Original Article

Effect of Yoga-Based Cardiac Rehabilitation Program on Endothelial Function, Oxidative Stress, and Inflammatory Markers in Acute Myocardial Infarction: A Randomized Controlled Trial

Satish Gurunathrao Patil[1,2], Edmin Christa Sobitharaj[3,4], Ambalam Mahendrakumar Chandrasekaran[4], Shankar S. Patil[5], Kalpana Singh[6], Ruby Gupta[7], Kishore Kumar Deepak[8], Ashok Kumar Jaryal[3], Dinu Santha Chandran[3], Sanjay Kinra[9], Ambuj Roy[10], Dorairaj Prabhakaran[4,9,11]

[1]Department of Physiology, SDM College of Medical Sciences and Hospital, Shri Dharmasthala Manjunatheshwara University, Dharwad, Departments of [2]Physiology and [5]Medicine, Shri B.M.Patil Medical College, Hospital and Research Centre, BLDE (Deemed to be University), Vijayapur, Karnataka, Departments of [3]Physiology and [10]Cardiology, All India Institute of Medical Sciences, Departments of [4]Clinical Trials and [7]Lab, Centre for Chronic Disease Control, [8]Center for Biomedical Engineering, Indian Institute of Technology, [11]Department of Epidemiology, Public Health Foundation of India, New Delhi, India, [6]Department of Biostatistics, Hamad Medical Corporation, Doha, Qatar, [9]Department of Non-communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK

Abstract

Aims: The aim of this study was to evaluate the effects of yoga-based cardiac rehabilitation (Yoga-CaRe) on the endothelial system, oxidative stress, and inflammatory markers in patients with acute myocardial infarction (MI). **Methods:** A sub-study was conducted in two clinical sites of the Yoga-CaRe trial (a multicenter randomized controlled trial). Participants with acute MI were randomized and allocated to either the Yoga-CaRe program (13 sessions with encouragement to home practice) or enhanced standard care (three educational sessions). Endothelial function, oxidative stress, and inflammatory biomarkers were assessed using biomarkers such as asymmetric dimethylarginine (ADMA), endothelial nitric oxide synthase (eNOS), endothelin-1 (ET-1), E-selectin, P-selectin, vascular cell adhesion molecule (VCAM), intercellular cell-adhesion molecule-1, total nitric oxide concentration (NOx), oxidized low-density lipoprotein (Oxd-LDL), superoxide dismutase, total antioxidant capacity (TAOC), tumor necrosis factor-alpha (TNFα), and C-reactive protein (CRP) at baseline and 12 weeks. Laboratory and statistical analysis were done by staff blinded to group allocation. **Results:** Eighty-two patients (of the 110 patients recruited) completed the study. The mean age was 53.1 ± 10.6 and 51.9 ± 10.7 years in enhanced standard care and Yoga-CaRe group, respectively. At 12 weeks, Yoga-CaRe significantly reduced ADMA, ET-1, and ICMA-1 than the enhanced standard care group. Although E-selectin and VCAM at 12 weeks were reduced in both groups, enhanced standard care had a significantly higher reduction than the Yoga-CaRe group. Among markers of oxidative stress, TAOC increased in the Yoga-CaRe group. We found no difference in eNOS, NOx, P-selectin, TNFα, CRP, and Oxd-LDL between the two groups. **Conclusion:** Yoga-CaRe improved the endothelial function (through a reduction in ET-1 and modulating adhesion molecules) and enhanced antioxidant capacity.

Keywords: *Acute myocardial infarction, cardiac rehabilitation, endothelial function, randomized controlled trial, yoga*

Introduction

Secondary prevention of myocardial infarction (MI) is associated with reduced morbidity and mortality, improvement in the quality of life, and longevity.[1,2] Cardiac rehabilitation (CR) is an effective intervention for the secondary prevention of cardiovascular diseases (CVDs). CR is the process of restoring desirable levels of physical, social, and psychological functioning after the onset of cardiovascular illness.[2,3] Yoga covers most of the elements of a comprehensive CR program: improved physical fitness, stress reduction, and lifestyle improvement.[4] Few clinical studies have found an improvement in the functioning, quality of life, and cardiovascular risk factors by yoga-based CR programs in patients with coronary artery disease.[5-7] Studies also suggest that yoga practice including meditation could retard or even regress early and advanced coronary atherosclerosis.[5,6] The yoga and cardiovascular health trial (YACHT), conducted in the United Kingdom, found no change in the estimated left ventricular filling pressure (E/e′), 6-min walk test, blood pressure (BP), heart rate (HR), VO2 max, and neuro-endocrine

Address for correspondence: *Dr. Kishore Kumar Deepak, Center for Biomedical Engineering, Indian Institute of Technology, New Delhi - 110 016, India. E-mail: kkdeepak@gmail.com*

How to cite this article: Patil SG, Sobitharaj EC, Chandrasekaran AM, Patil SS, Singh K, Gupta R, *et al.* Effect of yoga-based cardiac rehabilitation program on endothelial function, oxidative stress, and inflammatory markers in acute myocardial infarction: A randomized controlled trial. Int J Yoga 2024;17:20-8.

Submitted: 21-Feb-2024 **Revised:** 13-Apr-2024
Accepted: 16-Apr-2024 **Published:** 13-May-2024

Access this article online

Website: https://journals.lww.com/IJOY

DOI: 10.4103/ijoy.ijoy_40_24

Quick Response Code:

pathways in patients practicing yoga with and without CR following acute coronary events.[8] Yoga-based cardiac rehabilitation (Yoga-CaRe) trial, a multicenter randomized controlled trial conducted in India, evaluated the effects of yoga-based CR program (Yoga-CaRe) on cardiovascular events and quality of life. The trial found Yoga-CaRe to be safe and improved the quality of life in patients after acute MI significantly. Although improvements in cardiovascular events did not reach statistical significance in the intention-to-treat analysis, *post hoc* per-protocol analysis found Yoga-CaRe to be efficacious.[9] However, the precise mechanism of the benefit of yoga on CV health in patients with coronary artery disease remains to be elucidated.

Vascular inflammation, oxidative stress, and endothelial dysfunction are the major triggers for CVDs.[10,11] Vascular endothelial integrity is crucial for the maintenance of vascular homeostasis and the prevention of atherosclerosis.[12] MI is associated with endothelial dysfunction which is evident from the impaired flow-mediated dilatation (FMD) seen in brachial artery ultrasound in patients with MI. Studies suggest that endothelial dysfunction predates MI and atherosclerosis, but the latter is related to the presence and severity of endothelial dysfunction. The assessment of endothelial function in both coronary and peripheral circulation provides prognostic information on cardiovascular events.[13-15] Endothelial dysfunction appears to predict the prognosis of CVDs.[16] We presume that the favorable impact of Yoga CaRe on cardiovascular health may be through inducing beneficial changes in endothelial function, oxidative stress, and inflammation. Hence, in this study, we have investigated the effect of yoga-based CR program on endothelial function, oxidative stress, and inflammatory markers to explore the underlying mechanism of yoga-based CR program on cardiovascular health in patients with acute MI.

Methods

Study design and participants

This is a mechanistic sub-study of the Yoga-CaRe trial, a multicenter randomized controlled trial where Yoga-CaRe was compared with enhanced usual care, conducted in 24 hospitals across India.[9] The mechanistic sub-study was conducted in two tertiary care hospitals located in South and North India. The study was approved by the institutional ethics committees of both the centers as per the guidelines (2006) of the Indian Council of Medical Research. Prior informed written consent was obtained from patients for participation in the study. The trial was conducted between May 2015 and July 2017.

Patients were considered eligible for the study if they meet the following criteria (a) Patients with acute MI aged between 18 and 70 years. MI was confirmed by WHO's standard definition (the presence of ischemia symptoms, troponin elevation, and electrocardiographic changes). Those who have undergone a revascularization procedure during previous or current admission were also eligible. Patients referred from other hospitals and admitted to the clinical site for diagnostic or therapeutic reasons within 14 days of the acute MI were also eligible for participation. (b) Patients willing and able to attend the complete hospital-based Yoga-CaRe program. Patients were excluded if they (a) were not able to complete the study duration and/or cannot come for the follow-up, (b) regularly practice yoga, i.e. participants who practice more than 3 h of yoga per week, and (c) have any other diseases which limit the life years <1 year such as severe valvular diseases, recurrent ventricular arrhythmias, heart failure (Killip class IV), cancers, severe aortic incompetence, severe atrial fibrillation, end-stage renal diseases, and end-stage liver diseases. After obtaining the written informed consent, patients were randomly assigned in a 1:1 ratio to Yoga-CaRe or enhanced standard care group. Randomization was done using the Interactive Web Response System after providing the essential details for randomization. A total of 110 patients were recruited for the study. Of these, 82 patients (39 out of 55 in enhanced standard care and 43 out of 55 in Yoga-CaRe) completed the 12-week assessment. Blinding was not possible due to the nature of the intervention, although outcome measures and statistical analysis were carried out by team members who were blinded to group allocation.

The sample size was calculated with a 90% probability that the study will detect a treatment difference in endothelial marker at a two-sided 0.05 significance level, if the true difference between treatments and standard deviation (SD) was 9 and 12.6 units, respectively. Further, considering a dropout rate of 30%, we aimed to recruit a total of 110 participants (55 per arm) to achieve a total of 42 evaluable participants in each group.[17]

Interventions

An intervention of the Yoga-CaRe program or enhanced standard care was received as an adjunct to the usual medical care available at the hospital for 3 months. Patients of Yoga-CaRe arm received a Yoga-CaRe program as an adjunct to standard care which was developed through a systematic process.[4] The Yoga-CaRe program was delivered for 12 weeks by yoga instructors. These yoga teachers were trained for the delivery of the Yoga-CaRe program. The training of the yoga-CaRe program was given in 13 inhospital sessions spread over 12 weeks and then encouraged to practice regularly at home using an instruction booklet and video in the local language. Yoga-CaRe program included educational advice, Pranayama (controlled slow breathing practices), gentle asanas (maintained stretching exercise), relaxation techniques, and meditation. The first two sessions included education, pranayama, and meditation which were delivered individually and the remainder in groups at the hospital.

The duration of each group session was about 75 min. Each session was followed by a discussion on lifestyle and psychological concerns. The adherence to the Yoga-CaRe program was recorded during every visit of the patients to the hospital. Any difficulties faced by the patient regarding yoga practice at home were attended with priority and clarified by a yoga instructor.

Patients of the enhanced standard care arm received standard educational advice in three sessions spread over 12 weeks with the help of written instructions. The intervention to the enhanced standard care group was delivered by a health-care study team member other than the yoga instructor to avoid contamination of the treatment arms [Supplementary Tables 1-4].

Study outcomes

The primary outcome of the study was any change in the endothelial function biomarkers after 12 weeks. The secondary outcomes were any change in the oxidative stress, antioxidant capacity, and inflammatory markers between the 12th and 13th week of intervention.

Data collection

Data were collected at baseline and after 12 weeks in the morning between 8.00 am to 1.00 pm after a supine rest for at least 10 min. BP and HR were measured using a digital BP measuring device (OMRON HEM-7111). Blood samples were collected in plain tubes in the morning after overnight fasting. The serum was separated and stored at −70°C for further biochemical investigation. All the biochemical analysis was done at one center to minimize the variability caused by different processing protocols and kits and to maintain a standard protocol. The samples from the other center were transferred in dry ice with specialized insulated packages as per the standard protocol with biosafety measures. The sample analyses were done by a staff blinded to group allocation.

Biomarkers of the endothelial system included measurement of asymmetric dimethylarginine (ADMA), endothelial nitric oxide synthase (eNOS), and endothelin-1 (ET-1) and were assayed by the ELISA method (Biospes Co. Ltd, China). Nitric oxide concentration (NOx) was measured by the kinetic cadmium-reduction method.[18] Soluble E-selectin, soluble P-selectin, vascular cell-adhesion molecule (VCAM), and intercellular cell-adhesion molecule (ICAM) were assayed by ELISA using kits and internal controls from Quantikine (R and D Systems, Inc.). High-sensitivity C-reactive protein (hs-CRP) was assayed using kits from BioCheck. Inc. Oxidized low-density lipoprotein (Oxd-LDL) was measured as a marker of oxidative stress. Antioxidant capacity was determined by total antioxidant capacity (TAOC) and superoxide dismutase (SOD) activity. Oxd-LDL and TAOC were measured by the ELISA technique (Biospes Co. Ltd., China). SOD activity was determined by Marklund and Marklund method.[19] Inflammatory markers such as tumor necrosis factor-alpha (TNFα) and hs-CRP were measured by the ELISA method.

Statistical analysis

The data are expressed as mean ± SD. Gaussian distribution was tested using standard normality tests. Between-group differences in baseline demographic, clinical characteristics, and treatment profile were examined using Chi-square tests (categorical variables) and *t*-tests (continuous variables). Between-group intervention effects on the changes from baseline to 12 weeks were assessed using analysis of variance with the intervention arm as the group factor and baseline value as a covariate. All data analyses followed the intent-to-treat principle where participants were included in the intervention arm, they were randomized regardless of whether they participated in the intervention or not. We explored the effect of adherence on the results using the median of the inhospital sessions and home practice. All the analyses were done independently by a statistician blinded to study groups using Stata. The results were interpreted with a significance level of $P < 0.05$.

Results

Study participants

We recruited 110 patients for this sub-study between May 2015 and July 2017. Of these, 82 patients (39 out of 55 in enhanced standard care and 43 out of 55 in Yoga-CaRe) completed the 12-week assessment [Figure 1]. The mean age of the participants was 53.1 ± 10.6 and 51.9 ± 10.7 years in enhanced standard care and Yoga-CaRe group, respectively. About 20% of the participants were female [Table 1]. The prevalence of diabetes and hypertension was 18% and 13%, respectively. Only 30 patients (37%) underwent angiogram at baseline and among these, only 33% had multiple vessel involvement. Most patients were presented with ST-elevation myocardial infarction (95%). Tobacco use was reported by 40% of patients, alcohol use by 27%, and physical inactivity by 42% of patients. Almost all participants received antiplatelets and statins. At 12 weeks, the study group participants attended a median of 9 inhospital sessions (interquartile range: 7, 13) and practiced for 39 min at home (interquartile range: 23, 50).

Markers of vascular endothelial function

Compared to baseline, at the 12-week follow-up, ADMA decreased in the Yoga-CaRe group while it was increased in the enhanced standard care group; and the between-group difference in change from baseline was statistically significant (−0.44 [95% CI, −0.82–−0.07], $P = 0.02$). Similarly, the Yoga-CaRe group demonstrated statistically significant higher reductions in ET-1 (between-group difference: −7.73 [95% CI, −12.19–−3.28], $P = 0.001$) and ICAM-1(between-group difference: −75.47 [95% CI, −138.43–−12.51, $P = 0.019$]) [Table 2].

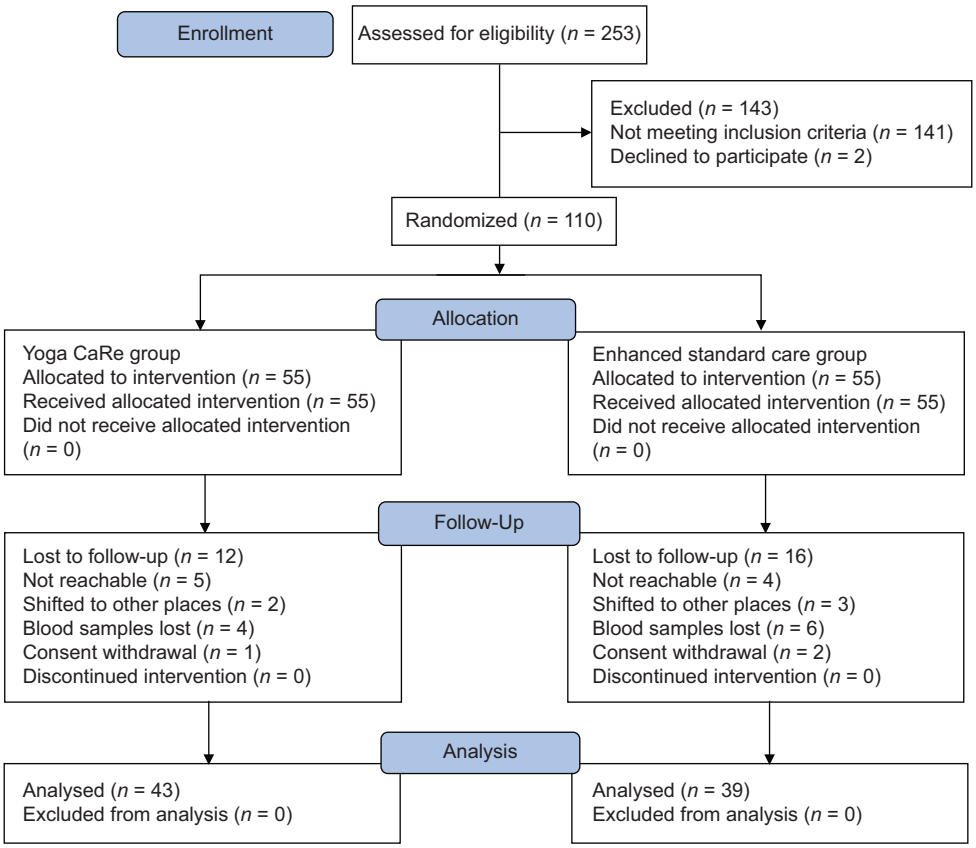

Figure 1: CONSORT flow diagram

Table 1: Baseline characteristics of all analyzed participants

	Enhanced standard care (*n*=39), *n*/*n* (%)	Yoga-CaRe (*n*=43), *n*/*n* (%)	*P*
Demography			
Age (years), mean (SD)	53.1 (10.6)	51.9 (10.7)	0.63
Female	9/39 (23)	7/43 (16)	0.44
Formal education >10 years	14/39 (36)	15/43 (35)	0.98
Clinical characteristics			
Medical history at admission			
Coronary artery disease	0/39 (0)	2/43 (5)	0.17
Diabetes mellitus	6/39 (15)	9/43 (21)	0.52
Hypertension	4/39 (10)	7/43 (16)	0.42
Current tobacco use	13/39 (33)	20/43 (47)	0.22
Current alcohol use	7/39 (18)	15/43 (35)	0.08
Physical inactivity	17/39 (44)	17/43 (40)	0.71
Characteristics of MI			
Multivessel disease on angiography	3/10 (30)	7/20 (35)	0.77
ST-segment elevation	39/39 (100)	39/43 (91)	0.05
Treatment profile			
Management at discharge			
Underwent PCI/CABG	10/39 (36)	21/43 (49)	0.03
Antiplatelets	39/39 (100)	43/43 (100)	NA
Statins	37/39 (95)	35/43 (81)	0.36
Beta-blockers	15/39 (38)	24/43 (56)	0.12
ACE inhibitors/ARB	14/39 (36)	27/43 (63)	0.02

PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass graft, ACE: Angiotensin-converting enzyme, ARB: Angiotensin II receptor blockers, Yoga-CaRe: Yoga-based cardiac rehabilitation program, SD: Standard deviation, NA: Not available, MI: Myocardial infarction

Table 2: Effect of Yoga-based cardiac rehabilitation program on markers of endothelial function, oxidative stress, and inflammatory mediators

Outcome	Timeline	Enhanced standard care (*n*=39), *n*(%)	Yoga-CaRe (*n*=43), *n* (%)	Regression coefficient (95% CI)[#]	*P*[†]
Markers of endothelial function					
ADMA	Pre	2.8 (1.6)	2.5 (0.7)	−0.44 (−0.82–−0.07)	0.02*
	Post	3.0 (1.6)	2.3 (0.7)		
eNOS	Pre	53.2 (13.5)	60.7 (13.9)	0.16 (−4.74–5.05)	0.95
	Post	53.4 (10.0)	57.9 (15.6)		
NOx	Pre	53.9 (29.0)	52.3 (20.0)	0.61 (−8.19–9.42)	0.89
	Post	54.3 (19.5)	54.6 (21.2)		
ET1	Pre	36.1 (8.5)	37.0 (15.7)	−7.73 (−12.19–−3.28)	0.001**
	Post	37.9 (10.5)	30.3 (10.1)		
E-selectin	Pre	44.5 (21.7)	52.2 (26.4)	10.76 (1.73–19.8)	0.02*
	Post	36.5 (20.9)	48.8 (20.0)		
P-selectin	Pre	81.9 (39.4)	90.3 (36.4)	11.87 (−6.07–29.81)	0.19
	Post	82.5 (35.0)	93.7 (46.3)		
ICAM-1	Pre	207.1 (138.1)	312.6 (105.7)	−75.47 (−12.51–−138.43)	0.019*
	Post	211.6 (156.9)	298.4 (114.1)		
VCAM-1	Pre	711.6 (378.1)	743.9 (355.2)	183.36 (64.15–302.57)	0.003**
	Post	493.8 (297.3)	660.1 (251.0)		
Markers of oxidative stress and antioxidant capacity					
Ox-LDL	Pre	38.1 (11.5)	46.1 (14.6)	0.49 (−4.49–5.47)	0.85
	Post	41.2 (14.6)	45.9 (10.7)		
SOD	Pre	12.7 (5.6)	12.0 (5.8)	−1.63 (−4.33–1.08)	0.24
	Post	12.0 (6.3)	10.2 (6.3)		
TAOC	Pre	2.1 (0.9)	1.9 (0.6)	0.28 (0.02–0.55)	0.03*
	Post	1.9 (0.8)	2.1 (0.8)		
Markers of inflammation					
TNF	Pre	0.5 (0.4)	0.8 (0.7)	−0.23 (−0.94–0.48)	0.52
	Post	1.0 (2.0)	0.9 (1.0)		
hs-CRP	Pre	12.4 (18.3)	10.5 (22.1)	−87.31 (−249.13–74.5)	0.29
	Post	73.4 (475.4)	6.0 (11.5)		

*Significant, **Very significant, [#]Coefficients estimated using ANCOVA adjusting for baseline values, [†]*P*-values for ANCOVA estimates. ADMA: Asymmetric dimethylarginine, eNOS: Endothelial nitrous oxide synthase, NOx: Total nitric oxide concentration, ET1: Endothelin-1, ICAM-1: Intercellular Adhesion Molecule 1, VCAM: Vascular cell adhesion molecule 1, Ox-LDL: Oxidized LDL, SOD: Superoxide dismutase, TAOC: Total antioxidant capacity, TNF: Tumor Necrosis Factor, hs-CRP: High-sensitive C-reactive protein, CI: Confidence interval

The biomarkers E-selectin and VCAM were reduced in both groups. However, the reductions were significantly higher in the enhanced standard care group than in the Yoga-CaRe group. Although there were favorable changes in the Yoga-CaRe group in the other biomarkers such as eNOS, NOx, and P-Selectin, these differences did not reach statistical significance.

Markers of oxidative stress and antioxidant capacity

There was no significant difference in the Oxd-LDL between groups. The TAOC was higher at the 12-week visit in the Yoga-CaRe group, while it was reduced in the enhanced standard care group (between-group difference: 0.28 [95% CI, 0.02–0.55, $P = 0.03$]) [Table 2]. However, there were no improvements in the SOD, the other marker of antioxidant capacity.

Markers of inflammation

Although there was an increase in the marker of inflammation TNF-α and reduction in hs-CRP and in the Yoga-CaRe group, they were not statistically significant within and between groups [Table 2].

Effect of adherence to yoga-based cardiac rehabilitation program

Good adherence (≥ median) to inhospital sessions and home practice was associated with better improvements in higher improvements in ADMA, ET-1, ICAM1, and TAOC than the low adherence group and the enhanced standard care.

Adverse events

There were no adverse events.

Discussion

We believe our study is one of the first to investigate the effect of yoga-based CR programs on endothelial function, oxidative stress, and inflammation in patients after acute MI. A significant reduction in ADMA, ET-1, and ICAM-1, and enhancement in TAOC in the Yoga-CaRe group than the enhanced standard-care group was observed, indicating an enhancement in improvement in endothelial function and antioxidant capacity with Yoga-CaRe. However, the reduction in E-selectin and VCAM levels was higher in the enhanced standard care group than in the Yoga-CaRe group. The Yoga-CaRe trial, a multicenter randomized controlled trial, has shown that the Yoga-based CR program is safe and effective in improving quality of life and returning to preinfarct activities after acute MI (n = 3959). Incidence of major cardiovascular events (composite of all-cause mortality, MI, stroke, or emergency cardiovascular hospitalization) was lower in patients receiving the Yoga-CaRe program than enhanced standard care but was statistically insignificant. However, no changes were noted in other outcomes such as tobacco cessation and compliance with medication.[9] Yoga-CaRe program is shown as a safe, simple, and potentially less expensive alternative model of CR. The mechanistic study was conducted to evaluate the potential pathways through the Yoga-CaRe program that influence the CVD pathway after acute MI.

The major factors that determine the prognosis of MI and secondary prevention of CVDs are endothelial function, oxidative stress, vascular inflammation, and autonomic function. Normal endothelial function is critical for maintaining vascular integrity.[12] The endothelium influences vascular tone through the release of vasodilators and vasoconstrictors (nitric oxide, ETs); vascular remodeling through growth-promoting, and growth-inhibiting factors; and vascular hemostasis through antiplatelet aggregation, anticoagulant, and fibrinolytic effects. Therefore, dysfunction of endothelium not only plays a major role in the pathogenesis of atherosclerosis and coronary artery disease but also predicts the prognosis of CVDs. A meta-analysis of observational studies examining the association between FMD and future cardiovascular events suggested that impairment of brachial FMD is significantly associated with future cardiovascular events and the relative risk of cardiovascular events per 1% increase in brachial FMD was 0.87.[16]

Sivasankaran *et al*. assessed the effect of a 6-week program (1.5 h. three times weekly) of yoga on endothelial function in subjects with and without coronary artery disease. They found a 69% improvement in endothelial-dependent vasodilation with yoga practice in patients with coronary artery disease.[20] While another study by Paul Labrador *et al*. did not find any change in FMD in subjects with coronary artery disease with 16 weeks of transcendental meditation practice.[21] In the present study, there was a significant reduction in the ADMA and ET-1 in patients receiving Yoga-CaRe intervention than enhanced standard care. ADMA is an endogenous competitive inhibitor of eNOS. An increase in ADMA concentration decreases the production of vascular nitric oxide and thus impairs endothelial function.[22] Nitric oxide is a potent vasodilator and key molecule of endothelium that maintains vascular homeostasis. ADMA is positively associated with the severity of endothelial dysfunction and atherosclerosis.[22-25] Elevated levels of ADMA independently predict future CV risk, adverse cardiovascular events, death, and all-cause mortality in individuals with coronary artery disease.[26-30] Therefore, the reduction in ADMA in the Yoga-CaRe group indicates an improvement in endothelial function and may be attributed to the reduction in future CV risk with the Yoga-CaRe program. However, we did not find any change in NOx and eNOS activity between the two groups that may be because of the administration of statin therapy to all the patients which increases the bioavailability of nitric oxide by upregulating the activity of eNOS and preventing the removal of nitric oxide by reactive oxygen species.[31] In our earlier study, we found an enhancement in NOx with yoga practice for 3 months in elderly hypertensive patients.[31] Recently, a systematic review and meta-analysis by Patil *et al*. showed that yoga is safe and effective for improving endothelial function.[32]

Further, endothelial dysfunction is characterized by a shift in the vasodilator to vasoconstrictor dominance resulting in reduced blood flow and poor prognosis after MI. The poor clinical outcomes after the MI are linked to vasoconstriction of coronary microcirculation by raised levels of ET-1.[33-35] ET-1 is a potent vasoconstrictor that exerts its effect through the ET-receptor. It is also implicated in reperfusion injury, no-reflow phenomenon, and coronary restenosis after percutaneous transluminal coronary angioplasty for acute coronary syndromes. These findings indicate that ET-1 regulates coronary flow in atherosclerotic arteries, particularly at stenosis. The raised level of ET-1 not only mediates coronary vasoconstriction, but is also involved in smooth muscle cell proliferation, platelet aggregation, and increased expression of adhesion molecules, leading to the promotion of atherogenesis, lesion growth, and coronary thrombosis.[36] Blockade of ET receptors was shown to cause vasodilation in patients with coronary artery disease[37] and after angioplasty[35,38] and increase long-term survival in experimental animals after MI.[39] These reports suggest that strategies that reduce ET-1 levels and inhibit its action may prevent coronary vasoconstriction and improve myocardial perfusion resulting in better prognosis after MI and angioplasty.[36] In the present study, there was a highly significant reduction in ET-1 concentration with 12 weeks of the Yoga-CaRe program in patients after MI, suggesting that the Yoga-CaRe program mimics ET-receptor blockers.

Thus, the reduction in ET-1 levels with the Yoga-CaRe program may be attributed to the improvement in the clinical outcomes in patients of the Yoga-CaRe group after MI.

Oxidative stress and vascular inflammation have been implicated in the development of endothelial dysfunction. Further, Ox-LDL is shown to induce ET-1 production in endothelial cells and human macrophages. Our current study has shown significant enhancement in TAOC in Yoga-CaRe group patients, but there was no change in oxidant levels. The enhancement in antioxidant defense with the Yoga-CaRe program may be because of less utilization of antioxidants due to decreased oxidative stress. We also estimated endothelial cell adhesion molecules and inflammatory markers. We found a significant reduction in ICAM in patients of the Yoga-CaRe group, whereas VCAM and E-selectin were reduced in the patients of both groups, the reduction was higher with enhanced standard care than in the Yoga-CaRe program. This mixed result may reflect a play of chance indicating the need for evaluation with larger sample size. Our findings suggest that the Yoga-CaRe program can restore normal endothelial function after MI. Further, our findings reinforced the yogic concept that yoga is a conscious process of gaining voluntary control over involuntary functions including the cardiovascular system at both gross and cellular levels through influencing the mind by physical postures, breath control, meditation, and control of diet. Moreover, the long-term benefits of yoga on cardiovascular health may be explained through favorable modifications at the molecular level in endothelial cells.

Strengths and limitations of the study

This is the first RCT reporting on the effects of yoga-based CR on the endothelial system and its mechanism underlying the favorable benefits of yoga on the heart after MI. A multicenter, parallel-arm, open-label, randomized controlled trial with end-point blinding design and unbiased statistical methods for data analysis are the key strengths of the methodology of this study.

Despite being well-designed and conducted, the study has few limitations. First, the study participants were relatively young with a fewer female population, lower rates of diabetes, hypertension (<20%), and multivessel involvement compared to real-world scenarios. This restricts the applicability of results to patients after acute AMI with a relatively high-risk profile. However, these are like most CR trials. Second, the attrition rate was relatively high. One-third of the patients randomized did not provide postintervention blood samples (samples from ten participants were inadequate for analysis or hemolyzed). However, the loss to follow-up and the inadequate samples were distributed equally between the two groups. The small sample size is a common limitation in yoga trials reported elsewhere in India and worldwide.

Conclusion

Yoga-CaRe improved endothelial function and antioxidant capacity in patients after acute MI. The most highly significant finding was a reduction in ET-1 concentration with 12 weeks of the Yoga-CaRe program in patients after MI, suggesting that the action of the Yoga-CaRe program mimics ET-receptor blockers. Thus, our results strengthen the concept of a novel therapeutic strategy of targeting a reduction in ET-1 for improving the prognosis after MI.

Acknowledgments

We would like to thank Dr. Prachi Srivastava, All India Institute of Medical Sciences, New Delhi, India.

Data availability statement

Data are available upon reasonable request. Note that raw data is available with the principal investigator. We are unable to attach all the raw data for each participant in this paper due to ethical restrictions.

Ethical statement

The study was approved by the institutional ethics committees of both the centers (Institutional Ethical Clearance no. 170/2016-17) and (Letter no. IESC/T-158/01.04.2015, RT-21/05.05.2015) as per the guidelines (2006) of Indian Council of Medical Research.

Financial support and sponsorship

The trial is supported by Indo-UK collaborative research grant - Indian Council for Medical Research, India (ICMR-58/1/9/MRC-ICMR/2009/NCD-II) and Medical Research Council, UK (MRC-MR/J000175/1); All India Institute of Medical Sciences, New Delhi and BLDE University, Vijayapur, Karnataka, India.

Conflicts of interest

There are no conflicts of interest.

References

1. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli Ducci C, Bueno H, *et al.* 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The task force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2018;39:119-77.
2. Thomas RJ, Balady G, Banka G, Beckie TM, Chiu J, Gokak S, *et al.* 2018 ACC/AHA clinical performance and quality measures for cardiac rehabilitation: A report of the American College of Cardiology/American Heart Association task force on performance measures. J Am Coll Cardiol 2018;71:1814-37.
3. Anderson L, Thompson DR, Oldridge N, Zwisler AD, Rees K, Martin N, *et al.* Exercise-based cardiac rehabilitation for coronary heart disease. Cochrane Database Syst Rev 2016;2016:CD001800.
4. Chattopadhyay K, Chandrasekaran AM, Praveen PA,

Manchanda SC, Madan K, Ajay VS, *et al.* Development of a yoga-based cardiac rehabilitation (Yoga-CaRe) programme for secondary prevention of myocardial infarction. Evid Based Complement Alternat Med 2019;2019:7470184.
5. Ornish D, Scherwitz LW, Billings JH, Brown SE, Gould KL, Merritt TA, *et al.* Intensive lifestyle changes for reversal of coronary heart disease. JAMA 1998;280:2001-7.
6. Manchanda SC, Narang R, Reddy KS, Sachdeva U, Prabhakaran D, Dharmanand S, *et al.* Retardation of coronary atherosclerosis with yoga lifestyle intervention. J Assoc Physicians India 2000;48:687-94.
7. Toobert DJ, Glasgow RE, Radcliffe JL. Physiologic and related behavioral outcomes from the women's lifestyle heart trial. Ann Behav Med 2000;22:1-9.
8. Tillin T, Tuson C, Sowa B, Chattopadhyay K, Sattar N, Welsh P, *et al.* Yoga and cardiovascular health trial (YACHT): A UK-based randomised mechanistic study of a yoga intervention plus usual care versus usual care alone following an acute coronary event. BMJ Open 2019;9:e030119.
9. Prabhakaran D, Chandrasekaran AM, Singh K, Mohan B, Chattopadhyay K, Chadha DS, *et al.* Yoga-based cardiac rehabilitation after acute myocardial infarction: A randomized trial. J Am Coll Cardiol 2020;75:1551-61.
10. Steven S, Frenis K, Oelze M, Kalinovic S, Kuntic M, Bayo Jimenez MT, *et al.* Vascular inflammation and oxidative stress: Major triggers for cardiovascular disease. Oxid Med Cell Longev 2019;2019:7092151.
11. Cai H, Harrison DG. Endothelial dysfunction in cardiovascular diseases: The role of oxidant stress. Circ Res 2000;87:840-4.
12. Versari D, Daghini E, Virdis A, Ghiadoni L, Taddei S. Endothelial dysfunction as a target for prevention of cardiovascular disease. Diabetes Care 2009;32 Suppl 2:S314-21.
13. Shimbo D, Grahame Clarke C, Miyake Y, Rodriguez C, Sciacca R, Di Tullio M, *et al.* The association between endothelial dysfunction and cardiovascular outcomes in a population-based multi-ethnic cohort. Atherosclerosis 2007;192:197-203.
14. Guazzi M, Reina G, Gripari P, Tumminello G, Vicenzi M, Arena R. Prognostic value of flow-mediated dilatation following myocardial infarction. Int J Cardiol 2009;132:45-50.
15. Lavine SJ. Prediction of heart failure post myocardial infarction: Comparison of ejection fraction, transmitral filling parameters, and the index of myocardial performance. Echocardiography 2003;20:691-701.
16. Inaba Y, Chen JA, Bergmann SR. Prediction of future cardiovascular outcomes by flow-mediated vasodilatation of brachial artery: A meta-analysis. Int J Cardiovasc Imaging 2010;26:631-40.
17. Patil SG, Aithala MR, Das KK. Effect of yoga on arterial stiffness in elderly subjects with increased pulse pressure: A randomized controlled study. Complement Ther Med 2015;23:562-9.
18. Cortas NK, Wakid NW. Determination of inorganic nitrate in serum and urine by a kinetic cadmium-reduction method. Clin Chem 1990;36:1440-3.
19. Marklund S, Marklund G. Involvement of the superoxide anion radical in the autoxidation of pyrogallol and a convenient assay for superoxide dismutase. Eur J Biochem 1974;47:469-74.
20. Sivasankaran S, Pollard Quintner S, Sachdeva R, Pugeda J, Hoq SM, Zarich SW. The effect of a six-week program of yoga and meditation on brachial artery reactivity: Do psychosocial interventions affect vascular tone? Clin Cardiol 2006;29:393-8.
21. Paul Labrador M, Polk D, Dwyer JH, Velasquez I, Nidich S, Rainforth M, *et al.* Effects of a randomized controlled trial of transcendental meditation on components of the metabolic syndrome in subjects with coronary heart disease. Arch Intern Med 2006;166:1218-24.
22. Landim MB, Casella Filho A, Chagas AC. Asymmetric dimethylarginine (ADMA) and endothelial dysfunction: Implications for atherogenesis. Clinics (Sao Paulo) 2009;64:471-8.
23. Böger RH, Bode Böger SM, Szuba A, Tsao PS, Chan JR, Tangphao O, *et al.* Asymmetric dimethylarginine (ADMA): A novel risk factor for endothelial dysfunction: Its role in hypercholesterolemia. Circulation 1998;98:1842-7.
24. Antoniades C, Shirodaria C, Leeson P, Antonopoulos A, Warrick N, Van Assche T, *et al.* Association of plasma asymmetrical dimethylarginine (ADMA) with elevated vascular superoxide production and endothelial nitric oxide synthase uncoupling: Implications for endothelial function in human atherosclerosis. Eur Heart J 2009;30:1142-50.
25. Sibal L, Agarwal SC, Home PD, Boger RH. The role of asymmetric dimethylarginine (ADMA) in endothelial dysfunction and cardiovascular disease. Curr Cardiol Rev 2010;6:82-90.
26. Parikh RV, Pargaonkar V, Ball RL, Kobayashi Y, Kimura T, Yeung AC, *et al.* Asymmetric dimethylarginine predicts impaired epicardial coronary vasomotion in patients with angina in the absence of obstructive coronary artery disease. Int J Cardiol 2020;299:7-11.
27. Schnabel R, Blankenberg S, Lubos E, Lackner KJ, Rupprecht HJ, Espinola Klein C, *et al.* Asymmetric dimethylarginine and the risk of cardiovascular events and death in patients with coronary artery disease: Results from the AtheroGene study. Circ Res 2005;97:e53-9.
28. Lu TM, Ding YA, Lin SJ, Lee WS, Tai HC. Plasma levels of asymmetrical dimethylarginine and adverse cardiovascular events after percutaneous coronary intervention. Eur Heart J 2003;24:1912-9.
29. Valkonen VP, Päivä H, Salonen JT, Lakka TA, Lehtimäki T, Laakso J, *et al.* Risk of acute coronary events and serum concentration of asymmetrical dimethylarginine. Lancet 2001;358:2127-8.
30. Meinitzer A, Seelhorst U, Wellnitz B, Halwachs Baumann G, Boehm BO, Winkelmann BR, *et al.* Asymmetrical dimethylarginine independently predicts total and cardiovascular mortality in individuals with angiographic coronary artery disease (the Ludwigshafen risk and cardiovascular health study). Clin Chem 2007;53:273-83.
31. Gorabi AM, Kiaie N, Hajighasemi S, Banach M, Penson PE, Jamialahmadi T, *et al.* Statin-induced nitric oxide signaling: Mechanisms and therapeutic implications. J Clin Med 2019;8:2051.
32. Patil SG, Khode V, Christa E, Desai RM, Chandrasekaran AM, Vadiraja HS, *et al.* Effect of yoga on endothelial function: A systematic review and meta-analysis. J Integr Complement Med 2024;30:233-49.
33. Omland T, Lie RT, Aakvaag A, Aarsland T, Dickstein K. Plasma endothelin determination as a prognostic indicator of 1-year mortality after acute myocardial infarction. Circulation 1994;89:1573-9.
34. Freixa X, Heras M, Ortiz JT, Argiró S, Guasch E, Doltra A, *et al.* Usefulness of endothelin-1 assessment in acute myocardial infarction. Rev Esp Cardiol 2011;64:105-10.
35. Guddeti RR, Prasad A, Matsuzawa Y, Aoki T, Rihal C, Holmes D, *et al.* Role of endothelin in microvascular dysfunction following percutaneous coronary intervention for non-ST elevation acute coronary syndromes: A single-centre randomised controlled trial.

Open Heart 2016;3:e000428.
36. Berger R, Pacher R. The role of the endothelin system in myocardial infarction – New therapeutic targets? Eur Heart J 2003;24:294-6.
37. Wenzel RR, Fleisch M, Shaw S, Noll G, Kaufmann U, Schmitt R, *et al.* Hemodynamic and coronary effects of the endothelin antagonist bosentan in patients with coronary artery disease. Circulation 1998;98:2235-40.
38. Kyriakides ZS, Kremastinos DT, Psychari SN, Kolettis T, Sbarouni E, Webb DJ. Coronary vasoconstriction after coronary angioplasty is attenuated by endothelin a receptor antagonism. Am J Cardiol 2001;87:1011-3.
39. Clozel M, Qiu C, Qiu CS, Hess P, Clozel JP. Short-term endothelin receptor blockade with tezosentan has both immediate and long-term beneficial effects in rats with myocardial infarction. J Am Coll Cardiol 2002;39:142-7.

Supplementary Table 1: The four phases of the Yoga-based cardiac rehabilitation program

Phase	Week after heart attack	Type of care
I		
Inpatient care	1 (session 1)	Individual face-to-face session- education
II		
Formal outpatient session- I	3 (session 2)	Individual face-to-face session- Yoga
III		
Formal outpatient session- II	5–7 (sessions 3–8; twice/week)*	Face-to-face group session- Yoga and education
	8–12 (sessions 9–13; once/week)*	(in addition, self-practice of Yoga at home during the rest of the week using the Yoga-CaRe program booklet and DVD)
IV		
Long-term maintenance of Yoga, dietary, and lifestyle changes at home	13+	Self-practice of Yoga at home almost daily using the Yoga-CaRe program booklet and DVD; and maintenance of dietary and lifestyle changes

*Self-supervised sessions with audiovisual material at home, 5–7 times per week. Yoga-CaRe: Yoga-based cardiac rehabilitation program. DVD: Digital Video Disc

Supplementary Table 2: Yoga-based cardiac rehabilitation program intervention session plan

Week	Session	Intervention program
1	1	Educational session
3	2	Pranayam, relaxation and meditation techniques
5	3 and 4	Health rejuvenating exercises, asanas, pranayam, relaxation, and meditation techniques
6	5 and 6	Health rejuvenating exercises, asanas, pranayam, relaxation, and meditation techniques
7	7 and 8	Health rejuvenating exercises, asanas, pranayam, relaxation, and meditation techniques
8	9	Health rejuvenating exercises, asanas, pranayam, relaxation, and meditation techniques
9	10	Health rejuvenating exercises, asanas, pranayam, relaxation, and meditation techniques
10	11	Health rejuvenating exercises, asanas, pranayam, relaxation, and meditation techniques
11	12	Health rejuvenating exercises, asanas, pranayam, relaxation, and meditation techniques
12	13	Health rejuvenating exercises, asanas, pranayam, relaxation, and meditation techniques
13	14	Group session - discussion on long-term maintenance of Yoga, dietary, and lifestyle changes at home

Supplementary Table 3: Components of Yoga-based cardiac rehabilitation program intervention	
Intervention component	**Practices**
Health rejuvenating exercises	Shoulder exercises Chest exercises Abdomen exercises
Yogic poses (asana)	
Standing poses	
Core poses	Kati-chakrasana (waist wheel pose) Tadasana (palm tree pose) Urdhva-hastottanasana (up stretched arms pose)
Elective poses	Ardhakati-Chakrasana (lateral arc pose) Trikonasana (triangle pose)
Sitting poses	
Core poses	Gomukhasana (cow face pose) Janushirsasana (head on the knee pose) Vakrasana (twisted pose)
Elective poses	Ardha-padmasana (half lotus pose) Vajrasana (adamant pose)
Lying poses	
Core poses	Ekpadottanasana (half-leg raise pose) Naukasana (boat pose) Ardha-pavanamuktasana (wind releasing pose)
Elective poses	Markatasana (monkey pose) Merudandasana (spinal cord pose)
Breath control exercises (Pranayama)	
Core breath control exercises	Anulom vilom/nadishodhana pranayama (without kumbhak) (alternate nostril breathing) Bhramari pranayama (bee breathing) Ujjayi pranayama (loud breathing)
Elective breath control exercises	Sitali pranayama (tongue hissing) Sitkari pranayama (teeth hissing)
Meditation (dhyana) and relaxation practices	
Core meditation and relaxation practices	Chanting Mindfulness meditation Shavasana (relaxation training)
Elective meditation and relaxation practices	Dirghasvasa preksha (perception of deep breathing) Antaranga trataka (internal concentrated gazing)

Supplementary Table 4: Details of yoga-based cardiac rehabilitation program intervention

Health rejuvenating exercises/asana/pranayam/ meditation and relaxation techniques	Procedure
Shoulder exercises	Stand erect. Keep your arms by your sides, with your fists closed. While inhaling, raise your shoulders up. While exhaling, bring them down. Repeat this four times
	Stand erect. Keep your arms by your sides, with your fists closed. Rotate your shoulders from back to front, and then from front to back. Repeat this four times
	Stand erect. Bend your arms with fingers touching the shoulders. While inhaling, rotate your arms from forward to backward. While exhaling, rotate them from backward to forward. Repeat this four times
Chest exercises	Stand erect. Bend your arms. Bring your palms to the chest, with middle fingers meeting at the middle of your chest. While inhaling, extend the left arm. While exhaling, bring your arm back to the initial position. While inhaling, extend the right arm. While exhaling, bring your arm back to the initial position. While inhaling, extend both the arms. While exhaling, bring both arms back to the initial position. Repeat this sequence four times
Abdomen exercises	Stand erect. Keep your arms in front of the thighs. While inhaling, raise your left arm to touch the ear. While exhaling, bring the arm down. While inhaling, raise your right arm to touch the ear. While exhaling, bring the arm down. While inhaling, raise both the arms to touch your ears. While exhaling, bring the arms down. Repeat this sequence four times
	Stand erect. Look straight ahead and become fully aware of your breath. Place your hands on the abdomen. On slow inhalation, feel the navel going out. On slow exhalation, feel the navel going in. Repeat this four times
	Stand erect. Look straight ahead and become fully aware of your breath. Place your hands on the abdomen. On quick inhalation, feel the navel going out. On quick exhalation, you should feel the navel going in. Repeat this four times
	Stand erect. Look ahead at the ground about 200 cm in front of your toes. Become fully aware of your breath. Place your hands on the abdomen. Inhale and exhale quickly. Repeat this four times
Kati-chakrasana	Stand erect. Look straight ahead. Keep your hands on the waist, with thumbs in front and other fingers at the back. Bend 30° forward. Inhale and exhale quickly. Repeat this four times. Inhale and return to your initial position. Exhale
	Stand erect with your feet about shoulder-width apart. Knees should be straight. Place your right hand on the left shoulder, and your left hand behind resting on the left waist. Inhale. While exhaling, rotate your trunk and head toward the left side as much as possible. Do not bend your neck forward. Maintain the final position for about 10 s–1 min, depending on your capacity. Inhale. While exhaling, return to your initial position. Relax. Repeat this on the opposite side
Tadasana	Stand erect with your feet about 15 cm apart. Raise your arms to the shoulder level. Then, further, raise your arms to the ears and simultaneously raise your heels. Interlock your fingers on the top. Stretch the whole body as much as possible. Maintain the final position for about 10 s–1 min, depending on your capacity. Come back in the reverse order. Initially, you may find balancing on your toes difficult, but you will achieve this with practice
Urdhva-hastottanasana	Stand erect with your feet about 15 cm apart. Interlock your fingers and raise the arms. Look straight ahead. Drop down to the left, bending from the waist. Try to get as low as possible so that your arms are parallel to the floor. Maintain the final position for about 10 s–1 min, depending on your capacity. Come back to the center. Repeat this on the opposite side
Ardhakati-Chakrasana	Stand erect with your feet slightly apart. Keep your hands on the sides of your respective thighs with fingers close together. Look straight ahead. While inhaling, raise the right arm to the shoulder level with your palm inward. Then, turn your palm upward, raise your hand and bring the inside of your upper arm close to the right ear. While exhaling, bend your trunk, head, and right hand sideways to the left. While bending, slide the left palm down your left thigh until it reaches the left knee. Maintain the final position for about 10 s–1 min, depending on your capacity. While inhaling, return back till the right hand comes straight above the head. While exhaling, lower the right arm to the side, turn the palm inward at the shoulder level, and bring the hand further down. Repeat this on the opposite side

Contd...

Supplementary Table 4: Contd...

Health rejuvenating exercises/asana/pranayam/ meditation and relaxation techniques	Procedure
Trikonasana	Stand erect with your feet 100 cm apart. Raise your arms sideways to the shoulder level. Slowly lean to the right, and try to bring your right hand close to the right toe. Your arms should be in one straight line. Your left hand should point upward. Turn the head upward and gaze at your left hand. Maintain the final position for about 10 s–1 min, depending on your capacity. Come back in the reverse order. Repeat this on the opposite side
Gomukhasana	Sit with both legs straight in front. Bend the right leg and keep it below the left leg. Place the right heel by the side of your left hip. Bend the left leg and place the left heel by the side of your right hip. Adjust your knees so that they are directly one above the other. Place the left hand behind your back, and the right hand above your shoulder. Bend your right hand at the elbow, and reach for the left-hand fingers. Interlock your left and right-hand fingers. If you are not able to interlock your fingers, keep your hands at the back. Keep your back and neck straight. Look forward and close your eyes. Maintain the final position for about 10 s–1 min, depending on your capacity. Come back in the reverse order. Repeat this on the opposite side
Janushirsasana	Sit with both legs straight in front. Bend your right leg at the knee and bring your right heel against the left groin. While inhaling, raise your arms. While exhaling, move forward and try to hold the left foot with your hands. If you are not able to hold the left foot, try to hold your left ankle. Maintain the final position for about 10 s–1 min, depending on your capacity. While returning to your initial position, raise your hands on inhalation and bring them down on exhalation. Repeat this on the opposite side
Vakrasana	Sit with both legs straight in front. Bend your right leg and place your right foot next to the left knee. Keep the spine straight and twist your waist toward the right side. Keep your right palm behind the spine. Look behind. Bring the left arm near to your right knee and hold the right big toe. If you are not able to hold your toe, hold your right knee. Maintain the final position for about 10 s–1 min, depending on your capacity. Come back in the reverse order. Repeat this on the opposite side
Ardha-padmasana	Sit with both legs straight in front. Fold the left leg and place the left foot on top of your right thigh. Without straining, try to place the heel of your left leg as near as possible to the abdomen. Fold your right leg. Adjust your body to a comfortable position. Keep your back, neck, and head straight. Place the hands on your knees. Close your eyes and relax your body. Maintain the final position for about 10 s–1 min, depending on your capacity. Come back to your initial position. Repeat this on the opposite side
Vajrasana	Sit with both legs straight in front. Fold your right leg and place the right heel under the right buttock. Similarly, place the left heel under the left buttock. Place the hands on your knees. Relax your arms and the whole body. Maintain the final position for about 10 s–1 min, depending on your capacity. Come back to your initial position
Ekpadottanasana	Lie in the supine position. Bring the feet together. Keep your palms close to the thighs. While inhaling, raise your right leg to make an angle of 60° with the ground, slightly bending your right knee. You may hold your thigh with your hands or use a towel to support your leg. Maintain the final position for about 10 s–1 min, depending on your capacity. Feel the strain in your legs and your abdomen. Do not tense your neck or face at all. While exhaling, bring your leg down to the initial position. Repeat this on the opposite side
Naukasana	Lie in the supine position. Bring the feet together. Keep your hands by the side of your body, and your palms on the ground. Bring your heels close to your hips. Raise your right leg to make an angle of 60° with the ground. Hold the right leg with your right hand. Raise your left leg to make an angle of 60° with the ground. Hold the left leg with your left hand. Gently raise your head, neck, and trunk. Maintain the final position for about 10 s–1 min, depending on your capacity. Come out of this pose before you feel any pain in your abdomen. Come back in the reverse order

Contd...

Supplementary Table 4: Contd...

Health rejuvenating exercises/asana/pranayam/ meditation and relaxation techniques	Procedure
Ardha-pavanamuktasana	Lie in the supine position. Bring the feet together. Bend your right leg, and bring the thigh and knee as near as possible to the chest. The other leg should remain straight. Place your hands over the knee and interlock your fingers. Gently pull the knee nearer to the chest. Keep your back and head on the floor. Maintain the final position for about 10 s–1 min, depending on your capacity. Come back to your initial position. Repeat this on the opposite side
Markatasana	Lie in the supine position. Bring the feet together. Stretch your arms to the sides. Keep your palms up. Fold your legs and keep them near your hips. Turn your knees toward the right side, and rest your right knee on the ground, your left knee on your right knee, and your left ankle on your right ankle. Keep your shoulders on the floor. Gently turn your neck to the left side. Maintain the final position for about 10 s–1 min, depending on your capacity. Come back to your initial position. Repeat this on the opposite side
Merudandasana	Take the supine pose. Bring the feet together. Stretch your arms to the sides. Keep your palms down. Bend your right leg, and place the right foot on your left knee. Gently twist the spine. Try to drop your right knee on the opposite side floor as much as possible. Keep your shoulders on the floor. Gently turn your neck to the right side. Maintain the final position for about 10 s–1 min, depending on your capacity. Come back to your initial position. Repeat this on the opposite side
Anulomvilom/nadishodhana pranayama	Sit in any comfortable pose or on a chair with your spine erect. Fold the index and middle fingers of your right hand. Close your eyes. Use your thumb and ring finger to practice this Pranayama. Close the right nostril with your thumb. Inhale slowly and completely through your left nostril. Close the left nostril with your ring finger. Open your right nostril, and exhale slowly and completely through it. Inhale through the right nostril. Close the right nostril with your thumb. Open your left nostril, and exhale slowly and completely through it. Try to keep the time of exhalation longer than inhalation. This constitutes one round of Nadishodhana
Bhramari pranayama	Sit in any comfortable pose or on a chair with your spine erect. Close your ears with your respective thumbs. Place your index fingers at the top of your eyebrows, close your eyes with your middle fingers, place your ring fingers on the sides of your nose, and your little fingers on the corners of your lips. Press all these points softly. Inhale deeply through your nose. Keep the mouth closed. Breathe out slowly producing a long continuous humming sound like a bee. Exhalation should be slow and long
Ujjayi pranayama	Sit in any comfortable pose or on a chair with your spine erect. Keep your hands on the knees. Close your eyes. Try to contract the inside of your throat after bending the neck a little. Inhale slowly through both nostrils, producing a hissing sound in such a way that its touch is felt from the throat to the chest. Exhale gently through both nostrils
Sitali pranayama	Sit in any comfortable pose or on a chair with your spine erect. Keep your hands on the knees. Close your eyes. Roll the tongue into a "U" shape, with the tip just outside of your lips. Inhale deeply through the rolled tongue. Exhale slowly through both nostrils
Sitkari pranayama	Sit in any comfortable pose or on a chair with your spine erect. Keep your hands on the knees. Close your eyes. Fold the tongue so that the tip of your tongue touches the upper palate. You may keep the two rows of teeth in contact. Inhale through your mouth with a hissing sound. Exhale slowly through both the nostrils. Continue this practice for 5 min
Chanting	Sit in any comfortable pose or on a chair with your spine erect. Keep your hands on the knees. Close your eyes. Relax your body. Inhale slowly and deeply through your nose. While exhaling, chant "M" loudly and prolonged with lips closed. A deep, long, continuous, and steady sound should vibrate all over the body. Do not push your breath beyond the comfort point
Mindfulness meditation	Sit in any comfortable pose or on a chair with your spine erect. Keep your hands on the knees. Close your eyes. Relax your body. Concentrate and feel- "The blockage in the arteries of my heart is opening. The blood circulation is getting normal"

Contd...

Supplementary Table 4: Contd...

Health rejuvenating exercises/asana/pranayam/ meditation and relaxation techniques	Procedure
Shavasana	Lie in the supine position. Keep your spine and neck straight, without any stiffness. Close your eyes
	Focus your complete attention on each part of your body one by one. Allow that particular part to relax, and feel it getting relaxed
	Relax your right big toe, and then relax your other right toes, right sole, right heel, right ankle, right calf muscle, right knee, right thigh, and right buttock. Now, relax your left big toe, then relax your other left toes, left sole, left heel, left ankle, left calf muscle, left knee, left thigh and left buttock. Relax your legs completely
	Relax your lower back, and then relax your middle back, upper back, lower abdomen, upper abdomen, and chest. Relax your trunk completely
	Relax your right-hand fingers, and then relax your right palm, right wrist, right forearm, right elbow, right arm, and right shoulder. Now, relax your left-hand fingers, and then relax your left palm, left wrist, left forearm, left elbow, left arm, and left shoulder. Relax your arms completely
	Relax your neck, throat, chin, jaws, lips, tongue, mouth, cheeks, nose, eyes, ears, temples, forehead, and scalp. Relax your neck and head completely
	Perceive your whole body, and feel it physically and mentally relaxed. If there is stiffness in any part of your body, then relax that particular part. Feel that your whole body is completely relaxed. Maintain this state for a few min
	To finish this meditation and relaxation practice, each and every part of your body needs to be charged with positive energy- start with your legs, then move on to the back of your trunk, abdomen, chest, arms, neck, face, and scalp. Feel your body get completely energized. Take three long breaths. Turn to your right side, put your right elbow below your neck and slowly sit up
Dirghasvasapreksha	Lie in the supine position. Keep your spine and neck straight, without any stiffness. Close your eyes. Relax all the muscles of your body and let them become limp
	Regulate your breathing and make it slow, deep, and rhythmic. Inhalation and exhalation should be performed knowingly. Exclude all thoughts and sensations. If you find yourself getting distracted, gently return your attention to your breath
	Focus your attention on the navel, and become fully aware of the expansion of your abdomen with inhalation and contraction of your abdomen with exhalation. Continue this for a few min
	Now, shift your attention from the navel and focus it on the junction of your nostrils. Each and every inhalation and exhalation needs to be perceived, that is, each and every breath needs to be watched and felt. Continue this for a few min
	To finish this meditation and relaxation, take three long breaths. Turn to your right side, put your right elbow below your neck and slowly sit up
Antarangatrataka	Sit in any comfortable pose or on a chair with your spine erect. Keep your hands on the knees. Close your eyes. Relax your body. Try to visualize a point of light such as a full moon in the dark sky. Concentrate on the object. Try to see the object clearly and steadily in the dark space, in front of your closed eyes