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RESEARCH ARTICLE

Understanding the Effect of Rajyog Meditation on Biomolecular and Behavioural Co-relates of Stress in Patients Undergoing Coronary Artery Bypass Graft Surgery

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ABSTRACT

Background: The role of psychological health in impacting the risk factors for heart disease is well recognized. Patients undergoing corrective surgery for Coronary Artery Disease undergo much anxiety and depression that negatively impact the overall health of the heart. Higher levels of biomarkers that promote atherosclerosis is frequently found in individuals with negative psychological health. Improving psychological health can lead to healthier surgical outcome. Various relaxation techniques including meditation are used to relax and reduce a person's stress and anxiety and are gaining importance in peri-operative stress management procedures.

Aim: It was the aim of present study to evaluate the role of Rajyog meditation in bringing down surgery related stress levels in patients undergoing Coronary Artery Bypass Grafting Surgery. This was sought to be achieved by measuring the variations in their circulating plasma endothelin-1 levels (molecular stress marker) after being imparted with relaxation therapy in the form of meditation followed by association analysis with subjective indicators of stress.

Design: Randomized controlled Trial

Setting: A total of 60 patients undergoing Coronary Artery Bypass Grafting Surgery, thirty each in non-intervention and intervention groups and fulfilling the inclusion criterion were enrolled in the study.

Intervention: Relaxation therapy in the form of Rajyoga Meditation was imparted for one month to patients only in the intervention group, before they underwent Coronary Artery Bypass Grafting Surgery.

Main outcome measures: Blood samples were collected before meditation, post-meditation/before surgery, post-meditation/after surgery and circulating plasma Endothelin-1 levels measured by sandwich ELISA. Clinical parameters were determined based on analysis of compiled questionnaires.

Results: The sleep quality improved and anxiety levels reduced after meditation (p = 0.002 and p= 0.005 respectively) in the intervention group as a whole. There was a drop in median plasma Endothelin-1 levels from 1.68 pg/ml to 1.38 pg/ml after meditation in the intervention group and a concomitant rise of median plasma Endothelin-1 levels from 1.0 pg/ml to 2.05 pg/ml in the non-intervention group.

Conclusions: The findings suggest that Rajyog meditation can bring about a beneficial difference in the subjective clinical parameters of patients and also a drop in plasma Endothelin-1 levels distinct from a rise in its levels in the non-intervention group.

Introduction

Amongst the various risk factors for CVD, Hypertension is a predominant causal factor and continues to be a major health concern[1]. Patients awaiting CABG undergo much fear and anxiety[2] and peri-operative stress management is important in bringing relief to the patient and determining the outcome of surgical procedures. Several relaxation techniques like yoga, exercises, music, deep breathing and meditation are being used for bringing relief from stress. Regular practice of Rajyog meditation- a relaxation technique, has been shown to have positive effects on cardiovascular physiology of healthy practitioners of meditation[3] [4]. Similar effects of transcendental meditation (TM) have been shown to subdue the sympathetic activity measured as reduced heart rate[5,6] In the area of cardiovascular diseases, reduction in stress response to relaxation techniques has focused on study of physiological parameters like lowering of blood pressure [7], heart rate[8] and breath rate[9] and body's response to hormones like norepinephrine[10]. Various humoral parameters, particularly plasma levels of oxidative stress markers have also been studied as indicators of stress[11]. Yet, pathophysiological mechanisms underlying emotional and behavioral stress leading to hypertension and CAD remain unclear.

In prevailing times of precision medicine, the study of biomarkers has gained attention because of their use in diagnosis, assessment of disease severity for risk-stratification of patients and as a guide in making clinical decisions and imparting treatments [12]. In this context, the study of stress biomolecules as predictors for risk of peri-operative cardiac complications becomes important. Endothelin -1 (ET-1), a potent 21 amino acid vasoactive peptide, has been reported to be associated with poor prognosis in congestive heart failure (CHF)[13]. Increased levels of ET-1 have also been reported to be specific and sensitive indicator of the patients with stress-induced acute coronary syndrome (ACS) [14]. In view of its role in cardiovascular functions, ET-1 receptor antagonists are widely being used in the treatment of cardiovascular diseases [15].

Subjective experience of the patient during clinical interrogation is usually inconsistent and is often considered to be a weak and partial correlate of the medical condition. A more reliable objective indicator of stress is required that would help in decision making in imparting suitable coping mechanisms to reduce the impact of stress in patients, both physically and psychologically. It was our hypothesis that plasma ET-1 levels (a plausible stress marker) may come down as a result of relaxation therapy in the form of meditation and this modulation of plasma ET-1 levels along with clinical co-relates of stress (sleep quality and anxiety) may serve as a reliable indicator of risk stratification of patients and pre-operative stress management in patients undergoing CABG. Accordingly, the objective of the study was to assess anxiety and sleep patterns in patients awaiting CABG before and after intervention in the form of Rajyog meditation before and after surgery, accompanied with measurement of circulating plasma endothelin levels as objective indicators of stress in the patients enrolled in the study.

In a study[16] on systematic evaluation of Endothelin-1 measurement in congestive heart failure patients (CHF) ET-1 was shown to be a unique predictor in HF prognosis, complementing a multi-marker profile in predicting risk to HF. Also, it was shown by serial measurement of ET-1 levels that those patients whose ET-1 levels decreased below a cut-off value over a period of time had better outcomes compared to patients whose ET-1 levels increased or remained stable[17]. In this study, we tried to assess the role of Rajyog meditation in lowering the circulating plasma ET-1 levels with the hope of bringing relief to the patients in facing surgical duress.

Based on available literature, the 2013 AHA scientific statement recommended only Transcendental Meditation among the various meditation practices for consideration in treatment plans for individuals with blood pressure greater than 120/80mm Hg [7]. The 2017 scientific statement by the American Heart Association on the potential benefits of meditation on cardiovascular risk could not draw any conclusions on the effectiveness of meditation on preventing heart disease but stated that meditation as an intervention may only be considered as an adjunct to guideline-directed cardiovascular risk reduction by those interested in lifestyle modification[18]. Estimation of CVD risk is the cornerstone of the 2021 guidelines of European Society of Cardiology[19] on CVD prevention in clinical practice and forms an important component of the proposed management schemes of the patients at risk.

The patients enrolled in this study already had established coronary artery disease and were undergoing corrective surgery for same. Long term resilience does come with regular practice of meditation, however, the goal in the present study was to understand the effect of Rajyog meditation in patients under distressful circumstance of much anxiety and uncertainty and a period of perceived or real crisis. Assessment of distress during the peri-operative phase is important and both subjective and objective measurements of stress may give a better indication of the relaxation achieved due to the imparted intervention in the form of Rajyog meditation.

Methods:

Study design: Randomized Controlled Trial

Selection of subjects: The cases included in this study included 60 adult patients undergoing routine coronary artery bypass grafting surgery (CABG) at the cardiothoracic science centre, All India Institute of Medical Sciences, New Delhi. Hospital Ethics Committee approval and written informed consent were taken for all the patients enrolled in the study. Patients on ventilator, ejection fraction of less than 30% (EF < 30%), pre-existing neuropsychological problem and patients with drug and alcohol abuse were excluded. The patients were randomly allocated between the intervention (study) and non-intervention (control) groups. The patients in the intervention (study) group were given relaxation therapy in the form of Rajyoga meditation after their primary check up in cardiothoracic surgical OPD while the patients in the non-intervention group were not given any relaxation therapy. The patients in the meditation group continued to practice meditation till the day of surgery (minimum of 30 days).

Intervention: Relaxation therapy in the form of Rajyoga Meditation was imparted to patients for a period of one-month in the meditation room by Brahmakumaris trained in the Art of Rajyog meditation and practicing it regularly as a part of their life. It is being observed as a holistic approach for preparing willing patients for surgery routinely at Cardio-Thoracic Centre, AIIMS[20]. Raja Yoga meditation incorporates guidelines about behaviour, physical posture and exercises for steadying the breath and ultimately the mind. The method of Raja Yoga was formally systematized in a collection of works - the Yoga Sutras, authored by Patanjali sometime between 200B.C. and 300A.D[21].

Scoring of Sleep pattern: The patients were categorized as good sleepers (+++), average sleepers (++) or poor sleepers (+).

Good Sleepers were those patients who failed to meet the criterion for difficulty in initiating and maintaining sleep (DIMS) and those who met the following requirements: (i) subjective sleep difficulty score below the mid-point of the 10 point scale; (ii) subjective sleep distress score of 3 or lower on a 10 point scale and (iii) no use of sleep medication.

Poor sleepers were those patients who met the criterion used for DIMS as well as in whom subjective rating of sleep difficulty above the midpoint of a 10-point scale. [22], [23], [24], [25].
The individuals who had the element of both poor sleepers and good sleepers were designated as average sleepers.

Scoring of Anxiety pattern: One clinical researcher without any prior knowledge of patient response conducted a questionnaire-based interview of anxiety on subjects enrolled in the study. The questions asked were like: "Do you feel tense and wound up? Do you worry a lot? Do you have panic attacks? Do you feel something awful is about to happen?" Each question was answered by the patient on a 4 point (0-3) response category, so that the possible scores ranged from 0-21, for anxiety. We considered a score of 0-3 as no anxiety (-), 4-7 as mild anxiety (+), 8-10 as moderate anxiety (++) and ≥ 11 as clinically relevant anxiety (+++) [26] [27].

Estimation of Plasma Endothelin levels: Patient Blood plasma was separated from EDTA treated

blood by centrifuging at 1500 x g for 15 min at R.T. 1ml of plasma from each patient sample was lyophilized and stored at -80°C until the time of assay. Estimation of plasma endothelin-1 levels was carried out according to manufacturer's instructions by an immunometric acetyl cholinesterase based – double antibody, sandwich ELISA kit (Cayman Chemical Co, MI, USA; catalog no. 583151) with a limit of detection of1.5 pg/ml.

Statistical Analysis: Data were presented as frequency (%) for categorical variables and mean (SD) or median (min-max) for continuous variables. The baseline categorical variables were compared between the groups using Chi-square test/Fisher's exact test and continuous variables were compared using unpaired t-test. The difference in plasma endothelin levels between the groups was tested using Wilcoxon signed rank sum test and within a group using Wilcoxon signed rank test. Wherever, the measured endothelin levels were > 0 but < 1pg/ml a value of 1pg/ml was taken for graphical representation and calculating the statistical significance of the differences observed. Sleep quality and anxiety scores were compared between two groups using χ^2 test/ Fisher's exact test. P-value ≤ 0.05 was considered statistically significant. The Stata 15.0 (StataCorp LP, Texas, USA) for Analysis was used.

Results:

Clinical dataset: After screening 78 patients undergoing checkups for elective CABG surgery as mentioned in methods, 60 were selected for the present study (**Figure 1**). The study group (n=30) and control group (n=30) of patients were comparable with respect to demographics & clinical profile. The statistical test applied for calculation of p-values for determining the significance of differences observed in the clinical parameters between the study and control groups is indicated in Table 1. Both the groups showed a greater incidence of Coronary Artery Disease (CAD) in males with the overall percentage of men and women enrolled in both groups being similar. The majority of the patients suffering from CAD belonged to the middle-income group and the group with good socio-economic status, the two economic strata together accounting for 73%-82% of the total number of patients enrolled in each group. The distribution of co-morbid factors, smoking (p=0.358), alcohol consumption (p=0.143) and association with non-vegetarian diet (p=0.381) was also comparable in the two groups. The difference in occurrence of high-risk factors, Hypertension (p=0.791) and Diabetes mellitus (p=0.083) between the two groups was also statistically insignificant (**Table-1**).

Figure 1: CONSORT flow diagram for randomized, controlled trial of intervention in the form of Rajyog Meditation in patients undergoing Coronary Artery Bypass Grafting Surgery.

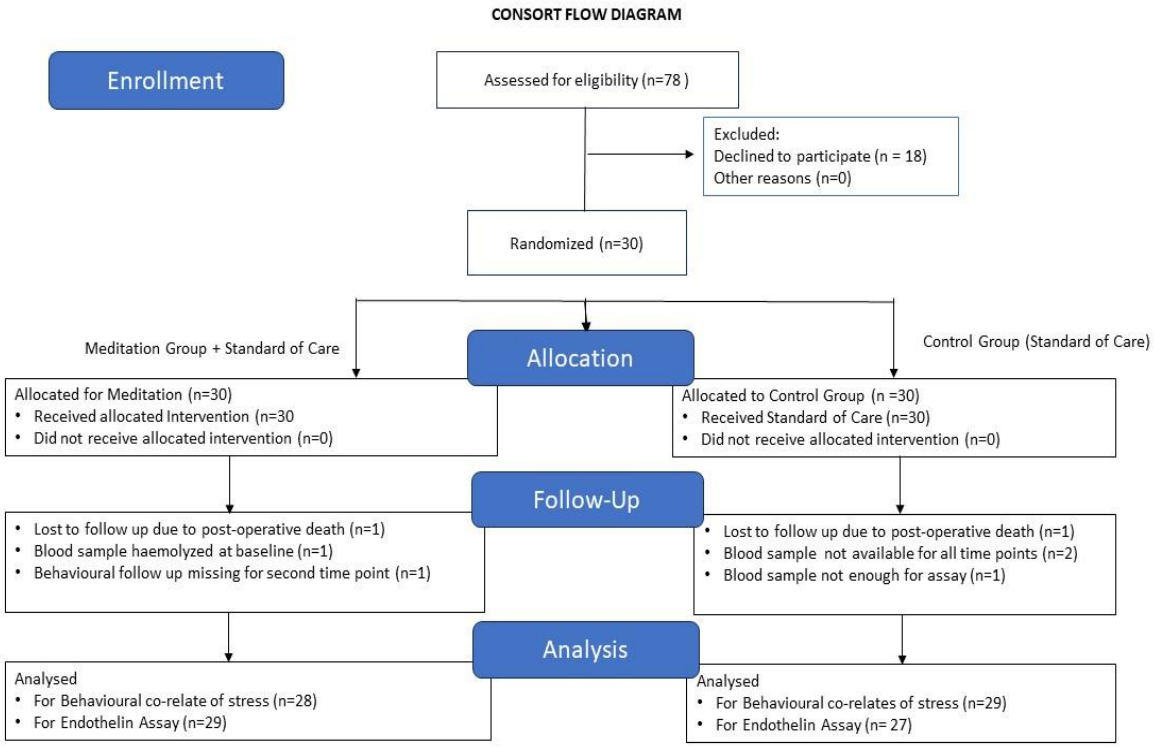

Table I: Baseline characteristics of patients enrolled in the study group (n=30) and control group (n=30).

Baseline Characteristics	Study Group (n=30)	ControlGroup (n=30)	*p*
Age Distribution			
Mean Age (yrs)	55.9 ± 9.4	58.9 ± 7.3	0.1833
Sex Distribution			
Females	3 (10%)	1 (03.3%)	
Males	27 (90%)	29(96.7%)	0.612
Consumption Habits			
Smoking	10 (34.5%)	13 (46.4%)	0.358
Alcohol Consumption	2 (7.1%)	6 (22.2%)	0.143
Non-Vegetarian Diet	21 (72.4%)	23 (82.1%)	0.381
Physical Activity			
Nil	1 (3.7%)	1 (3.7%)	
Mild	17 (63%)	11 (40.7%)	
Moderate	4 (14.8%)	3 (11.1%)	
Good	5 (18.5%)	12 (44.4%)	0.188
Socio-Economic status			
Poor	1 (3.33%)	2 (7.14%)	
Lower Middle	7 (23.33%)	3 (10.71%)	
Middle	12 (40%)	14 (50%)	
Good	10 (33.33%)	9 (32.14%)	0.599
Occurrence of Hypertension	12 (41.4%)	11 (36.7%)	0.791
Occurrence of Diabetes mellitus	16 (55.2%)	9 (31.0 %)	0.083

Plasma Endothelin levels: Circulating plasma endothelin levels in the two groups were measured before meditation/before surgery (baseline), post-meditation/before surgery (follow-up1) and post meditation/ after surgery (follow-up 2). **Table 2** shows the number of patients (n) whose circulating plasma endothelin levels were measured in respective groups.

Table 2: Circulating Plasma Endothelin levels (pg/ml) in patients belonging to the Meditation and Control Groups

	Meditation group		Control group		p-Value b/w groups
	n	Median(P_{25}-P_{75}) pg/ml	n	Median (P_{25}-P_{75}) pg/ml	
Baseline	29	1.68(1-2.73)	29	1(1-4.03)	0.2008
follow-up 1 **p value[a]**	29	1.38(1-2.86) **0.991**	27	2.05(1-4.36) **0.686**	0.9664
follow-up 2 **p Value [b]**	29	2.08(1-4.96) **0.551**	27	1.1(1-3.93) **0.615**	0.229

p-value[a] indicates comparison between baseline ET-1 levels and the circulating ET-1 levels measured before surgery after meditation within each group.
p-value[b] indicates comparison between baseline ET-1 levels and the circulating ET-1 levels measured after surgery within each group.

A wide variation was observed in plasma ET-1 levels of both intervention and non-intervention groups at different time-points with the maximum observed values being 16.17 pg/ml in the intervention group and 17.04 pg/ml in the control group. The median values for plasma ET-1 levels as shown in **Table 2** were only marginally higher than the reported values of ≤ 1pg/ml for healthy subjects. These differences in plasma ET-1 levels between different time points, within the two groups, as well as between the two groups was statistically not significant.

CLINICAL CO-RELATES OF STRESS:

Practicing Rajyoga improved Sleep Quality: In the clinical setting, patients' sleep quality was

assessed by an established questionnaire at the time the patient was initiated into the relaxation therapy (Baseline), a day before surgery (Follow-up1) and a day after surgery (Follow-up 2) in the study group. In the intervention group of patients imparted with relaxation therapy in the form of Rajyog mediatation, the percent number of individuals who shifted to the (+++) scoring group of sleep quality before and after meditation is shown in **Table 3.** Before meditation only 20% of the individuals scored a +++ in sleep quality, whereas, after meditation this percentage went up to 55.17%. This quantum jump in percentage number of patients with a Good quality of sleep was statistically significant with $p \leq 0.002$ (**Table 3a**) as was the drop in the percentage of patients with (+) and (++) score. Further, the percentage of good sleepers in the study group increased from 55.17% to 62.07 % after surgery and in the control group from 23.33% to 62.07 %. This increase in percentage of good sleepers after surgery was statistically significant ($p = 0.011 \leq 0.05$) only in the control group and not in the study group (follow-up1 vs follow up-2 p-value $= 0.15 \geq 0.05$). **Table 3** shows the percent of poor sleepers, average sleepers and good sleepers in the intervention and non-intervention groups at different time-points. It is clear from the table that the percentage of good sleepers (23.33%) in the control group before surgery was lower as compared to the poor sleepers (40%) and average sleepers (36.67 %) and this percentage of good sleepers increased to 62.07% after surgery. The sleep quality of patients falling in the category of good sleepers (+++) increased from 20% to 55.17% after meditation (before surgery) and to 62.07% after surgery in the intervention group. This increase in percentage of good sleepers from follow-up1 to follow-up2 time points in the intervention group was statistically insignificant ($p \leq 0.15$). At the time of initiation, before-meditation/ before-surgery and at the time after-meditation/after-surgery there was no significant difference {$p \leq 0.406$ and $p \leq 0.675$ in the overall sleep quality of patients in the two groups. However, the sleep quality between the intervention and non-intervention groups was significantly ($p=0.021$) different post-meditation before surgery. For the control group without meditation the improvement in sleep quality observed is due to surgical outcome only.

Table 3: Comparison of Sleep Quality observed between the groups (Control and meditation) at different time points before surgery and after surgery.

	Meditation group		Control group*		
Sleep Quality	**N**	**n (%)**	**N**	**n (%)**	**Pr-Value**
Baseline	30		30		0.406
Good		6, (20.00)		7 (23.33)	
Average		16 (53.33)		11 (36.67)	
Poor		8 (26.67)		12 (40)	
Follow-up1	29		*		-
Good		16 (55.17)	-	-	
Average		9 (31.03)	-	-	
Poor		4 (13.79)	-	-	
Follow-up2	29		29		0.675
Good		18 (62.07)		18 (62.07)	
Average		8 (27.59)		6 (20.69)	
Poor		3 (10.34)		5 (17.24)	

Table 3a: Comparison of sleep quality within each group as indicated by p-values

	Meditation group	Control group
Baseline vs Follow-up 1	0.002	*
Baseline vs Follow-up 2	0.003	0.011

***For the control group sleep quality was assumed to be stable as per the personality type of the individual at the time of initiation and before surgery since no meditation was imparted to the control group of patients.**

Anxiety Pattern among patients was assessed simultaneously with sleep quality at the time the patient was enrolled for the study, a day before the surgery and a day after the surgery in both the groups and only the patients in the study group were imparted relaxation therapy after initial assessment of behavioral patterns. **Table 4** shows that at the time of initiation the prevalence of

anxiety patterns was similar in both the study and control groups with the percentage of patients scoring severe anxiety being 36.67% and 43.33%, those scoring moderate anxiety being 23.33% and 16.6% and those reporting no anxiety being 40% each in the study and control groups respectively.

None of the patients had an anxiety level ≥ 11. The difference in the anxiety levels between the study and control groups was statistically non-significant at the time of initiation ($p = 0.779$) and a day after surgery ($p=0.372$) but on the day before surgery the difference between the anxiety patterns of the two groups was significant ($p=0.026 \leq 0.05$). A day before the surgery, in the intervention group the overall relief in anxiety among patients was reflected in a higher percentage (72.41%) of patients scoring a (-) compared to 40 % in the control group. Seventeen individuals (57%) in the meditation group did not show any change in the anxiety pattern. In the remaining 13 patients (43%) who did reflect a change in anxiety levels, number of patients where a score of (++) became (+) was 3; where a score of (++) became (-) it was 3; and where the score reduced from (+) became (-) the number of patients was 6.

Table 4: Comparison of Anxiety levels observed between the groups (Control and meditation) at different time points before surgery and after surgery

Anxiety	Meditation		Control		Pr-Value
	N (total)	n (%)	N (total)	n (%)	
Baseline	30		30		0.779
Nil-Mild		12 (40)		12, (40)	
Moderate		7 (23.33)		5 (16.6)	
Severe		11 (36.67)		13 (43.33)	
Follow-up 1	29		-	-	-
Nil-Mild		21 (72.41)	-	-	-
Moderate		4 (13.79)	-	-	-
Severe		4 (13.79)	-	-	-
Follow-up 2	29				0.372
Nil-Mild		27 (93.10)	29	24 (82.76)	
Moderate		1 (3.45)	29	4 (13.79)	
Severe		1 (3.45)	29	1 (3.45)	

In the meditation group Baseline vs Follow up1 p-value ≤ 0.007 and Baseline vs Follow-up 2 the p-value ≤ 0.0007. For the control group without meditation the decrease in anxiety observed is the relief due to surgical procedure only and the baseline vs Follow up2 p-value ≤ 0.005.

Discussion

The present study sought to understand the scope of meditation in peri-operative patient management systems, whether relaxation technique in the form of meditation can bring relief to patients undergoing much stress and anxiety of the corrective coronary artery bypass grafting surgery. What is it that meditation does to bring relief from stress? Can perception/anticipation of stress during a surgical procedure be soothed and an ensuing emergency reaction be prevented by a counter relaxation response by practice of Rajyog meditation? Can a short course in Rajyog meditation prior to surgery modulate stress biomolecules and is there any co-relation of these markers with behavioural indicators of stress? These questions both from basic science and clinics served as triggers for our study that was challenging.

For long various research groups have focused on different types of meditative practices to find an answer. Dr Wallace [28] described a wakeful hypometabolic physiological state that resulted from the practice of Transcendental Meditation. This state during which the EEG shows an increased alpha and an occasional theta-wave activity is different from sleep and hypnosis. The restful state that resulted from the regular practice of Transcendental Meditation widely known as the Relaxation Response[29] was accompanied by decreased sympathetic nervous system activity and an increased intensity and frequency of EEG alpha and theta waves. The beneficial effects of meditation in cardiovascular risk reduction and on psychological and physiological responses to stress have been reviewed by Levine G.N[30]. What emerges is that the regions of brain that are engaged during meditation are those that regulate attention and emotion[31] and that there is a neural plasticity in different regions of the brain.

A causal role of meditation in altering brain morphology was observed by voxel-based morphometric comparison of brain scans of practitioners of Rajyog meditation with non-practitioners of meditation. The altered brain structure was reflected in higher global gray matter volume and enhanced positive thoughts in individuals practicing Rajyog meditation[32].

Three aspects of the current study in patients undergoing CABG surgery are a) elevated plasma endothelin levels; b) disturbed sleep and increased anxiety and c) role of rajyog meditation in bringing down ET-1 levels and in bringing relief from disturbed sleep and increased anxiety in patients awaiting surgery.

Several studies have pointed towards a positive co-relation between increased plasma endothelin-1 concentration and cardiovascular disorders[33-41]. Venous plasma endothelin concentration in CABG before surgery has been reported to be 1.16 pg/ml and increased levels (1.71 pg/ml) after sternotomy [42]. In the present study all the subjects whether in the intervention group or non-intervention group were suffering from coronary artery disease and had mean plasma ET-1 levels slightly higher than the reported normal values. The intervention group and non-intervention group as a whole did not show significant variation in the mean plasma endothelin-levels. There was a wide variation in individual plasma ET-1 levels that were higher than <1pg/ml (normal values) at different time-points before and after meditation and before surgery/post-meditation and after surgery/post meditation. Within the meditation group there was a noticeable trend in a drop in median values of plasma endothelin levels after meditation before surgery from 1.68 pg/ml to 1.38 pg/ml. In contrast, in the non-intervention group the trend was towards an increase in median values of plasma endothelin levels from 1.0 pg/ml to 2.05 pg/ml presumably due to a rise in anxiety levels with the approach of date of surgery. These trends in plasma ET-1 values are suggestive of an association with anxiety levels of the patient and need to be investigated further. One patient in the study group who showed a high ET- 1 level of 16.17 pg /ml before surgery - before meditation showed a concomitantly high ET-1 level of 12.18pg /ml after meditation- before surgery and 6.05 pg/ml of ET-1 after meditation- after surgery. The drop in ET-1 levels at this high level of expression in this patient tempts us to draw conclusion about the positive effect of meditation and surgical procedures in bringing stress relief to the patient. However, a large number of data labels were below the acceptable sensitivity range of the assay. Due to the low circulating levels and short plasma half-life[37,43, 26, 29] the measurement of plasma ET-1 levels is difficult. Endothelin-1 is a very potent vasoconstrictor [4430] and extremely low levels of ET-1 can produce a sustained constriction for half an hour. While, this quantity of ET-1 may make it very potent and efficient in the discharge of its function in the body, the low range of occurrence of many data labels limits the inference one can draw about the stressful /relaxed condition of the patients. Earlier studies[14 9] showed a co-relation between stress-induced ACS and increased inflammatory status, associated with enhanced ET-1 release. However, their report was limited by the lack of data pertaining to ET- 1 levels prior to stress exposure. In its present form our data is limited by low circulating levels of plasma ET-1 and assay sensitivity and it would be pre-mature to drop circulating plasma ET-1 levels as an indicator of stress. Moreover, given the subtlety of meditation practice, it is our surmise that for the technique to be effective at the molecular level, one needs to be highly motivated and should be practicing the art as a daily routine. In other words, the response of subjects enrolled in study is dependent upon quality of meditation practice imbibed by the patient and individual personality variations.

Sleep quality is affected by a number of medical and psychological factors. In the present study, 26.67% of the enrolled subjects in the intervention group and 40% of the subjects in the non-intervention group were poor sleepers with a score of (+). There was a significant improvement in the sleep quality of patients after meditation with the percent of good sleepers reaching upto 55.17% after meditation from a small 20% before meditation before surgery. In the non-intervention group in the absence of meditation, the sleep quality of patients was assumed to be stable as per the personality type of the individual. However, 53.33% of the individuals did not show any change in sleep pattern. This result is in accord with research findings that suggest sleep disturbance to be a multifactorial process that has many co-relates persisting from pre-surgical period throughout recovery. After surgery, there was a marginal increase from 55.17% to 62.07 % of individual shifting to the (+++) category of good-sleepers in the study group and a significant jump from 23.33% to 62.07% of good sleepers in the control group. The improvement in the sleep quality of subjects in the control group may be explained partially due to a successful surgery [4531] and partially due to lingering effects of general anaesthesia, plus side effects of pain killers. The

good sleep quality brought about by mediatation before surgery may prepare the patient better to undertake the rigours of surgical procedures both mentally and physically and may be able to cope better with the postoperative pain and decreased mobility.

Pre-operative anxiety in patients awaiting surgery has been assessed and reported in a wide body of literature against a backdrop of surgical procedures. Stress and anxiety has also been reported in patients with coronary artery disease[2,46, 1, 32] and with adverse cardiovascular outcomes[47]. However, the findings related to anxiety as a risk factor for CVD are conflicting[48]. It is assumed that endothelial damage resulting from excessive activation of hypothalamic-pituitary-adrenal axis and sympathetic nervous system with increased release of plasma catecholamines eventually leads to the development of CAD[49]. It is this hyperactivity of the sympathetic nervous system and the hypothalamic -pituitary-adrenal axis that is believed to be downmodulated by the practice of meditation with beneficial effects and in reducing negative behavioral activity. At the time of enrollment 36.67% of the patients in the study group and 43.33% in the control group demonstrated an anxiety score of (++). This percentage was similar to the percentage of patients (40% each in study and control groups) who reported no anxiety at the same time point. There was a significant difference ($p=0.026 \leq 0.05$) in the anxiety levels of patients between the study and control groups after meditation and before surgery. The percentage of patients with nil anxiety score (-) rose upto 72.41% from 40 % after meditation in the study group. The differential of 32% who transited into the (-) score included patients from both (++) and (+) anxiety score. This is indicative of the beneficial effect of the relaxation technique in bringing down the anxiety levels in patients with mild and moderate anxiety levels in pre-operative phase. Since the study did not have any patient with clinically relevant anxiety (+++), no inference can be deduced about the effect of meditation on this group of patients. In the post-operative period the percent of individuals with (++) and (+) anxiety levels went down drastically and those with nil anxiety levels increased to 93.10% in the study group and 82.76% in the control group. There was no significant difference in the absolute numbers of patients with a (-) anxiety score between the study and control groups after surgery. However, within each group the difference was remarkable ($p = 0.0007$ for study group and $p = 0.005$ for control group) before and after surgery. These p-values of tests of significance are suggestive of the complementary role of meditation to routine surgical procedures in bringing psychological and emotional relief to patients. An earlier study [50,33] had reported that patients who were taught self-hypnosis relaxation techniques were significantly more relaxed postoperatively compared to the control group. They demonstrated the role of self-hypnoses relaxation techniques on patients undergoing coronary artery bypass surgery. In our study we did not have this limitation since behavioral co-relates were assessed before meditation/ before surgery, post meditation/ before surgery and post meditation/ post-surgery. Statistical analysis of subjective indicators of stress did show clear differences in sleep quality and anxiety levels that could be clearly attributed to the practice of meditation as distinct from the difference in these parameters attributable to successful surgical procedure.

Conclusions

Interest in various forms of relaxation techniques is being renewed for their beneficial effects in relieving stress and mental tension. Age old practices like meditation can bring about a host of physiological changes in an individual and the art of meditation is gaining popularity in peri-operative stress management in bringing relief to the patient.

Our results indicated an overall positive effect of meditation on sleep quality and reduced anxiety levels in patients undergoing CABG even though some patients showed stable behavioral patterns. The plasma endothelin levels also varied greatly between individuals. However, there was no significant difference in the ET-1 levels between the group of patients who were imparted relaxation therapy in the form of meditation and those who did not receive any training in the art of Rajyog meditation. For the effect of the meditation practice to be reflected at the molecular level, we believe that a long term, regular practice in the art is required. A short-term training of one month as was followed in our study is insufficient to produce any stable changes at the molecular level.

Our studies showed a significant improvement in sleep quality and a positive relief in anxiety that could be attributed to relaxation brought about by meditation. With the current data set it is difficult to draw any co-relation in the apparent difference observed between plasma ET-1 levels and the clinical co-relates of stress. There is however, a positive trend in increased endothelin levels with increased anxiety levels a day before the surgery. The source of Rajyog meditation – the

Yog *Sutras*-compiled by sage Patanjali almost 2000 years ago -illustrate the essence of Rajyog meditation in the second *sutra* in Sanskrit as follows: *yogas chitta vritti nirodhah* (योगश्चित्तवृत्तिनिरोधः) meaning practicing yoga allows for the calming and restraint of a fluctuating mind. Since, Rajyog meditation is a spiritual discipline, it is tempting to surmise that regular practice and integration into the lifestyle of an individual would be more efficacious in stress-coping abilities of individuals and especially among patients undergoing CABG.

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Abbreviations

ACS – Acute Coronary Syndrome; **CAD**- Coronary Artery Disease; **CABG**- Coronary Artery Bypass Grafting Surgery; **CHF**- Congestive Heart Failure; **CVD**- Cardiovascular Disease; **DIMS**- Disorders of initiating and maintaining sleep; **EEG**- Electro encephalogram; **EF**- Ejection Fraction; **ELISA** – Enzyme Linked Immunosorbent Assay; **ET-1** - Endothelin-1; **HF**-Heart Failure; **TM**-Transcendental Meditation.

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