patients in India. Further, we initiated to test the efficacy of this validated yoga program in rehabilitation of post MI patients with left ventricular dysfunction in India in a larger randomized control trial.

The implications of this study are broad and comprehensive. Firstly, compared to the conventional exercises, yoga, besides being effortless, offers minimum risk for the patients (Mehta, Mehta, & Pai, 2017). Secondly, if incorporated into the rehabilitation program, better prognosis for cardiac patients may be anticipated (Longfellow, 1993; Pischke, Scherwitz, Weidner, & Ornish, 2008). Thirdly, it helps reduce chronic health-related anxiety and depression (Gard, Noggle, Park, Vago, & Wilson, 2014).

The limitations of the current study are the fact that there is no direct correlation with heart failure symptoms in traditional yoga texts and that most benefits indicated are purely interpretations. Most of the studies focusing on the physiological responses to various practices of yoga have been demonstrated on the healthy participants and similar effects are assumed in the patient population.

The module, if demonstrated to be effective by clinical studies, may add a safe and well-accepted therapeutic option in the rehabilitation of cardiac patients following MI, which can further be applied in the hospitals and at the community level.

The yoga module thus developed was incorporated into the cardiac rehabilitation program of the patients suffering from left ventricular dysfunction following acute MI in a randomized control trial, the methodology of which is described in the following section.

5.0 METHODS

5.1 PARTICIPANTS

5.1.1 SAMPLE SIZE

G*power version 3.1.3 (Faul, Erdfelder, Lang, & Buchner, 2007) was used to calculate the sample size based on the results of a previous study.(Hari Krishna et al., 2014) A priori computation of the required sample size with a probability error alpha= 0.05, for a power of 0.8 yielded a result of 48 as the total sample size with 24 in each group. Anticipating dropout, we recruited an additional 20 percent so that our sample constituted a total of 66 patients.

5.1.2 SELECTION AND SOURCE OF PARTICIPANTS

The study was conducted between 2015-2017 at Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bangalore, Karnataka, India.

5.1.3 INCLUSION CRITERIA

The study was open to adults of both genders (age30-65 years) who were able to consent for themselves (presumed from completion of the consent form). Patients were included if they had (1) Recent MI on conservative medical management- without involving any revascularization procedures like Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Grafting (CABG) [10 days to 2 months post-MI] (2) Left ventricular dysfunction [New York Heart Association (NYHA) classes I and II] (3) LVEF between 30% and 50%.

5.1.4 EXCLUSION CRITERIA

Patients were excluded if (1) they had LVEF < 30% (2) Class III and IV heart failure (3) unstable cardiac symptoms like angina (4) recurrent ischemia (5) concurrent pulmonary disease like COPD (6) uncontrolled arrhythmia (7) severe musculoskeletal disease like osteoarthritis restraining the patient to perform yoga (8) hypertension (a systolic blood pressure of >160 mm Hg or a diastolic blood pressure of >100 mm Hg) (9) valvular heart disease and (10) patients with hematologic, renal, or hepatic dysfunction.

5.1.5 ETHICAL CONSIDERATION

The study was cleared by the institutional ethics committees of Swami Vivekananda Yoga Anusandhana Samsthana (SVYASA) University, Bangalore as well as Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bangalore, India. The trial was registered with the Central Trial Registry of India (CTRI/2015/02/005563). Written informed consent was obtained from all participants at the time of enrollment.

5.2 DESIGN OF THE STUDY

This study is a randomized control trial involving two groups, namely Yoga group and Control group. The participants were randomly assigned to either of the groups.

Randomization

Randomization was stratified by two groups- control and yoga. The participants were randomly assigned to either of the groups at 1:1 ratio. The sequential sampling method was adopted, wherein, an interim analysis was done after reaching the determined sample size a-priory (16 in each group) with the power of the sample size of 80 and based on the results, additional participants were recruited so as to acquire the adequate power of the study. The allocation was determined based on minimization using the software MinimPy (Saghaei, 2011) with the following randomization parameters: Biased coin minimization probability method, Marginal balance distance measure, and 0.7 Base probability. The baseline characteristics of the study population are given in Table 1. The cardiac sonographer, laboratory staff, and the subjects were blinded to the group. The analyst performed the randomization using MinimPy 0.3 and the group status was written in a concealed slip of paper and this was directed to the cardiac patient through yoga therapists.

5.3 VARIABLES STUDIED

Demographic data, including age, sex, education, employment status, marital status, socioeconomic status (SES), and ethnicity were recorded. Cardiac measures: LVEF was assessed to evaluate the cardiac function using standard Trans Thoracic Echocardiography (TTE), which is the imaging of choice recommended for the measurement of LVEF (Amiel et al., 2012; Raghuram et al., 2014). The assessment of the QOL of the participants was performed using the Duke Activity Status Index (DASI) (Storti et al., 2011). DASI is a valid and reliable self-administered functional capacity tool that measures the performance of a set of 12 common activities of daily living under four major activity domains. Metabolic equivalents (METs) were derived from DASI scores (George, Kasbekar, Bhagawati, Hall, & Buscombe, 2011; Vibulchai, Thanasilp, Preechawong, & Broome, 2014). Biochemical measures: The total plasma triglycerides (Tg), cholesterol, Low-Density Lipoproteins (LDL) and High-Density Lipoproteins (HDL) were assessed using the shotgun technique (Fernandez et al., 2013). Psychosocial measures: Anxiety and depression were assessed using the Hamilton Anxiety Rating Scale (HAM-A) and Cardiac Depression Scale (CDS) respectively. Data on all outcome measures were collected at the baseline and on completion of 12 weeks.

Testing the feasibility, utility, and reliability of administering CDS and HAM-A in the context of Indian culture.

The Cardiac Depression Scale (CDS) was developed in Melbourne, Australia, keeping in mind the drawbacks of the previous scales with respect to the cardiac patients. It is the only scale developed based on responses from cardiac patients (Ski, Thompson, Hare, Stewart, & Watson, 2012). The CDS is a 26 item self administered questionnaire, in which the patient is expected to give a rating between 1 ('Strongly disagree') to 7 ('Strongly agree') on a seven

point Likert scale against each question. The innovators of this scale have taken steps to avoid fixed responses from the respondents by introducing positive as well as negative worded items at random intervals. The questionnaires are easily administered (taking ≈ 5 minutes to complete and one minute to score) with 95% sensitivity and 85% specificity in diagnosing major depression, as indexed using the Mini International Neuropsychiatric Interview while also detecting less severe depressive symptoms. Given that the scores from a symmetrical 'normal' distribution without skewness and with excellent kurtosis, it is possible to use raw scores and parametric statistics without any logarithmic transformation of data (Ski et al., 2012). However, the CDS questionnaire has not been validated for the psychometric testing among the Indian population with cardiovascular disease. This makes it important to test CDS and its psychometric properties in Indian population.

The Hamilton anxiety rating scale was developed in England by Max Hamilton and is one of the earliest scales to measure the severity of anxiety symptoms and is extensively used in the clinical and research domains till date. The HAM-A is often used as the primary outcome measure in case of Generalized Anxiety Disorder (GAD) and is often used in other disorders to rate the severity of anxiety symptoms (Katherine Shear et al., 2001).

The scale comprises of 14 items, each one of which is scored on a 5-point Likert scale where "0=not present" and "4=severe". The total score ranges between 0 and 56, with a score <17 indicating "mild severity", 18-24 indicating "mild to moderate severity" and scores between 25-30 indicating "moderate to severe" anxiety levels. The reliability and the concurrent validity of the HAM-A and its sub-scales was proved to be sufficient to be used in patient care and research(Wolfgang Maier, Philipp, & Heuser, 1998).

Inter-rater reliability has been reported as an Intra-class Correlation Coefficient of 0.74–0.96.

HAM-A correlates well with the Beck Anxiety Inventory. The scale is designed to measure both psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints related to anxiety) and has been translated into Cantonese, French and Spanish. This time-tested scale could be confidently implemented as an assessment tool by any trained research raters (Katherine Shear et al., 2001). Nevertheless, the items on HAM-A have not been validated for the psychometric testing of the Indian population with cardiovascular disease, making it an interesting area to investigate to decipher psychometric properties in Indian context.

This section of the study was executed with an intent of examining the cross-cultural validity, feasibility, utility and reliability of administering CDS and HAM-A in assessing the depressive symptoms and severity of anxiety respectively, among Indian patients with recent MI.

VALIDATION

The CDS and HAM-A questionnaires were administered on an individual basis to the patients in the hospital by trained health care professionals. The response of the patients were tabulated using Microsoft excel spreadsheet. The 26 depression items of the CDS were scored from 1 to 7. Items 2, 4, 12, 15, 19, 20, and 23 were reverse scored (1 = 7, 2 = 6, 3 = 5, 4 = 4 ,5 = 3, 6 = 2, 7 = 1) and the final score of each patient generated and consolidated (Fig. 27).

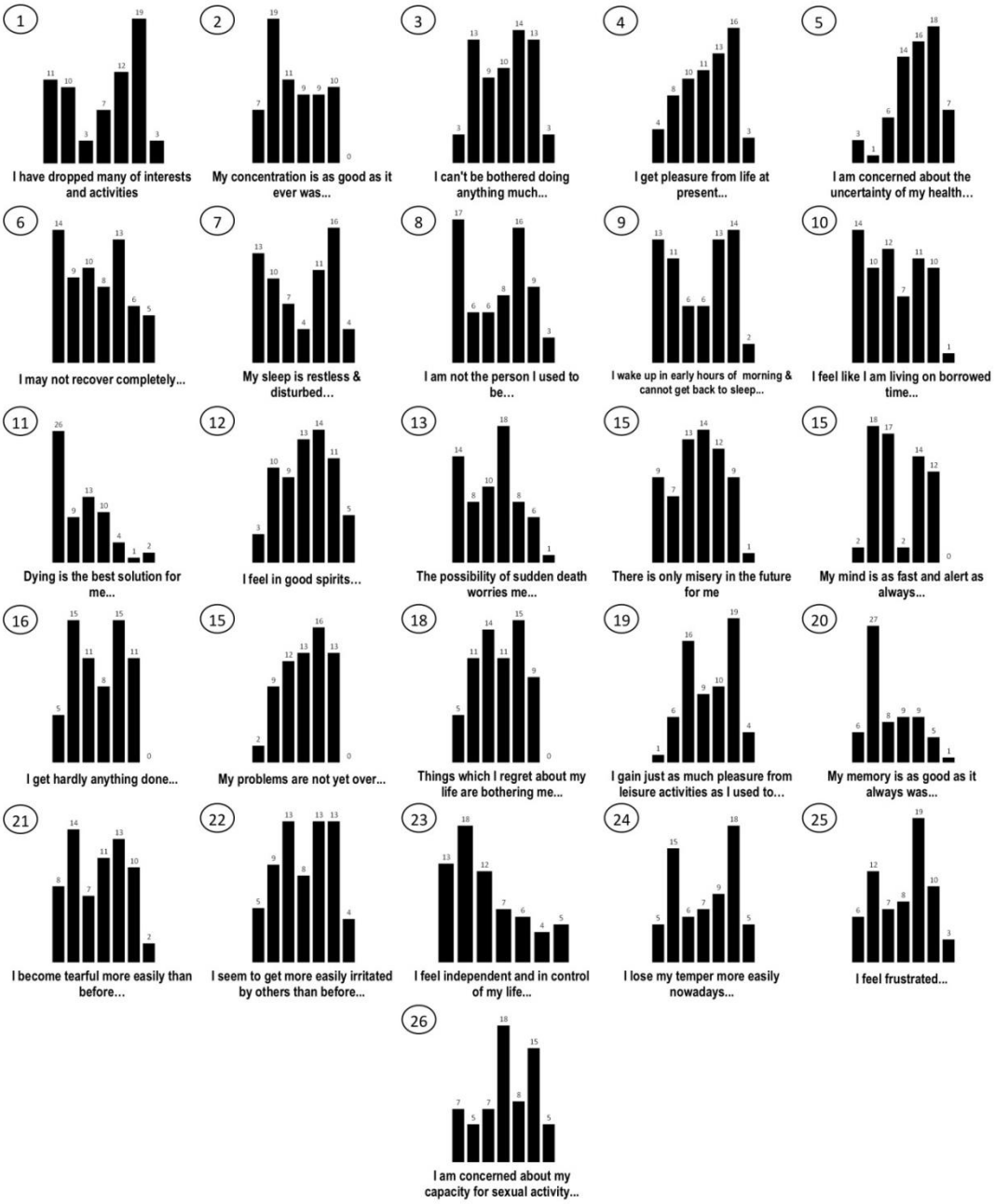

Figure 27: Patient scoring pattern- Cardiac Depression Scale

The 14 anxiety items of HAM-A were scored from 0 to 4 and the sum of all the 14 scores generated and documented (Fig. 28).

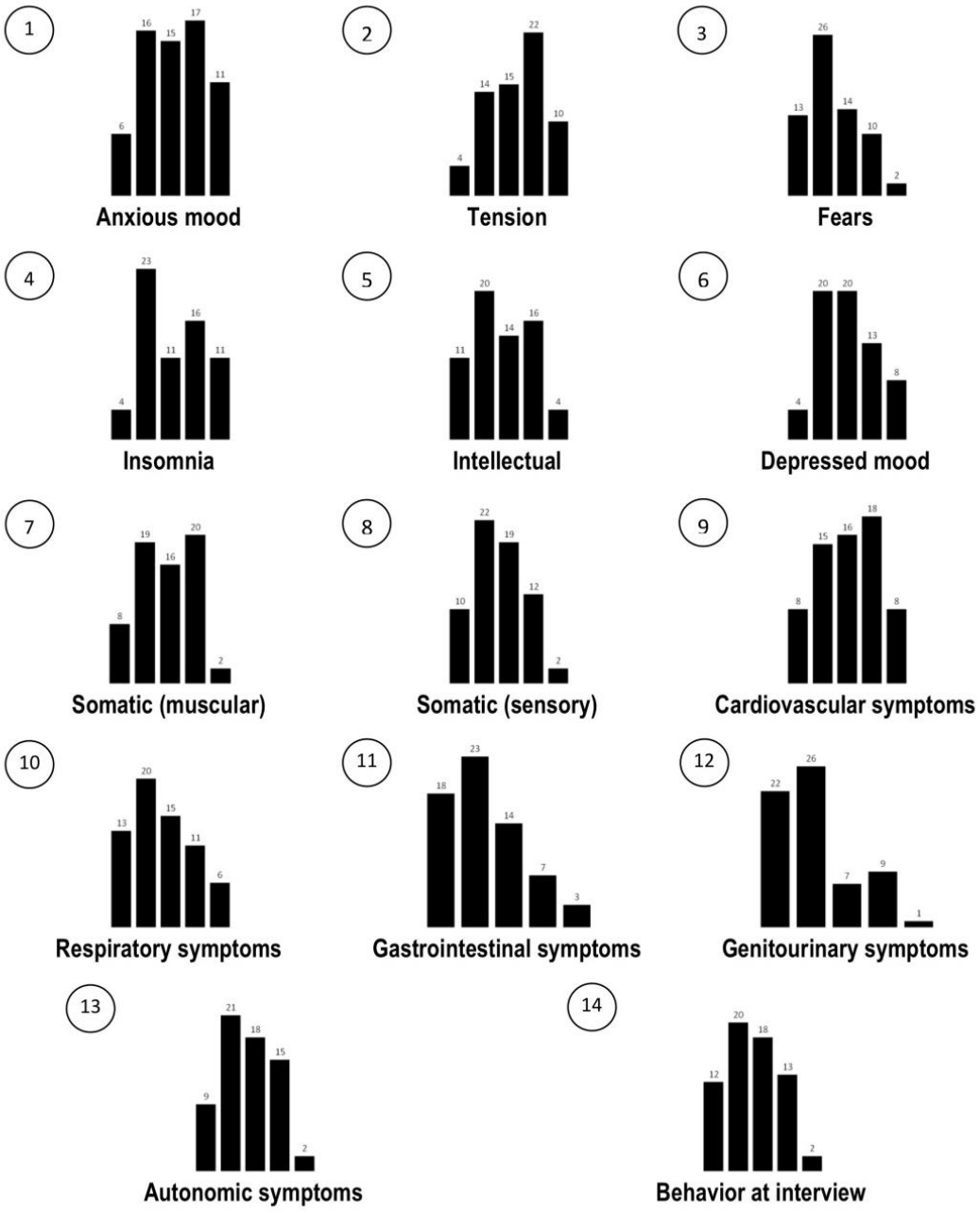

Figure 28: Patient scoring pattern- Hamilton Anxiety Rating Scale

ANALYSIS

Statistical analysis was performed using SPSS inter-rater reliability analysis. Cronbach alpha was estimated and reported.

FINDINGS

The average time taken in the administration of CDS and HAM-A were 10 minutes each. The elderly patients took significantly longer duration to complete the questionnaire as compared to their younger counterparts. To estimate the reliability of the CDS and HAM-A scale in the Indian participants Cronbach's alpha was calculated to measure internal consistency. There was high internal consistency for both CDS (Cronbach alpha = 0.93) (Table 7) and HAM-A (Cronbach alpha = 0.92) (Table 8).

		N	Mean	Variance	SD	
Statistics for Scale		26	98.32	719.972	26.832	
	Mean	**Minimum**	**Maximum**	**Range**	**Max/Min**	**Variance**
Item Means	3.782	2.508	4.862	2.354	1.939	.237
Item Variances	3.014	2.085	4.268	2.183	2.047	.361
Inter-Item Correlations	.334	-.270	.794	1.064	-2.938	.031
Item Total Statistics	Scale Mean If Item Deleted	Scale Variance If Item Deleted	Corrected Item total Correlation	Squared Multiple Correlation	Alpha If Item Deleted	
Q.1	94.28	659.391	.550	.526	.924	
Q.2	94.95	679.420	.441	.527	.926	
Q.3	94.25	675.407	.478	.507	.925	
Q.4	94.08	668.728	.562	.614	.924	

Q.5	93.46	679.190	.501	.450	.925
Q.6	94.78	654.453	.623	.690	.923
Q.7	94.49	653.504	.589	.784	.924
Q.8	94.72	652.328	.629	.646	.923
Q.9	94.63	658.987	.565	.787	.924
Q.10	94.94	652.746	.685	.797	.922
Q.11	95.82	663.278	.656	.652	.923
Q.12	94.12	666.172	.596	.748	.923
Q.13	95.02	669.297	.555	.658	.924
Q.14	94.65	653.763	.757	.777	.921
Q.15	94.65	668.420	.595	.700	.924
Q.16	94.62	665.740	.641	.609	.923
Q.17	94.23	660.899	.768	.783	.921
Q.18	94.60	661.650	.713	.730	.922
Q.19	93.88	664.891	.649	.641	.923
Q.20	95.22	667.140	.624	.691	.923
Q.21	94.63	676.674	.437	.487	.926
Q.22	94.25	674.438	.469	.694	.925
Q.23	95.22	673.640	.450	.543	.926
Q.24	94.18	669.309	.473	.766	.925
Q.25	94.34	663.852	.590	.709	.923
Q.26	94.09	724.366	-.079	.385	.933
			Alpha	**Standardized Item Alpha**	
Reliability Coefficients for 26 Items			.927	.929	

Table 7: Internal consistency- Cardiac Depression Scale

		N	Mean	Variance	SD	
Statistics for Scale		14	24.77	142.881	11.953	
	Mean	**Minimum**	**Maximum**	**Range**	**Max/Min**	**Variance**
Item Means	1.769	1.094	2.328	1.234	2.129	.126
Item Variances	1.313	1.095	1.562	.467	1.427	.029
Inter-Item Correlations	.522	.270	.839	.569	3.107	.010
Item Total Statistics	Scale Mean If Item Deleted	Scale Variance If Item Deleted	Corrected Item total Correlation	Squared Multiple Correlation	Alpha If Item Deleted	
Q.1	22.58	119.454	.803	.824	.931	
Q.2	22.44	122.440	.747	.757	.932	
Q.3	23.33	125.843	.664	.661	.935	
Q.4	22.64	124.551	.606	.507	.937	
Q.5	23.03	121.713	.746	.652	.932	
Q.6	22.73	124.166	.695	.683	.934	
Q.7	22.92	127.057	.588	.464	.937	
Q.8	23.14	125.043	.715	.656	.934	
Q.9	22.69	124.758	.615	.453	.936	
Q.10	32.11	119.274	.807	.751	.931	
Q.11	23.47	126.253	.601	.561	.937	
Q.12	23.67	124.605	.710	.711	.934	
Q.13	23.05	123.982	.752	.697	.932	
Q.14	23.16	123.816	.735	.737	.933	
			Alpha	**Standardized Item Alpha**		
Reliability Coefficients for 14 Items			.938	.939		

Table 8: Internal consistency- Hamilton Anxiety Rating Scale

We found that post MI, Indian subjects also demonstrated anxiety and depression which was well reflected by the CDS and HAM-A scores, validating that these scales are also applicable in Indian subjects, demonstrating the high flexibility and robustness of the scale. There were no complaints from the patients regarding the length of the interview or difficulty in understanding the majority of the questions included in the questionnaires.

Cardiac depression scale

The cardiac depression scale (CDS) constitutes of 26 multiple Likert questions in a questionnaire that forms a scale. With a minimum score of 26 and a maximum score of 182 and higher scores depicting more severe depressive symptoms, 67% of the patients scored between 75 and 125.

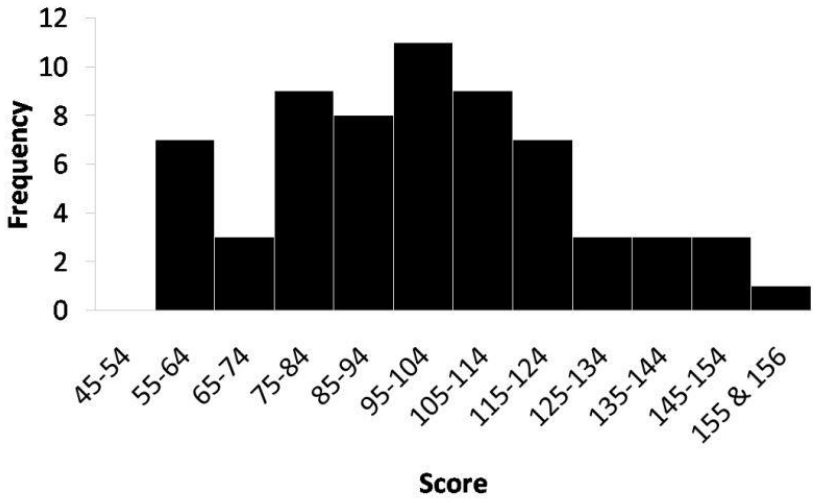

Figure 29: Histogram- Cardiac Depression Scale Questionnaire.

Additionally the CDS score distribution indicates the score frequency was between 95-104, indicating clinically significant depressive symptoms. Fifty percent patients demonstrated poor memory (Fig. 27, item #20), 46% reflected no independence (Fig. 27, item #23) and 39% indicated poor concentration (Fig. 27, item #2). On the other hand, 53% indicated that

dying was not the solution for them and 36% patients showed positivity towards life, proper sleep cycle and demonstrated overall positive quality of life (Fig. 27, item #8, #9, #10).

Hamilton Anxiety scale (HAM-A)

The HAM-A scale is composed of 14 questions. The distribution of the score as illustrated as a histogram in Figure 30 shows that the majority of the score was between 20-29 (Fig. 30). Out of the total of 66 patients, 22 of them scored <17 indicating mild severity, 12 patients scored between 18 and 24 indicating mild to moderate severity, 12 patients scored between 25 and 30, indicating moderate to severe and 20 patients scored >30 indicating severe form of anxiety.

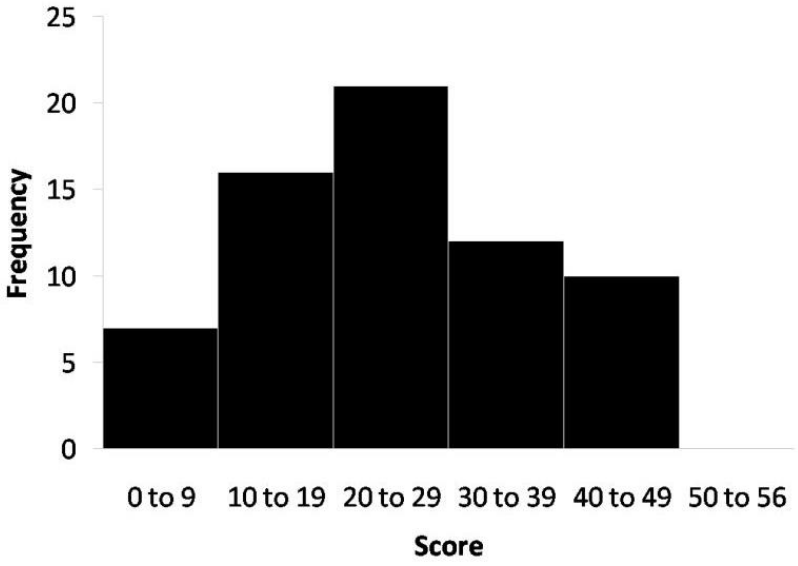

Figure 30: Histogram- Hamilton Anxiety scale (HAM-A)

Approximately 48% of the patients rated either 'severe' or 'very severe' for "**Tension**: Feelings of tension, fatigue, startle response, moved to tears easily, trembling, feelings of restlessness, inability to relax" (Fig. 28, item#2). Also, the majority of the responders rated 'severe' or 'very severe' for questions about Anxious mood (Fig. 28, item #1), insomnia (Fig.

28, item #4), and cardiovascular symptoms (Fig. 28, item #9). The items with a considerable percentage of patients rating 0 "Not present" were item numbers 12, 11, 10 and 3 i.e. questions related to 'gastro-urinary symptoms', 'gastrointestinal symptoms', 'respiratory symptoms' and that of 'fear' respectively (Fig. 28).

DELIBERATION

Scales such as the CDS and the HAM-A are beneficial for researchers across the globe in the screening of depression and anxiety respectively in the patient population. The majority of the scales similar to CDS and HAM-A are frequently developed in the western part of the world where the patterns of psychological problems and the response of the individual to such problems differs significantly from the other parts of the world, thereby challenging their cross-cultural adaptability.

Our experience during the interview process as well as the opinion of the respondents was suggestive of ease in the flow as well as consistency in response to the items on the CDS and HAM-A questionnaires without any confusion. The majority of the respondents had no complaints and when confusion arose, it was pertaining to specific items among a small number of respondents. Item numbers 3 and 16 of the CDS "I can't be bothered doing anything much..." and "I get hardly anything done..." respectively, were difficult to apprehend for the majority of the respondents, where the interviewers' intervention was required. The finding suggests that rephrasing and further validation of the scale would help minimize response bias. Similarly, in case of HAM-A, terminologies like 'frigidity' under Genitourinary symptoms, item number 12 as well as 'fidgeting' and 'furrowed brow' under behavior at interview, item number 14 is not frequently used terms in the Indian scenario. Item number 26 of CDS " I am concerned about my capacity for sexual activity..." as well as

item number 12 of HAM-A, speaking of the 'genitourinary symptoms' are likely to put the respondent through embarrassment since, such topics are considered very personal and less discussed readily in the Indian scenario except in cases where the health care professional has a good rapport with the patient and has gained his/her confidence as well.

Overall, there were no major problems encountered in the process of administration of either of the scales. These scales are designed to be comprehensive, brief, flexible, and appropriate for use in Indian clinical setting.

This study is a part of the randomized clinical trial, which aims to evaluate the efficacy of IAYT based cardiac rehabilitation program adjunct to conventional pharmacological management in the improvement of cardiac function and minimizing the symptoms of anxiety and depression in patients with left ventricular dysfunction following MI.

5.4 INTERVENTION

The participants were randomly assigned to two groups, namely, Group 1- yoga and Group 2- control. Compilation and expert validation of a yoga module for the purpose of the current RCT was performed(Sharma, Pailoor, Choudhary Ram, & Shrestha, 2019).

Yoga group

The yoga group received one hour supervised yoga module comprising of Asanas (physical postures), Pranayama (breathing techniques) and relaxation techniques thrice a week for a period of 12 weeks along with the standard pharmacological therapy prescribed for the condition. Certified yoga therapists with a minimum qualification of Masters of Science (M.Sc.) in yoga and a minimum experience of 3 years in the field of yoga conducted the sessions in the hospital yoga center under the supervision of senior yoga therapists/ cardiologists. The patients were encouraged to practice the same one hour yoga, as per the

module, at home during the other days of the week, for which, the participants were provided with handouts and a digital versatile disc (DVD) consisting of explanation and demonstration of the practices for their convenience. Participants were instructed to mark the days of their home practice in a diary.

Control group

The control group received standard care that included pharmacological treatment and the instructions of the cardiologist.

5.5 DATA EXTRACTION

- Baseline readings of all parameters were taken at the commencement of intervention.
- Interim reading was taken at 3 months.
- Final reading was taken at 6 months from the commencement date.
- Descriptive statistics were used to analyze the baseline data for demographic and outcome variables.
- Inferential statistical tests were chosen based on the distribution.
- Statistical software R version 3.1.1 and SPSS for Windows (version 17.0; SPSS, Chicago, IL, USA) were used for analysis purpose.

5.6 DATA ANALYSIS

All data used in this manuscript were tested for normal distribution. A histogram depicting the data distribution was plotted for the cardiac function (LVEF), psychological parameters (CDS, HAM-A), quality of life parameters (DASI, MET) and for the biochemical (LDL, HDL, Tg, Total Cholesterol, Ratio of HDL and Total Cholesterol) parameters. Both the raw and log-transformed data were plotted (Supplement Figure 1). Baseline comparison between control and yoga groups using Wilcoxon-Rank sum test were performed to identify any

baseline differences in the data. Data collection and analysis were performed using SPSS for Windows (version 17.0; SPSS, Chicago, IL, USA). All the tests were two-tailed and the significance threshold was $P = 0.05$.

6.0 RESULTS

A total of 867 subjects were screened, 233 met the selection criteria, of which 66 agreed to participate in the study (Fig. 31).

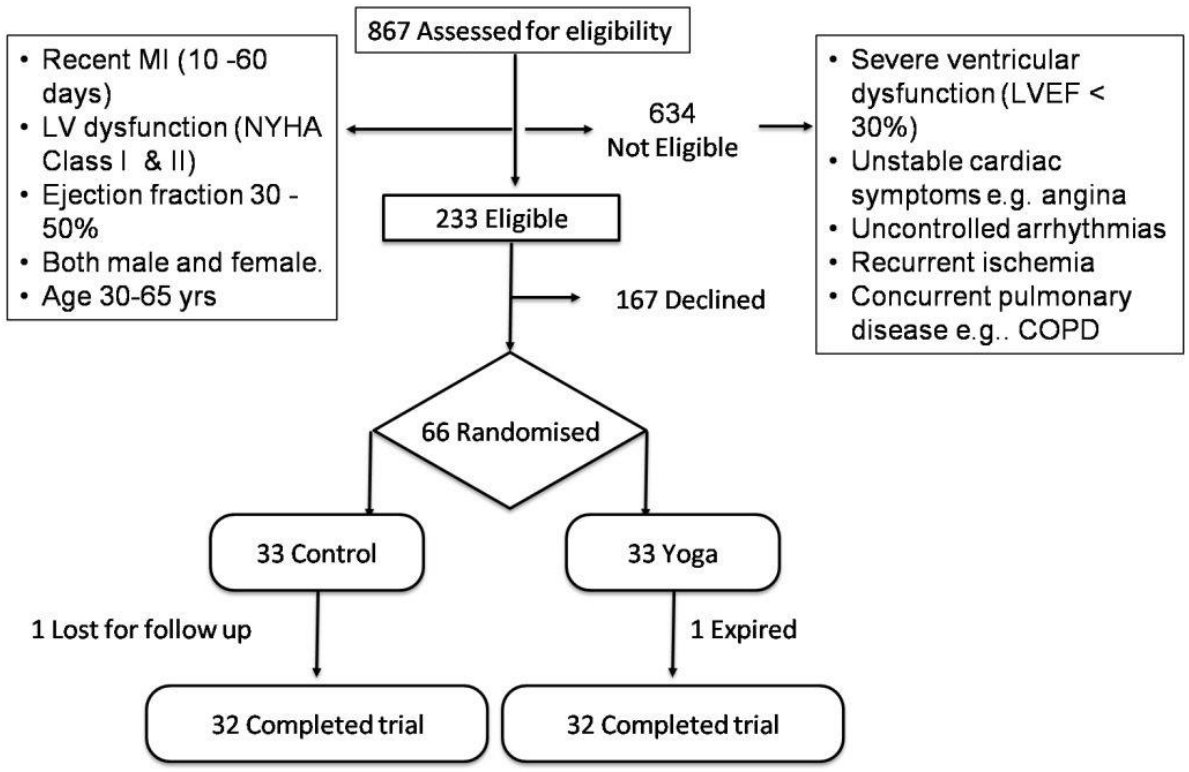

Figure 31: Flow chart illustrating study outline

Participants were 52.3 years old on average (SD = 9.9) and predominantly male (86.3%). These subjects were randomly allocated to control (n=33) and yoga (n=33) groups. Of these subjects, 32 were classified as Class II and 34 as Class I using