

Effectiveness of a Yoga-based Cardiac Rehabilitation (Yoga-CaRe) Program: A Multi-centre Randomised Controlled Trial of Patients With Acute Myocardial Infarction From India

Dorairaj Prabhakaran MD, DM
Executive Director, CCDC & Vice-President, PHFI

Late breaking Clinical trials – AHA '18

Funding: Indian Council for Medical Research (India) & Medical Research Council (UK)



LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



Yoga-CaRe Trial
Investigators



Audience Response and Q&A System Instructions

- **On your phone or tablet via the AHA app**
 - Locate and open the session
 - Tap or click “Polling/Social Q&A” button



Polling / Social Q&A

- **On your phone, tablet or laptop via web browser**
 - **URL: aha2018.cnf.io**
 - Locate and open the session

Polls will appear on your device when speakers activate slides containing ARS questions.

Yoga-CaRe Trial – The Rationale

- **Cardiac Rehabilitation (CR) is a Class I indication in post MI patients and has become an integral part of cardiac care in High Income Countries.**
- **CR is virtually non-existent in Low-Middle Income Countries due to its high cost and the need for a multidisciplinary team.**
- **Even In high income countries uptake of CR is 25-35% and is particularly poor among the elderly and women who may prefer gentler and simpler approaches.**
- **High unmet need for CR.**

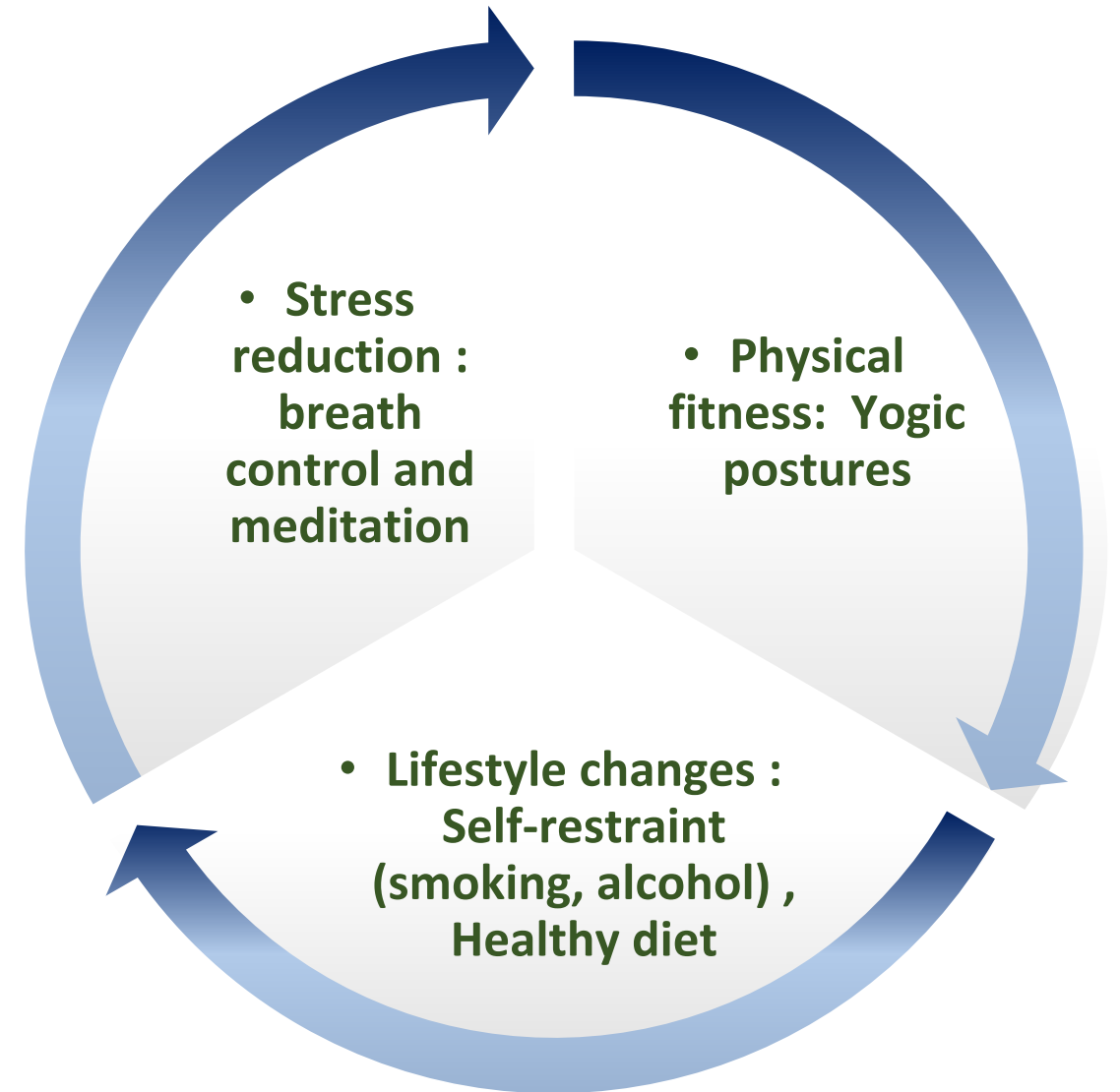
In India, need for developing a low-cost, culturally acceptable and effective cardiac rehabilitation, a need that would be filled by Yoga-CaRe should it prove to be efficacious.

Why Yoga ?

Cardiac Rehabilitation



Yoga



Aims

To compare the effectiveness of Yoga based Cardiac Rehabilitation (Yoga-CaRe), with Enhanced Standard Care (ESC) in post myocardial infarction patients on cardiac morbidity and mortality and quality of life.

Outcomes

1. Primary Outcomes

- a) Time to occurrence of first cardiac event (composite of death, nonfatal myocardial infarction and stroke) & emergency cardiac admissions
- b) Quality of life (EQ-5D-5L) at 12 weeks

2. Secondary Outcomes

- a) Return to pre-infarct daily activities at 12 weeks (RNLI)
- b) Smoking cessation at 12 weeks
- c) Compliance to prescribed medications at 12 weeks

Methods

- **Study sites : 24 centers in India**
- **Study design: PROBE**
- **Trial duration: 50 Months (Aug'14-Sept'18)**
- **Sample size – 3959 Participants**
 - **80% power to detect 20% reduction in cardiovascular events (assumption-20% event rate in control)**
 - **99% power to detect difference in quality of life**
- **Analysis**
 - **ITT**
 - **Per protocol**
- **Inclusions**
 - **Age – 18-80 years**
 - **Within 14 days of acute myocardial infarction (WHO/3rd Universal Definition)**
 - **Willing and able to attend the complete CR program**
- **Exclusions**
 - **Patients not likely to complete follow up**
 - **Self reported regular practice of Yoga (> 3hours a week)**
 - **Participation in other clinical trials**
 - **Comorbidity which limits life expectancy <=12 months**

Intervention and Enhanced Standard Care

Development : Structured process.

- Literature review; Consultation with yoga experts, CR experts and Post MI patients
- Refinement : Feedback from an internal stakeholder group and an external panel of international experts
- Piloted with yoga teachers and post MI patients

Components of Yoga :

- 3 health rejuvenating exercises
- 15 postures
- 5 breathing techniques 5 meditative techniques

Structure: Yoga-CaRe sessions aligned to CR phases

Week1: Education on life style (Session 1)

Week 3: Meditation and breathing (Session 2)

Weeks 5-7: Full Yoga training sessions, twice per week (Sessions 3-8)

Weeks 8-13: Full Yoga training sessions , once per week (Sessions 9-13)

Week 14+: Self practice at home

Control group received enhanced standard care:

- 3 session educational information before discharge from the hospital and subsequently at weeks 5 and 12
- Printed leaflet
- Delivered by nurse or another member of cardiac care team either individually or in groups to avoid contamination

Personnel: Trained Yoga instructors to deliver pre-selected Yoga practices and health education

Consort – Flow Diagram

Assessed for eligibility (n=6737)

Excluded (n=2727)
-Not meeting inclusion criteria; IC (n=200)
-Declined to participate (n=2527)

Randomized (n=4010)

Excluded (n=51) did not meet IC
-Yoga CaRe group (n=35)
-Enhanced Standard Care group (n=16)

Evaluable (n=3959)

Did not receive allocated intervention (≤1 session; n=160)

- Death/event before intervention (n=34)
- Consent withdrawal (n=5)
- Others Incomplete information (n=121)

Yoga-CaRe (n=1970)

Enhanced Standard Care (n=1989)

Did not receive allocated intervention (n=22)

- Death / event before 17 days (n=20)
- Consent withdrawal (n=2)

ITT Analysis (n=1970)

ITT Analysis (n=1989)

Baseline Characteristics

Variables	Enhanced Standard care n=1989	Yoga-CaRe n=1970
Age, years Mean(SD)	53.4 (10.8)	53.4 (11.0)
Women	14.1%	13.8%
STEMI	76.0%	75.0%
Anterior wall MI	57.8%	57.1%
Vessel involvement - Single	55.6%	56.4%
Past history of CAD	21.2%	22.3%
Diabetes	29.1%	28.1%
Hypertension	28.7%	30.1%
Current tobacco	29.8%	31.0%
Physical inactivity	54.3%	53.9%

Baseline Characteristics -2

Variables	Enhanced Standard care n=1989 (%)	Yoga-CaRe n=1970 (%)
Revascularization	62.1	60.7
PCI	58.2	57.4
CABG	4.5	3.9
Antiplatelet	98.5	98.5
Dual antiplatelet	83.5	84.3
ACE/ARB	49.4	51.4
Beta blockers	62.6	62.6
Statins	93.2	93.2

High standard of contemporary cardiac care in both arms

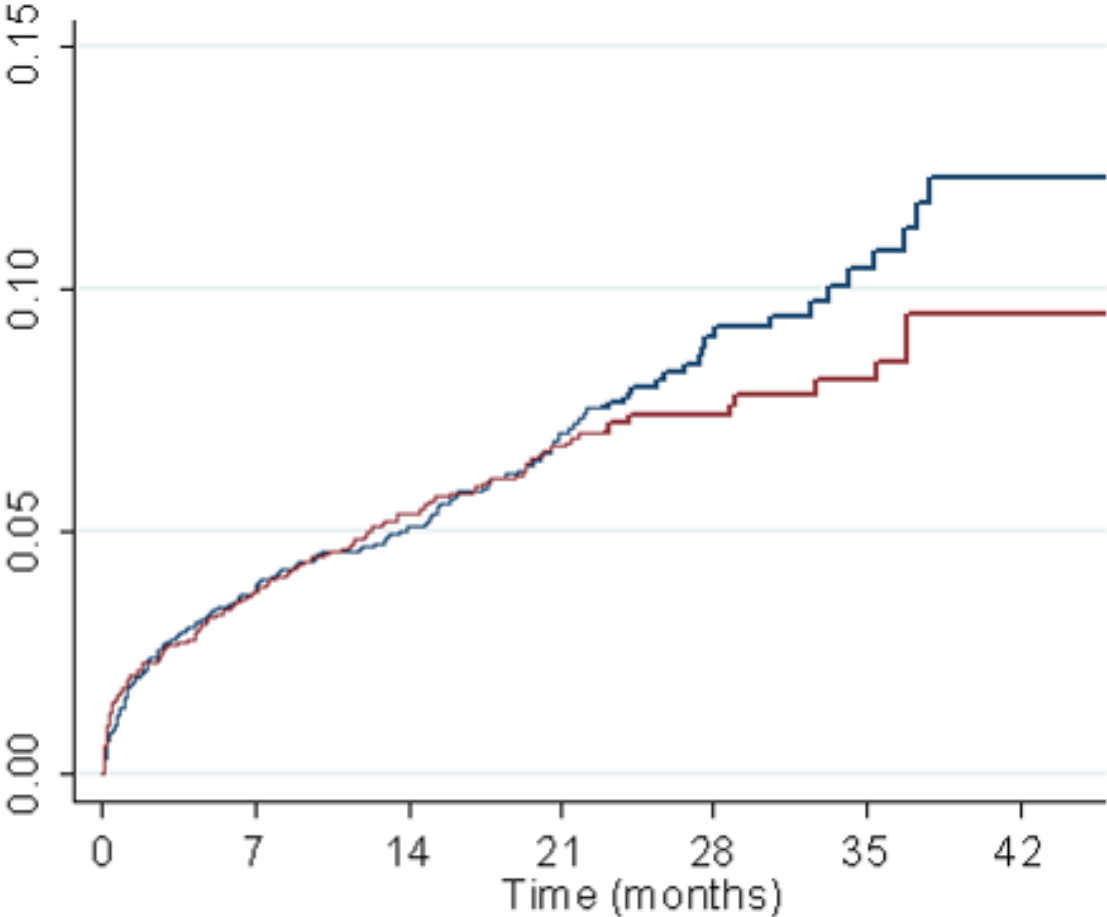
Primary Outcomes (ITT)

Co-Primary Outcome 1	ESC (n=1989) n (%)	YC (n=1970) n (%)	Hazards Ratio, 95% CI (unadjusted)	p-Value
<u>First Co-Primary outcome</u>	<u>146 (7.3)</u>	<u>131 (6.7)</u>	<u>0.91 (0.72, 1.14)</u>	<u>0.33</u>
Death	77 (3.9)	78 (4.0)	1.02 (0.75, 1.40)	0.99
Non fatal Myocardial Infarction	15 (0.8)	13 (0.7)	0.88 (0.42, 1.84)	0.73
Non fatal Stroke	3 (0.2)	4 (0.2)	1.34 (0.30, 6.0)	0.43
Emergency Cardiovascular hospitalisations	59 (3.0)	48 (2.4)	0.82 (0.56, 1.20)	0.26

HR remains same after adjusting for baseline covariates, risk profiles and treatments at discharge

Numerically fewer outcomes in the Yoga-CaRe group, but not statistically significant

Primary Outcomes (ITT) - Kaplan Meir plot of Cardiovascular Events



HR[CI] = 0.91[0.72, 1.15]

Log rank test, p=0.41

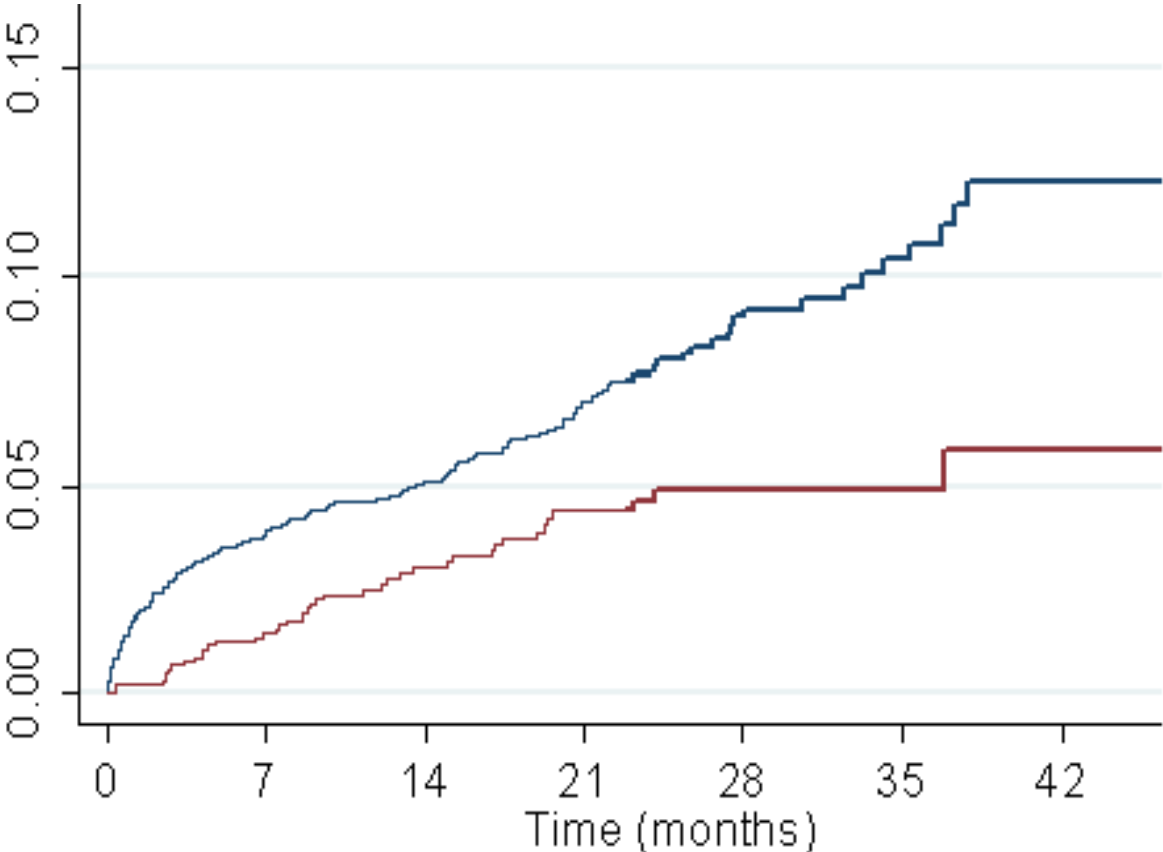
Less than half the number of events as compared to the original assumption

Number at risk

Enhanced Standard Care	1989	1767	1381	1038	477	242	87
Yoga CaRe	1970	1750	1378	1019	467	248	89

— Enhanced Standard Care — Yoga CaRe

Primary Outcomes (Per-protocol): Kaplan Meir plot of Cardiovascular Events



Number at risk

Enhanced Standard Care	1989	1767	1381	1038	477	242	87
Completers	1059	956	711	468	208	116	67



Primary Outcome (ITT)

Co-Primary Outcome 2	ESC (n=1989) Mean (CI)	YC (n=1970) Mean (CI)	Regression Coefficient, 95% CI (unadjusted)	p
Mean Change in EQ-5D VAS Score (from baseline to three months)	<u>9.2 (8.4, 10.1)</u>	<u>10.7 (9.9, 11.5)</u>	<u>1.4 (0.3, 2.5)</u>	<u>0.002</u>

Coefficient remained significant after adjusting for baseline covariates, risk profiles and treatments at discharge

“Improvement in the Self-rated quality of life was significantly greater in the Yoga-CaRe group”

Secondary outcomes: ITT Analysis

Outcomes at three months	Unadjusted Regression coefficient (CI)	p-Value
Change in health states - EQ-5D	-0.03 (-0.19, 0.13)	0.72
Return to Pre-infarct daily activities	<u>1.17 (0.11, 2.23)</u>	<u><0.001</u>
Outcomes at three months	Unadjusted Odds Ratio (CI)	p-Value
Health states (≤ 6)	<u>1.16 (1.01, 1.34)</u>	<u>0.04</u>
Tobacco cessation	1.14 (0.89, 1.46)	0.11
High compliance to medication	1.04 (0.91, 1.19)	0.52

Conclusions

- Yoga-CaRe, a yoga based CR, is safe, **feasible** and significantly improves quality of life and return to pre-infarct daily activities.
- **The clinical outcomes were not different between the two groups (Inadequate power to detect the planned difference due to lower event rate than estimated).**
- Per-protocol analysis showed Yoga-CaRe program to be efficacious in improving clinical outcomes suggesting a potential dose-response relationship.
- Yoga-CaRe has the potential to be an alternative to the conventional CR programs and address the unmet needs of cardiac rehabilitation for patients in low- and middle-income countries.

- Based on the results, do you recommend Yoga-CaRe programme for your patients
 - Yes
 - No
 - Unsure

Live Content Slide

When playing as a slideshow, this slide will display live content

Poll: Based on the results, do you recommend Yoga-CaRe programme for your patients

Contributors

**Dorairaj Prabhakaran (India) & Sanjay Kinra (UK) –
Principal Investigators**

Co-Investigators & Research Team

Ambuj Roy	Subash Chander Manchanda
Ajay Vamdevan	K Srinath Reddy
Nish Chaturvedi	Alun Hughes
Ian Roberts	Stuart Pocock
Shah Ebrahim	Chandrasekaran AM
Kalpana Singh	Kaushik Chattopadhyay
Kavita Singh	Divya Soni
Dimple Kondal	Praveen Pradeep
Raji Devarajan	Nikhil Tandon

**Trial Steering Committee, Data Monitoring and Ethics
Committee & Endpoint Adjudication Committee**

Acknowledgement:

Clinical site – Research Team

Indian Council for Medical Research

Yoga-CaRe Instructors

Medical Research Council

Top Clinical Sites

DMC Ludhiana
CH Pune & Bengaluru
IGMC Shimla
SJICSR Bengaluru
SJICSR Mysuru
JSS Hospital
KPKH Belagavi
SGRH New Delhi
LSSH Guntur
KGMU Lucknow
BLDE Vijapura
CARE Hyderabad
AIIMS New Delhi
GKNM Coimbatore

Site-Investigators

Bishav Mohan
Davinder Singh Chadha
Sanjeev Asotra & PC Negi
Prabhavathi
K Sadananda
Nagaraj Desai & Sunil Kumar
Prasad
Subash Chander Manchanda
PV Ragahv Sarma
Sharad Chandra
Shankar Patil
Calambur Narasimhan
Ambuj Roy
S Natarajan

Trial Participants & families