate VO<sub>2</sub> max. The other baseline and day-90 data which were considered retrospectively by investigators for statistical analysis included the BMI, SBP, DBP and the conventional treatment information. The BMI for day 1 and day 90 of the patients was evaluated by checking the weight and the height from the medical data records of patients and using the formula: *weight in kilograms/(height in meters)<sup>2</sup>*. Likewise, the baseline and the day 90 readings of SBP as well as the DBP were noted down from the medical records of the patients in the study. The dependency on standard medications was calculated both on

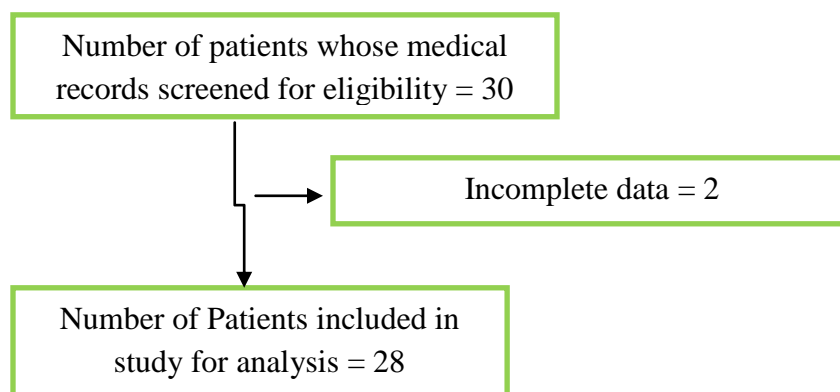
day 1 as well as day 90 of HFRT, and the change in the medicine intake pattern was assessed.

Data was entered and coded in Microsoft Excel spreadsheet. R Version 3.4.1 software was used to analyze the data. Categorical data were represented in the numeric form and continuous data were presented as the mean ± SD. The paired t-test was used to assess the difference between baseline values and 90<sup>th</sup> day after the treatment and graphs were used to represent the assessed parameters.

### RESULTS

A total of 30 patients' data was screened for inclusion in the study. However, based on the availability of complete data and the inclusion criteria, 28 patients were selected, and their data were analyzed. Figure 1 gives the screening process of patients. The majority of the enrolled patients were males (75%), with the mean age being 55.79 ± 9.83 years. The mean ejection fraction (EF) of the patients was noted (57.32 ± 8.58) which was in the normal range. Table 2 gives the baseline demographic details of the patients enrolled.

**Figure 1: Patient Enrolment Flow Chart**



**Table 2: Baseline characteristics of the study participants**

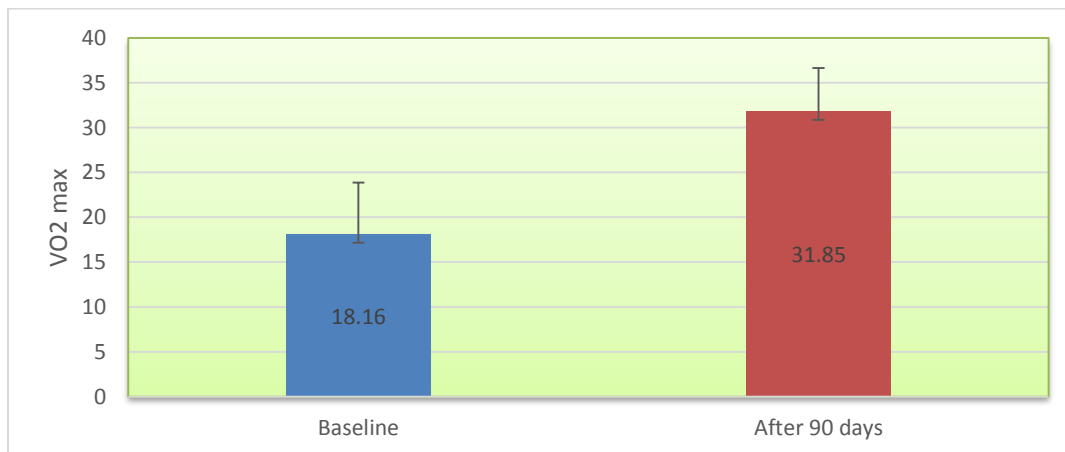
| Variable              | N = 28       |
|-----------------------|--------------|
| Age (years)           | 55.79 ± 9.83 |
| Ejection Fraction (%) | 57.32 ± 8.58 |
| <b>Gender</b>         |              |
| Male                  | 21 (75)      |
| Female                | 7 (25)       |

Results are expressed in mean ± SD and N(%)

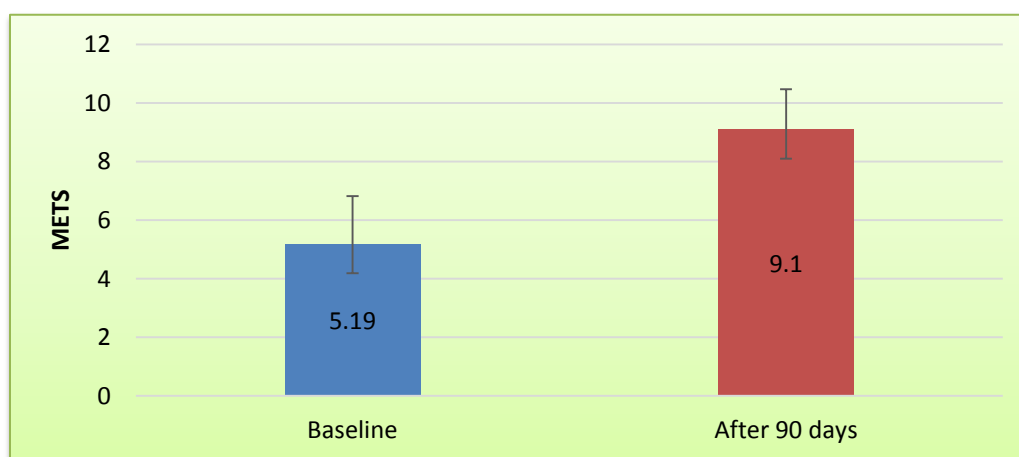
The VO<sub>2</sub> max of the patients, based on a treadmill test, was significantly increased after 90 days (p<0.01), with the mean difference being 13.69 ml/kg.min. (Table 3, Figure 2)

The maximum workload signified by metabolic equivalents (METS) increased significantly after day 90, as compared to mean day 1 values (p<0.01), with the increase being by a mean value of 3.91 units. (Table 3, Figure 3)

**Figure 2: Comparison of VO<sub>2</sub> max between baseline values and 90<sup>th</sup> day (N = 28)**

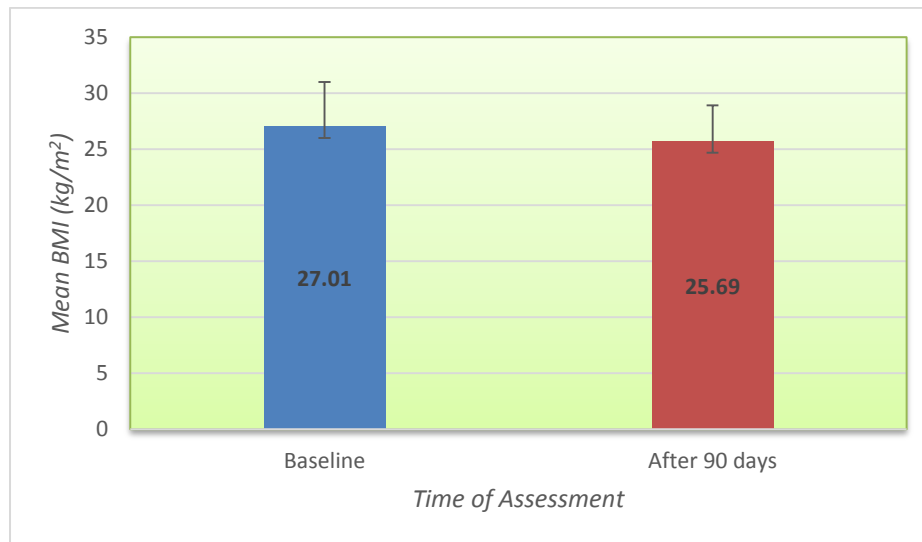


**Figure 3: Comparison of METS between baseline values and 90<sup>th</sup> day (N = 28)**



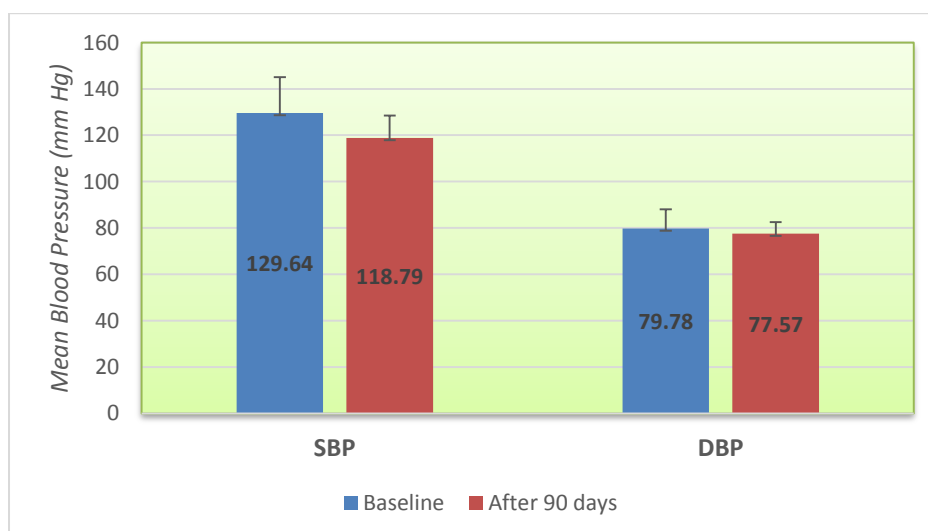
We noted a significant improvement in the mean BMI of the patients on day 90, when compared to that on day 1 ( $p < 0.01$ ). The decrease in the mean BMI was by a margin of  $1.32 \text{ kg/m}^2$ . (Table 3, figure 4)

**Figure 4: Comparison of Body Mass Index between baseline values and 90<sup>th</sup> day (N = 28)**



The mean SBP also decreased significantly on day 90 when compared to that on day 1, the mean difference being of 10.86 mm Hg ( $p < 0.01$ ). The DBP also decreased on day 90, by a mean margin of 2.21 mm Hg, but this decrease was not statistically significant ( $p = 0.18$ ). (Table 3, Figure 5)

**Figure 5: Comparison of SBP, DBP between baseline values and 90th day (N = 28)**



**Table 3: Comparison of Clinical parameters between baseline values and 90<sup>th</sup> day of the treatment by HFRT**

| Variable            | Baseline (Day 1) | After 90 days | Difference | p-value |
|---------------------|------------------|---------------|------------|---------|
| VO <sub>2</sub> Max | 18.16 ± 5.71     | 31.85 ± 4.80  | 13.69      | <0.001  |
| METs                | 5.19 ± 1.63      | 9.10 ± 1.37   | 3.91       | <0.001  |
| BMI                 | 27.01 ± 3.98     | 25.69 ± 3.21  | 1.32       | <0.001  |
| SBP                 | 129.64 ± 15.36   | 118.79 ± 9.69 | 10.86      | <0.001  |
| DBP                 | 79.78 ± 8.24     | 77.57 ± 5.00  | 2.214      | 0.184   |

*BMI, Body Mass Index; SBP, Systolic blood pressure, DBP, Diastolic blood pressure; maximal oxygen uptake; METS: Maximum Work Load*

We calculated the consumption of allopathic medications on day 1 and day 90 of HFRT. Most of the participants were treated with statins (46.43 %), angiotensin II receptor blockers (35.71 %), beta blockers (28.57 %), antiplatelet agents (21.43 %) and nonsteroidal anti-inflammatory drugs (25 %). After 90 days of HFRT, the participants

dependent on statins (28.57 %), calcium channel blockers (3.57 %), beta blockers (25 %), antiplatelet (14.29 %) and angiotensin II receptor blockers (28.57%) were reduced. The percentage of patients not on any conventional medication increased from 10.71% on day 1 of HFRT to 17.86% on day 90 of HFRT. Table 4 gives a tabular representation of consumption of conventional medications in our study.

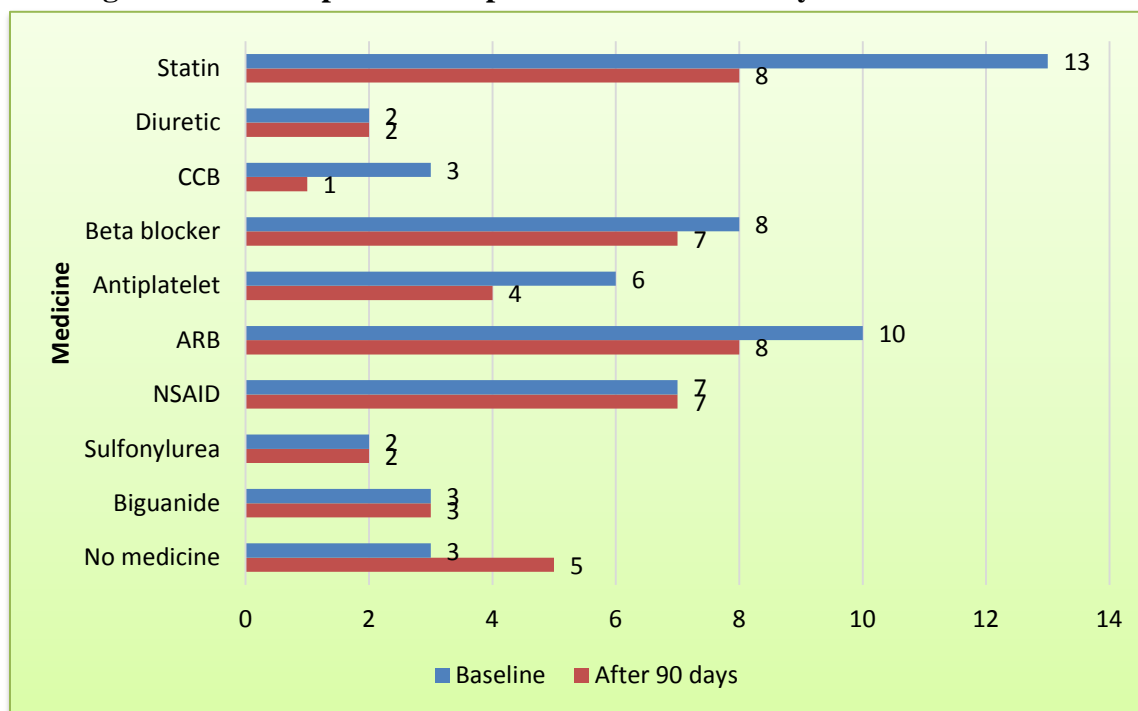
**Table 4: Consumption of allopathic medicines on days 1 and 90 of HFRT**

| Medicine     | Baseline   | After 90 days |
|--------------|------------|---------------|
| Statin       | 13 (46.43) | 8 (28.57)     |
| Diuretic     | 2 (7.14)   | 2 (7.14)      |
| CCB          | 3 (10.71)  | 1 (3.57)      |
| Beta blocker | 8 (28.57)  | 7 (25)        |
| Antiplatelet | 6 (21.43)  | 4 (14.29)     |
| ARB          | 10 (35.71) | 8 (28.57)     |
| NSAID        | 7 (25)     | 7 (25)        |
| Sulfonylurea | 2 (7.14)   | 2 (7.14)      |
| Biguanide    | 3 (10.71)  | 3 (10.71)     |
| No medicine  | 3 (10.71)  | 5 (17.86)     |

*NSAID: Nonsteroidal anti-inflammatory drugs; ARB: Angiotensin II receptor blockers; CCB: Calcium channel blockers*



**Figure 6: Consumption of allopathic medicines on days 1 and 90 of HFRT**



## DISCUSSION

CHF is one of the most common cause of CVD, and one of the most common causes of death worldwide. HFpEF is one of the two functional types of CHF and has overtaken the other type (HFrEF) according to multiple prevalence studies. The risk factors for HFpEF are multiple, and there is no known prevention strategy other than the management of the risk factors which include hypertension, diabetes and obesity. The prevention as well as early treatment strategies (which is early revascularization) seem to be effective in decreasing the risk and severity of acute myocardial infarction. The conventional drugs used for the management of CHF include beta blockers which have been found to have anti-oxidant and anti-inflammatory properties. Many herbal drugs have been known to have these properties and hence, *Ayurveda* seems to be

a feasible alternative option for research in patients suffering from CHF. *Ayurveda* physicians utilize *Panchakarma* therapy as an add-on therapy for treatment of CHF and HFRT is a combination of *Panchakarma* with allied therapies.<sup>14</sup> Therefore, we evaluated the effect of HFRT in patients of CHF having preserved ejection fraction. We found that the VO<sub>2</sub> max, which is nothing but the maximal aerobic capacity (MAC), was significantly improved after 90 days of HFRT therapy. We also found that the maximum workload, signified by metabolic equivalents (METS), augmented significantly after 90 days of HFRT. The BMI and SBP were also significantly decreased in the patients after 90-day HFRT, signalling a positive response on the risk factors of CHF, viz. obesity and hypertension. The dependency of patients on multiple concomitant medications like



statins, beta blockers and ARBs decreased significantly after HFRT, leading to less chances of adverse effects in these patients which result from polypharmacy.

Functional capacity is the ability of a person to perform his routine activities involving physical exertion. VO<sub>2</sub>max, also known as maximal aerobic capacity, signifies the maximum rate of oxygen consumption measured during incremental exercise. It is the most widely accepted marker of aerobic fitness<sup>15</sup> a compromise or decrease in the VO<sub>2</sub> max indicates a decrease in the cardiorespiratory function. In our study, the VO<sub>2</sub>max was found to be significantly increased at the end of 90 days, thereby indicating an improvement in the patient's exercise capacity.

A metabolic equivalent (MET) is the resting metabolic rate and signifies the amount of oxygen which is consumed at rest. In exercise testing, as the exercise intensity is gradually increased, the increase in intensity from stage to stage is normally about 1 to 2 METS, or even more, in normal individuals. However, the increase is small in functionally compromised individuals, like those with CHF. It represents the energy expenditure of physical activities as a multiple of resting metabolic rate. In our study, the METs were significantly improved in the patients after 90 days of HFRT, signifying an improvement in the exercise capacity of all the patients.

BMI is considered as a crucial indicator of a sedentary lifestyle as well as impending or prevalent obesity. CHF patients having a high BMI are at greater risk of mortality.<sup>16,17</sup>

Hypertension is a known risk factor for CHF

development and modifies the prognosis. Hence, approaches have been developed to deliver sustained blood pressure control in patients suffering from HTN, to prevent CHF.<sup>18</sup>

Management of HFpEF is complex, and the main aim of managing this type of CHF is treatment of the various risks or aggravating factors associated with it, like obesity and HTN.<sup>19</sup> HFRT comprises of *Snehana* (External oleation or massage), *Swedana* (Passive heat therapy), *Hridayadhara* (Decoction dripping therapy) and *Basti* (Per rectal drug administration) which seem to act in cohesion to improve the parameters in CHF patients. In cases of heart failure, as in normal individuals, the increase in the work load proportionately increases the oxygen consumption of the left ventricle. The work of the heart though fails to rise proportionately. This leads to a disproportionate increase in aerobic energy uptake and thus, a fall in left ventricular efficiency occurs.<sup>20</sup> Therefore, there is a need to maintain the oxygen demand of the failing heart, especially in HFpEF where there is diastolic dysfunction and ultimate systolic function as well. It has been theorized that *Snehana* may be reducing the sympathetic activity, ultimately leading to reduction in the vascular tone and increase in the vasodilator reserve. *Swedana* leads to increase in sweating which may cause peripheral vasodilation and thus, a decrease in the systemic vascular resistance. This will cause reduction in the afterload, decrease the cardiac work load and hence, reduce myocardial oxygen demand. A rise of body temperature due to passive heating

suggestively increases the cutaneous vascular conductance which leads to an equivalent elevation in systemic conductance.<sup>21</sup> *Hridaydhara* will lead to relaxation of the patient both mentally and physically, which may have a beneficial effect on the BP of the patient. Research has shown that pro-inflammatory conditions may also increase the chances of causing diastolic dysfunction, as seen in HFpEF.<sup>22</sup> According to a research involving obese patients, *Basti* moderated immune responses by regulating pro-inflammatory cytokines, immunoglobulins and functional properties of T-cells. These changes are related to a decrease in the body weight, which is sustained even after three months of treatment<sup>23</sup> this finding may explain the beneficial effect of *Basti* in patients with HFpEF.

Present study has a few limitations. Study was carried over a period of 90 days, so long-term effects still need to be studied. A bigger sample size covering multiple centres will also help generate more evidence.

### CONCLUSION

HFRT showed promise as a treatment modality for the management of patients of HFpEF. HFRT significantly improved VO2 max and METs along with a significant reduction in the SBP and BMI. HFRT also reduced the dependency of patients on standard concomitant medications.

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