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)
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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

- Stress Reduction: Counselling/medication for depression
- Physical fitness: Exercise
- Lifestyle changes: Smoking cessation, Nutrition counselling and other healthy behaviors

Yoga

- Stress reduction: breath control and meditation
- Physical fitness: Yogic postures
- Lifestyle changes: Self-restraint (smoking, alcohol), Healthy diet
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
- Week 1: Education on lifestyle (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
Excluded (n=2727)  
- Not meeting inclusion criteria; IC (n=200)  
- Declined to participate (n=2527)  

Assessed for eligibility (n=6737)  

Randomized (n=4010)  

Evaluable (n=3959)  

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

Yoga-CaRe  (n=1970)  

Enhanced Standard Care  (n=1989)  

Did not receive allocated intervention (≤1 session; n=160)  
- Death/event before intervention (n=34)  
- Consent withdrawal (n=5)  
- Others incomplete information (n=121)  

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

<table>
<thead>
<tr>
<th>Variables</th>
<th>Enhanced Standard care n=1989</th>
<th>Yoga-CaRe n=1970</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years Mean(SD)</td>
<td>53.4 (10.8)</td>
<td>53.4 (11.0)</td>
</tr>
<tr>
<td>Women</td>
<td>14.1%</td>
<td>13.8%</td>
</tr>
<tr>
<td>STEMI</td>
<td>76.0%</td>
<td>75.0%</td>
</tr>
<tr>
<td>Anterior wall MI</td>
<td>57.8%</td>
<td>57.1%</td>
</tr>
<tr>
<td>Vessel involvement - Single</td>
<td>55.6%</td>
<td>56.4%</td>
</tr>
<tr>
<td>Past history of CAD</td>
<td>21.2%</td>
<td>22.3%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>29.1%</td>
<td>28.1%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>28.7%</td>
<td>30.1%</td>
</tr>
<tr>
<td>Current tobacco</td>
<td>29.8%</td>
<td>31.0%</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>54.3%</td>
<td>53.9%</td>
</tr>
</tbody>
</table>
## Baseline Characteristics -2

<table>
<thead>
<tr>
<th>Variables</th>
<th>Enhanced Standard care</th>
<th>Yoga-CaRe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revascularization</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>n=1989</td>
<td>n=1970</td>
</tr>
<tr>
<td></td>
<td>(%)</td>
<td>(%)</td>
</tr>
<tr>
<td>PCI</td>
<td>62.1</td>
<td>60.7</td>
</tr>
<tr>
<td>CABG</td>
<td>4.5</td>
<td>3.9</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>98.5</td>
<td>98.5</td>
</tr>
<tr>
<td>Dual antiplatelet</td>
<td>83.5</td>
<td>84.3</td>
</tr>
<tr>
<td>ACE/ARB</td>
<td>49.4</td>
<td>51.4</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>62.6</td>
<td>62.6</td>
</tr>
<tr>
<td>Statins</td>
<td>93.2</td>
<td>93.2</td>
</tr>
</tbody>
</table>

*High standard of contemporary cardiac care in both arms*
# Primary Outcomes (ITT)

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

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

HR[CI] = 0.54 [0.38, 0.76]
Log rank test, p<0.001

Completers = those who participated in ≥10 Yoga-CaRe sessions
Primary Outcome (ITT)

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

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

<table>
<thead>
<tr>
<th>Outcomes at three months</th>
<th>Unadjusted Regression coefficient (CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in health states - EQ-5D</td>
<td>-0.03 (-0.19, 0.13)</td>
<td>0.72</td>
</tr>
<tr>
<td>Return to Pre-infarct daily activities</td>
<td>1.17 (0.11, 2.23)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcomes at three months</th>
<th>Unadjusted Odds Ratio (CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health states (&lt;6)</td>
<td>1.16 (1.01, 1.34)</td>
<td>0.04</td>
</tr>
<tr>
<td>Tobacco cessation</td>
<td>1.14 (0.89, 1.46)</td>
<td>0.11</td>
</tr>
<tr>
<td>High compliance to medication</td>
<td>1.04 (0.91, 1.19)</td>
<td>0.52</td>
</tr>
</tbody>
</table>
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
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 Chattopadhayay
Kavita Singh  Divya Soni
Dimple Kondal  Praveen Pradeep
Raji Devarajan  Nikhil Tandon

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

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

Acknowledgement:

Clinical site – Research Team
Indian Council for Medical Research

Yoga-CaRe Instructors
Medical Research Council

Trial Participants & families