



# Tertiary Prevention of Ischemic Heart Disease: Post Coronary Artery Bypass Surgery

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## ABSTRACT

Coronary heart disease is more prevalent in Indian urban populations and there is a clear declining gradient in its prevalence from semi-urban to rural populations. Epidemiological studies show a sizeable burden of coronary heart disease in adult rural (3–5%) and urban (7–10%) populations. Thus, of the 30 million patients with coronary heart disease in India, there would be 14 million who are in urban and 16 million in rural areas. In India, about 50% of coronary heart disease-related deaths occur in people younger than 70 years compared with only 22% in the West. Extrapolation of these numbers estimates the burden of coronary heart disease in India to be more than 32 million patients. In India, there are large spectrums of patients who present at tertiary stage when first examined. These patients are left with very little margin of safety. Heart disease is one of the commonest causes of mortality and morbidity worldwide. Coronary artery bypass graft (CABG) surgery is a frequently used cardiothoracic revascularization to treat coronary artery disease (CAD).

In addition to physical impairments and activity restrictions in the immediate postoperative period, patients encounter some obstacles to exhibit improvements in quality of life in the long run. Cardiac tertiary prevention programs generally consist of the prevention of disease progression and patient suffering. Aim of these interventions is to reduce the negative impact of disease by restoring function and reducing disease-related complications and therefore, include the rehabilitation of disabling conditions. Cardiac rehabilitation programs are interventions aimed to reduce mortality and morbidity of patients with ischemic heart diseases through promoting a healthier lifestyle among patients. These programs are used to restore, maintain, or improve both physiologic and psychosocial outcomes and finally the quality of life in patients through a combination of exercise, education and psychological support.

**Keywords:** Cardiac surgery, Cardiac tertiary prevention programs, Coronary artery bypass grafting, Coronary heart disease.

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## INTRODUCTION

Coronary heart disease is more prevalent in Indian urban populations and there is a clear declining gradient in its prevalence from semi-urban to rural populations. Epidemiological studies show a sizeable burden of coronary heart disease in adult rural (3–5%) and urban (7–10%) populations. Thus, of the 30 million patients with coronary heart disease in India, there would be 14 million are in urban and 16 million in rural areas.<sup>1-3</sup> In India about 50% of coronary heart disease-related deaths occur in people younger than 70 years compared with only 22% in the West. Extrapolation of these numbers estimates the burden of coronary heart disease in India to be more than 32 million patients.<sup>4</sup> In India there are large spectrum of patients who present at tertiary stage when first examined. These patients are left with very little margin of safety. Heart disease is one of the commonest causes of mortality and morbidity worldwide. Coronary artery bypass graft (CABG) surgery is a frequently used cardiothoracic revascularization to treat coronary artery disease (CAD).<sup>5</sup> In addition to physical impairments and activity restrictions in the immediate postoperative period, patients encounter some obstacles to exhibit improvements in quality of life in the long run. Cardiac tertiary prevention programs generally consist of the prevention of disease progression and patient suffering. Aim of these interventions is to reduce the negative impact of disease by restoring function and reducing disease-related complications and, therefore, include the rehabilitation of disabling conditions.<sup>6-8</sup> Cardiac rehabilitation programs are interventions aimed to reduce mortality and morbidity of patients with ischemic heart diseases through promoting a healthier lifestyle among patients. These programs are used to restore, maintain, or improve both physiologic and psychosocial outcomes and finally the quality of life in patients through a combination of exercise, education and psychological support.



## Literature Search Methods

A literature search was performed in Medline, Google, PubMed, using the following headings: 'Cardiovascular disease-related mortality in India', 'primary, secondary and tertiary prevention of coronary heart disease', 'tertiary prevention of coronary heart disease', 'coronary artery bypass grafting', and 'cardiac surgery'.

## Literature Search Results

To evaluate patients' quality of life, the short form 36 (SF-36) questionnaire (Persian standard version) was completed for all patients at an average time of 23.4 months afterward CABG. The reliability and validity of the Persian version of the SF-36 have been well established.<sup>9,10</sup> Short form-36 is a 36 item scale that generates scores for eight items which can finally establish physical and mental component summary scores. Physical component summary score includes physical functioning, role limitations due to physical health, bodily pain, and self-perception of general health. Mental component summary score includes vitality, social functioning, role limitations due to emotional problems, and mental health. Short form-36 scores were calculated according to the methods determined by the authors of the questionnaire.<sup>11,12</sup> A questionnaires was used to collect data on age, sex, medical history and attendance in cardiac tertiary prevention programs.

Patients in CR group were attended in a cardiac tertiary prevention program 10.6 ± 1 weeks after operation at Isfahan Cardiac Research Center.<sup>13</sup> The program was at least 8 weeks long and consisted of exercise training and dietary and psychological counseling.

Morbidity and mortality were assessed via telephone interviews approximately 23.4 ± 1 months after CABG.<sup>14-17</sup> The interview was comprised of questions related to the recurrence of angina, subsequent cardiovascular associated hospitalization and/or contact with the healthcare system, such as emergency department. During this interview, participants were asked about chest pain and shortness of breath on the basis of the NYHA, and the occurrence of any neurological symptoms representative of transient ischemic attack or stroke. Patients were also questioned regarding their level of activity, their employment status and their restoration to previous level of performance in social activities after surgery.

Statins appear to exert several beneficial, non-lipid related actions in many cardiothoracic surgical operations, namely CABG, valve surgery, heart and lung transplantation, pulmonary lobectomy/pneumonectomy and thoracic aortic aneurysm surgery.<sup>18</sup> Current evidence suggests that a large percentage of cardiothoracic surgical

patients are under treated with respect to statins. This has considerable implications for perioperative, as well as long-term morbidity and mortality rates.<sup>19,20</sup> In the last few years, there is accumulating evidence that statins (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) exert several non-lipid related actions.<sup>21,22</sup> Statins have an established role in primary and secondary prevention of cardiovascular events. Besides this, however, a number of studies suggest that statins exert pleiotropic actions in patients undergoing percutaneous or open surgical procedures.<sup>23</sup> Early studies showed that atherosclerosis frequently develops in saphenous vein coronary bypass grafts leading to occlusion rates as high as 40% at 10 to 12 years.<sup>24, 25</sup> Following an observational study following up 1041 post-CABG patients for 20 years showed that one in five patients underwent repeat CABG and another 7% had percutaneous transluminal coronary angioplasty during this time period.<sup>26,27</sup> These progressive atherosclerotic obstructive changes are especially common in patients with hyperlipidemia. The key role of managing hyperlipidemia in these patients was demonstrated in the post-CABG trial.<sup>28</sup> Compared with moderate lipid-lowering treatment with lovastatin [target low-density lipoprotein cholesterol (LDL-C): 132–136 mg/dl],<sup>29</sup> aggressive lovastatin treatment aiming at target LDL-C levels <100 mg/dl<sup>30</sup> resulted in a reduced percentage of grafts per patient with angiographically detected atherosclerosis progression after a mean follow-up of 4.3 years (39 vs 27%, respectively;  $p < 0.001$ ). Similar results were reported regarding the mean percentage of grafts per patient with occlusion or new lesions. The post-CABG trial was designed to have adequate power to detect treatment-related differences in angiographic characteristics but not in clinical events. As a result, a reduction in the number of clinical events was not seen. Nevertheless, a 29% lower rate of revascularization procedures was observed in the aggressive compared with the moderate treatment group ( $p = 0.03$ ).<sup>31</sup> In an extended follow-up report of the post-CABG trial evaluating the long-term (7.5 years) effects of moderate as compared with aggressive lipid-lowering treatment with lovastatin, the initial 29% difference in the revascularization rates between the two groups<sup>31</sup> increased to 42% (or 30% increase;  $p = 0.0006$ ).<sup>32</sup> Similarly, a significant 24% difference was observed in the composite end-point (death from cardiovascular or unknown causes, non-fatal myocardial infarction (MI), stroke, CABG or percutaneous transluminal coronary angioplasty) between the moderate and aggressive lipid-lowering groups (40.4 vs 32.0%, respectively = 0.001).<sup>32</sup> The long-term clinical benefit in post-CABG patients assigned to aggressive lipid-lowering treatment provides rationale

for postoperative initiation of high-dose statin treatment in these patients. Following the post-CABG trial, several other studies on patients undergoing CABG showed that statin treatment is beneficial in these patients with respect to the incidence of postoperative adverse cardiovascular outcomes (unstable angina, MI, arrhythmia, stroke and cardiac death). The possible mechanisms through which statins exert their beneficial actions in CABG are reviewed elsewhere.<sup>33-35</sup> Briefly, these include reduction of inflammation and oxidative stress, improvement of vascular endothelial function and management of postoperative hyperlipidemia/dyslipidemia.<sup>33-35</sup> Lipid-lowering in post-CABG patients is crucial; hyperlipidemia is responsible for the development of atherosclerotic changes in vein grafts eventually leading to graft occlusion.<sup>34,35</sup> Preoperative statin therapy in CABG patients improves postoperative myocardial perfusion of bypassed areas.<sup>36</sup> It also significantly reduces cytokine release [such as interleukin (IL-6<sup>37-39</sup> and IL-8<sup>37</sup>)] and neutrophil adhesion to the venous endothelium via a nitric oxide-mediated mechanism. Preoperative statin treatment is also associated with improved perioperative mortality rates<sup>40-43</sup> and reduced risk of postoperative thrombocytosis and thrombotic complications.<sup>44</sup> Postoperative thrombocytosis occurs in 20 to 30% of the patients undergoing CABG and it is associated with an increase in late thrombotic complications.<sup>45</sup> Furthermore, pre-CABG statin use is associated with a 33% reduction in the odds of developing a postoperative infection and a 20% reduction in the odds of requiring a prolonged post procedural hospitalization.<sup>46</sup> Another beneficial action of statins in CABG patients is stroke prevention, which is one of the most serious complications of this procedure,<sup>47</sup> a recent prospective study showed that, compared with non-use, statin treatment for at least 4 weeks prior to surgery was significantly and independently associated with a lower risk of perioperative cerebrovascular events [odds ratio (OR) 0.26; 95% confidence interval (CI) 0.06–0.86;  $p = 0.027$ ].<sup>47</sup> Acute renal failure occurs in 1 to 5% of the patients following CABG surgery.<sup>48-50</sup> It is associated with mortality rates as high as 60%<sup>48,49</sup> and substantial increases in the lengths of intensive care and hospital stay.<sup>48-50</sup> A large, multi-center trial including 19,625 patients undergoing isolated CABG surgery showed that patients with preoperative non-dialysis-dependent renal dysfunction had significantly higher in-hospital mortality (adjusted OR 3.0;  $p < 0.001$ ), stroke (adjusted OR 2.0;  $p = 0.33$ ), atrial arrhythmia (adjusted OR 1.5,  $p = 0.003$ ), prolonged ventilation (adjusted OR 2.1;  $p < 0.001$ ), postoperative hospital stay  $> 6$  days (adjusted OR 2.6;  $p < 0.001$ ) and follow-up mortality rates (adjusted OR 2.7;  $p < 0.001$ ).<sup>51</sup> A retrospective cohort study including 1802 CABG patients suggested that preoperative statin

therapy might be renoprotective in patients undergoing CABG.<sup>52</sup> By multivariate analysis, preoperative statin use was associated with an almost 50% lower incidence of new postoperative renal insufficiency (OR 0.54, 95% CI 0.18–0.82;  $p = 0.047$ ).<sup>52</sup> Statins exert several beneficial actions on saphenous venous bypass graft patency rates. A 4-year prospective study with a median follow-up of 32 months (mean: 38.54–0.54 months) investigated predictors of symptom recurrence (recurrent angina, MI and congestive heart failure) and adverse cardiac events (MI, coronary reintervention and any cardiac-related mortality including sudden cardiac death) in 591 patients undergoing CABG.<sup>53</sup> Following the procedure, statins were used in 391 patients (66.1%). Postoperative statin use was associated with both decreased symptom recurrence [hazard ratio (HR) 0.157, 95% CI 0.075–0.330;  $p < 0.0001$ ] and adverse cardiac events (HR 0.178, 95% CI 0.076–0.418;  $p < 0.0001$ ).<sup>53</sup> Similar results were also reported in other studies;<sup>31,54-58</sup> statins improve endothelial cell function and inhibit smooth muscle cell proliferation in human saphenous veins, thus, effectively decreasing progression of atherosclerosis in the vein grafts used in CABG.<sup>31,54-58</sup> An interesting study evaluated the predictive role of preoperative C-reactive protein (CRP) levels in the long-term outcome of 843 patients undergoing CABG.<sup>59</sup> Among operative survivors (753 patients with low CRP ( $< 1.0$  mg/dl) and 87 with high CRP (1.0 mg/dl)),<sup>60</sup> patients in the low CRP group had significantly better 12-year overall survival rate (74.1 vs 63.0%;  $p = 0.004$ ) and survival freedom from fatal cardiac events (86.7 vs 78.1%;  $p = 0.008$ ).<sup>61-64</sup>

## DISCUSSION

Primary, secondary and tertiary prevention are three terms that map out the range of interventions available to health experts. Prevention includes a wide range of activities aimed at reducing risks or threats to health. Primary prevention aims to prevent disease or injury before it ever occurs. Secondary prevention aims to reduce the impact of a disease or injury that has already occurred. This is done by detecting and treating disease or injury as soon as possible to halt or slow its progress, encouraging personal strategies to prevent injury or recurrence, and implementing programs to return people to their original health and function to prevent long-term problems. Examples include: regular examinations and screening tests to detect disease in its earliest stages, low-dose aspirins and/or diet and exercise programs to prevent further heart attacks, suitably modified work so ill workers can return safely to their jobs. Aim of tertiary prevention is to soften the impact of an ongoing illness that has long-lasting effects. This is done by helping



people manage long-term health problems. In order to improve as much as possible their ability to function, their quality of life and their life expectancy by cardiac rehabilitation programs. Examples include: cardiac rehabilitation programs, chronic disease management programs. Support groups that allow members to share strategies for living well and vocational rehabilitation programs to retrain workers for new jobs when they have recovered. The burden of cardiovascular disease and its risk factors in India calls for an effective public health approach to stop the epidemic. Efforts to put in place an intervention program. Intervention program should be complemented with a robust surveillance mechanism so as to monitor, evaluate and guide policies and program. It has been demonstrated in a pilot mode that it is possible to establish surveillance for cardiovascular disease risk factors at community levels. It has been scaled up to the national level, and is now included in the National Programme for Prevention and Control of Diabetes and Cardiovascular Diseases. The future of surveillance systems lies in its timeliness, systems approach and enduring partnerships with public. Consolidating on the gains will push the path for the forward. Two systematic reviews that analyzed<sup>48</sup> randomized controlled trials reported a 20% decrease in all-cause mortality and a 27% reduction in cardiac mortality in participants of cardiac rehabilitation programs at 2 to 5 years after surgery. The improvement in general health status has been shown 5 years after CABG. It has been demonstrated that patients who attended cardiac rehabilitation recognized their health and overall life situation to be better. There was no difference in the incidence or severity of cardiac associated symptoms and hospitalization between cardiac rehabilitation attendants and non-attendants corroborating the results from another study that investigated the impacts of attendance at cardiac rehabilitation on the outcomes after myocardial infarction.

As patients' perceptions of their health despite of the physical health, determine the likelihood of their return to work after CABG, it is conceivable to observe that cardiac rehabilitation program participants had returned to their previous level of performance in society more than control group. Similar reports in the literature have shown that more rehabilitation participants returned to work and fewer dropped out afterwards cardiac rehabilitation.

## CONCLUSION

While rehabilitation participants are not healthier than their control counterparts, they appear to have a better perception of their health problems and are thus, able to cope better. These findings are comparable with the

results of above mentioned randomized studies reporting better self-perception of health status and viewpoint of overall life situation among post-CABG patients who participated in cardiac rehabilitation programs.

Although, the results of current observational study should be interpreted with caution, and also considering that self-selection of patients participating in cardiac rehabilitation programs may be redolent of their better motivation, the improved health-related quality of life of patients who participated in cardiac rehabilitation after CABG can be interpreted as evidence of the positive effect.

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