CHAPTER II: REVIEW OF LITERATURE

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2.1 Search Strategies

An electronic data base search on prevalence of CAD, its epidemiology & risk factors, pathophysiology of coronary dysfunction, & Quality of life in cardiac patients, exercise testing & training in cardiac patients, clinical outcomes in CAD patients, cardiac rehabilitation status worldwide and separately in India & Iran was performed. In detailed electronic search of comparative randomized clinical trials on Hospital versus Home-based cardiac rehabilitation programs also was performed in Pub Med, Cochrane Library, Pro-quest and Blackwell online journals, BiomedCentral, clinical trials.gov, Evidence Based Medicine Resources(EBM) including Center for Evidence Based Medicine(CEBM), NHS Center for Reviews and Disseminations(CRD), Center for Evidence Based Physiotherapy (CEBP), PEDro, Sum Search database, as well as a hand search on published national studies in both countries was done from the earliest up to August 2007 which was regularly updated till April 2011.

2.2 CVD: Its Prevalence, Epidemiology & Risk Factors

CVD has become the leading cause of death worldwide. This predominance of cardiovascular aetiology was well recognized in developed countries since 70s, representing about 49% of the global mortality, despite important country-to-country variations and a strong tendency to an age-adjusted rate decline in CVD mortality.2-7,42,45 A sharp increase in CVD deaths in Eastern Europe, giving them a mortality rate of 4-5 times greater than that seen in other European countries (such as France, Spain and Italy), which contributes 15% of total world mortality. An emerging epidemic in CVD in developing countries, caused by the decline of disease related to infections and malnutrition and an increase in lifestyle-related pathologies (such as CHD and cancers). Predictions on long term CVD mortality in these countries conclude that a dramatic rise is inevitable if nothing is done to prevent it. Such a rise will affect a relatively younger population and will contribute to a 2.8 times higher rate of age-adjusted disability compared with developed countries. In the face of these facts, the
beneficial effects of cardiac rehabilitation and prevention can no longer be ignored.²

Most Middle Eastern countries such as Iran are joining the global obesity pandemic and its consequences (such as CVD) and the problem becomes more significant when we consider the trend of westernization can potentially put the population of these countries at higher risk of CVD and its risk factors than western countries. As Horton has highlighted, we have an unusual opportunity to act in order to prevent the needless deaths of millions by focusing on risk factors of cardiac disease in low- and middle-income countries.⁵⁷ Kelishadi, Saraf-Zadegan and Nadery (2002) mentioned that the prevalence of CAD has increased in Iran and the mean age of its incidence has decreased. They noticed that concurrently an increasing trend in risk factors for atherosclerosis has been shown in children and adolescent Iranian population.⁴⁴ Bahrami, Sadat-Safavi and Pourshams (2006) concluded that prevalence of obesity and overweight as a risk factor of CVD in Iran-as well as other Middle East countries- is as high as US. They noticed that however, Iranian women are more obese than American women; Iranian men are less obese than their American counterparts. According to their results, prevalence of hypertension and diabetes as other CVD risk factors was similar to US population.⁵⁷ Ghadimi, Bishesari and Allameh (2006) mentioned that few data exist about the clinical epidemiology of myocardial infarction and its complications and mortality rate in Iran. In a one year follow up study, they concluded that MI patients in Iran are younger than in developed countries with higher rates of in-hospital mortality than international statistics.⁵⁸ Chinikar, Maddah and Hoda (2006) postulated that advancing age and diabetes are independent predictors for development of CAD in overweight and obese Iranian women population which is consistent with other countries.⁵⁹ Larijani, Fakhrzadeh and Mohaghegh (2003) studied the burden of CHD on Iranian oil industry. They concluded that direct cost of CHD to Iranian oil industry estimated at 22770 million IR Rials. Working days lost to workers hospitalized for CHD amounted to 62832. They noticed that heavy burden of CHD on Iranian oil industry necessitates the introduction of an industry-wide prevention program.⁶⁰
Hajiloo, Tajik and Sanati (2006) found carriage of L-section 206Leu mutant allele and its association with susceptibility of CAD in Iranian population.\textsuperscript{61} Pahlavan and Frobert (2004) noticed the importance of socio-economic status in cardiovascular disease and the need for health promotion and lifestyle changes.\textsuperscript{62} Azizi, Rahmani and Ghanbarian (2003) found higher levels of total cholesterol, LDL and TG and slightly lower HDL in adult population in Tehran (Capital of Iran) compared with industrialized countries.\textsuperscript{63} Haidari, Mghadam and Chinicar (2001) indicated that a relatively high proportion of Iranian patients with CAD unlike western counterparts have normal levels of traditional lipid risk factors. They postulated that serum concentration of apolipoprotein B (apoB) is the best discriminating factor to predict the presence or absence of atherosclerosis in Iranian normo-lipidemic individuals and young patients undergoing coronary angiography.\textsuperscript{64} Azadbakht, Mirmiran, Smailzadeh and Azizi (2006) studied the Dietary Diversity Score (DDS) and its relation to CVD risk factors in a adult population in Tehran; Iran, and found an inverse association. They postulated that increase in variety of vegetables is helpful in reducing the CVD risk factors.\textsuperscript{65} Daryani, Berglund and Anderson (2005) compared the CHD risk factors among immigrant women from Iran and Turkey with women of Swedish ethnicity. They found heavier weight and abdominal obesity, unfavorable lipid profile and higher degree of physical inactivity in immigrants from Iran and Turkey than Swedish ethnic women.\textsuperscript{66} Gupta and Gupta (2000) reviewed the studies determining CHD prevalence in India. They found that CHD prevalence increased in urban areas from 1% in the 1960s to 9% in the 1990s. In rural areas the rate increased from 2% in the 1970s to 4% in 1990s.\textsuperscript{45} Rajasekhar, Srinivasa Rao and Latheef (2004) mentioned that there will be an increase of 111% in CVD deaths in India by the year 2020, and this is much higher than that predicted in any other region both in Asia as well as outside India. They noticed higher prevalence of CHD in South India. According to them, traditional risk factors like serum cholesterol, blood pressure and smoking account for not more than 50% difference in mortality of CHD. This
led to studies on newer risk factors like fibrinogen, Lp(a), antioxidants etc. In India, Dube (jaipur), Nand (Haryana), and Singh (Moradabad) have reported deficiency of serum vitamin E levels in CHD patients.\(^5\)

Physical inactivity is a well-established risk factor for CHD in western population and is associated with about two fold increase in risk of CHD. It has been postulated that people from Indian ethnicity have an increased susceptibility to CHD both due to genetic factors predisposing to high levels of metabolic cardiovascular risk factors associated with insulin resistance e.g. central adiposity, glucose intolerance, hyperinsulinaemia, and dyslipidaemia as well as to environmental influences which lead to weight gain, rise in blood cholesterol and blood pressure.\(^6\)

Rastogi, Vaz and Spiegelman (2004) for the first time in India highlighted the adverse health consequences of physical inactivity and the importance of leisure time exercise in prevention of CHD and the potential benefit of exercise in urban India where physical inactivity levels are now comparable with west.\(^7\)

Studies of Asian–Indian immigrants show that they suffer between 1.5 to 4.0 times higher CHD mortality compared to other ethnic groups. It is also shown that Asian-Indians in Britain suffer MI at a younger age than Caucasian population with a mean age difference of 5.5 years.\(^67\)

Studies conducted in countries with national health care system have noted approximately twice the risk of hospitalization for ischemic heart disease or MI among South Asian immigrant men relative to native-born men aged 45-64. They also experience the onset of symptomatic heart disease at a younger age than native-born population.\(^68\)

The INTERHEART investigators reported that the prevalence of dyslipidemia (abnormal apolipoprotein apoB/ apoA ratio) among controls without acute MI was higher among study participants living in the five South Asian countries (45%) compared to other 47 countries (35%).\(^4\)

Data from the Seven Countries study showed that large differences in CHD mortality were observed between countries and these differences were most likely due to differences in ethnic group susceptibility and environmental risk factors.\(^5\) The relative importance of CHD varies across regions and from country to country. Gender differences in CHD risk are also important. Middle
age men have a 2-5 times higher risk than women but this risk ratio differs between populations.  

Thus, these studies show the effect of ethnicity, culture and food intake etc. in prevalence of CVD and its risk factors. A crucial question of public health relevance concerns the differences in level of risk factors between populations and generalizability of western guidelines for the prevention and management of CHD to other countries.  

2.3 Pathophysiology of Coronary Dysfunction and effect of Exercise

Over last 2 decades, exercise training has assumed a major role in both the primary and secondary prevention of coronary artery disease mostly because of its positive effects on myocardial perfusion. It increases physical performance, lifts the angina threshold in patients with symptomatic CAD and improves myocardial perfusion. However, which mechanisms mediate the apparent improvement of myocardial perfusion after training therapy is a matter of continuing debate.  

Basically, regional myocardial hypoperfusion in CAD results from a combination of 3 pathogenetic components: (1) vascular stenosis, (2) microvascular dysfunction, and (3) microrheology and hemostasis. All 3 components may be affected by exercise training in patients with stable CAD. “Regression of coronary atherosclerosis” and Collateral formation” are among favorite successful theories.  

A) Regression of coronary atherosclerosis: the first era of clinical research was guided by the concept that the extent of coronary stenosis represented the key determinant of myocardial perfusion. In this phase, which paralleled the expansion of interventional cardiology, the angiographically visible static coronary stenosis was regarded as the therapeutic target. This led to the hypothesis that exercise training would result in a net regression of coronary stenosis. Three prospective randomized studies have been published assessing the influence of exercise training in combination with cholesterol lowering on the progression of CAD. They share not only the “Regression hypothesis” but also a methodological approach of quantitative coronary angiography.
The Lifestyle Heart Trial analyzed the effect of lifestyle changes, including a strictly vegetarian diet, stress management techniques, smoking cessation and 3 hours of exercise training per week, on the degree of coronary artery stenosis. They showed that in the intervention group, a regression of coronary artery stenosis from 40±17% to 38±17% and in the control group stenosis increased from 43±16% to 46±19%. They showed that this difference was even more pronounced at 5-year follow up.\(^7\)

In Stanford Coronary Risk Intervention Project, 300 patients with CAD were randomly assigned to receive either the usual care or multifactorial risk reduction, including a low-fat diet, lipid-lowering medication, and exercise training. Serial coronary artery angiograms on a yearly basis showed an attenuation of disease progression in the intervention arm, with a decline in minimal luminal diameter by 0.024±0.067 mm/ year compared with a regression of 0.045±0.073 mm/ year in the control group.\(^7\)

In the Heidelberg Regression Study, 113 patients with documented CAD were randomly assigned to a bifactorial intervention with a low-fat diet and regular exercise or to a control group. The regimen was effective in halting the progression of coronary atherosclerosis.\(^2\) After 1 year follow up, the mean luminal diameter was unchanged in the training group (0.0± 0.038mm), but it decreased in usual care group by 0.13± 0.045 mm.\(^3\)

In a retrospective analysis, a correlation between exercise-associated energy expenditure and change in minimal stenosis diameter revealed that a regression of coronary stenosis may only be expected when using>2200 Kcal/week which is equivalent to 5to 6 hours of regular exercise per week. These findings make the regression of coronary stenosis an unlikely mechanism to explain the improved myocardial perfusion in majority of patients who undergo exercise training.\(^4\)

**B) Formation of collaterals:** Evidence in animal studies suggested that long-term intensive exercise led to an improvement in coronary collateralization. In humans, data derived from clinical studies are equally controversial.\(^6\)

Belardinelli (1996) in a subgroup analysis of an 8-weeks exercise training trial ischemic cardiomyopathy involving 23 patients found a significant increase in coronary collateralization as quantified by visual classification of retrograde filling of the infarct-related vessel.\(^7\)
In Heidelberg Regression Study, which involved patients with stenotic CAD and preserved left ventricular function, they concluded that (1) angiography is not sensitive enough to detect the formation of small intramyocardial collateral vessels that will be recruited only during exercise and (2) the stimuli for collateralization are different in patients with stenotic CAD, stable angina pectoris and post-infarct patients with complete vessel occlusion.\(^6^9\)

### 2.4 Quality of Life in Cardiac Patients

Several clinical studies have shown that acute MI causes a decline in the social, physical, and psychological functionality of affected patients. These changes in quality of life (QOL) can impair the patient’s ability to perform even basic daily tasks.\(^7^6\)

Since the goals of any health and social care intervention including cardiac rehabilitation are placing emphasis on patient’s quality of life as well as quantity of life and improvement in health-related quality of life (HRQOL), therefore, HRQOL is an important aspect of the evaluation of secondary prevention programs in heart disease. Researchers have used several generic and disease specific instruments in their attempts to index HRQOL among people with ischemic heart disease. A review on instruments used to measure HRQL for people with ischemic heart disease identified four generic and nine disease-specific instruments.\(^6^8\)

An electronic data base search and literature review on quality of life outcome measures in cardiac patients was performed using the Pub Med, Cochrane Library, DARE data base, pro-quest on line data base, Blackwell on line journals, Ovid gateway, clinicaltrials.gov, BiomedCentral, Evidence Based Medicine Resources(EBM) including Center for Evidence Based Medicine(CEBM), NHS Center for Reviews and Disseminations(CRD), Center for Physiotherapy Evidence Based Data base(CEBP), PEDro, Sum Search database, and Google search engine along hand search in available published national studies in both countries from the earliest. Results revealed that 3 types of quality of life outcome measures are available: 1) Generic outcomes: are intended to be broadly applicable across different interventions and patients with different characteristics; 2) Disease specific outcomes: focus
on the complaints that are attributable to a specific diagnosis or patient population; 3) and another more recent approach is the individualized (patient generated) measures: which allow patient from their own perspective to identify the aspects that contribute to their overall quality of life.\textsuperscript{24} Data base review revealed more than 150 quality of life outcome measures which cardiac disease specific outcomes including:

Mac New Quality of Life Questionnaire\textsuperscript{32} which is a revised version of Mac New Quality of Life after Myocardial Infarction Questionnaire, Ferrans and Power Quality of Life Index-cardiac version III\textsuperscript{30}, Living with Heart Failure Questionnaire\textsuperscript{77}, Seattle Angina Questionnaire\textsuperscript{78}, Myocardial Infarction Dimensional Assessment Scale (MIDAS)\textsuperscript{29}, Cardiovascular Limitations and Symptoms Profile(CLASP)\textsuperscript{29}, Heart Surgery Symptom Inventory(HSSI).\textsuperscript{33}

With increasing body of knowledge about the quality of life and many new outcome measures, there is a need of choosing the appropriate outcome. Among generic HRQOL outcome measures SF-36 has demonstrated high validity and reliability in various disease populations including cardiac patients.\textsuperscript{79}

Shephard and Franklin (2001) mentioned about the value of QOL measurements in management of patients with cardiac disease and reported that further research is needed to determine the optimum test instrument and best method of interpreting resultant scores.\textsuperscript{77}

Smith, Taylor and Mitchell (2000) compared 4 QOL instruments including SF-36, Quality of Life Index, and Quality of Life after Myocardial Infarction and Schedule for the evaluation of individual quality of life (SEIQoL) which is a patient generated outcome in cardiac patients. They reported that SF-36 Role-Physical subscale produced the highest sensitivity score in cardiac patients. Their study suggested that there is lack of sensitivity in all 4 studied outcomes in cardiac patients and there is need for clinicians to develop a more sensitive quality of life measure in cardiac patients.\textsuperscript{30}

Dempster and Donnelly (2000) concluded that SF-36 appears to offer the most reliable, valid and sensitive assessment of quality of life. However, a few of the SF-36 subscales lack a sufficient degree of sensitivity to detect change in a patient's clinical condition. They noticed that the SF-36 and the quality of life after myocardial infarction questionnaire (version 2) are the most
appropriate currently available generic and disease specific measures of health related quality of life, respectively.\textsuperscript{32, 80}

Dougherty, Dewhurst, Nichol and Spertus (1998) compared three QOL instruments including SF-36, Seattle Angina questionnaire and Quality of life–Cardiac Index (version III) in stable angina patients. They postulated that all quality of life (QOL) instruments demonstrated acceptable test-retest reliability when administered over a 2-week interval.\textsuperscript{81}

Although some authors suggested that Mac New Quality of Life Questionnaire is the most appropriate disease specific outcome measure of quality of life among people with ischemic heart disease, there is ambiguity about the allocation of some items and it needs to be modified to provide more useful indicators of health related quality of life.\textsuperscript{32}

Despite many studies have shown the use of SF-36 instrument and its efficiency in cardiac patients in other countries, there is not much available published literature on use of these outcome measures in cardiac patients in our population.

2.5 Exercise Testing & Training in Cardiac Patients

For many years, exercise training has been the cornerstone of cardiac rehabilitation programs. Its place remains important to preserve or restore patient’s fitness and quality of life, and to optimize secondary prevention. Beyond the improvement of physical capacity, exercise training improves glucose tolerance and the lipid profile (increase of HDL, decrease of triglycerides) can restore endothelium-dependent vasodilation and to lower atheroma progression. It also seems to have beneficial effects on the autonomic nervous system.\textsuperscript{2, 36}

Ehsani, Martin, Heath and Coyle (1982) studied the effects of intense and prolonged exercise training on the heart echocardiographically in coronary artery disease patients. They suggested that prolonged and vigorous exercise training in selected patients with coronary artery disease can elicit cardiac adaptations.\textsuperscript{82}

Ciske, Dressendorfer, Gordon and Timmis (1986) studied cardio-respiratory responses to graded treadmill tests administered 1 month after myocardial
infarction or coronary bypass surgery and again after 4 weeks of aerobic training and compared in 24 patients taking beta blockers and 15 control patients. They found VO₂ max was significantly increased (p ≤0.05) by 16% in the beta-blocker group and by 21% in controls. However, the group taking beta blockers showed no significant change in oxygen pulse (VO₂/heart rate) at the fixed work load or at the ventilatory threshold, whereas the controls increased VO₂/heart rate at the fixed work load by 9% (P<0.05) and at the ventilatory threshold by 22% (p ≤0.05).83

Ades and Grundval (1999) assessed the effect of an aerobic conditioning program on cardiopulmonary markers of fitness on elderly cardiac patients. They postulated that in spite of older patients following coronary events are substantially less fit than younger patients; they obtained a similar relative improvement of aerobic capacity with a graded conditioning program.84

Brodie, Liu and Jackson (2003) established the difference in the exercise response profile of the enzymes lactate dehydrogenase (LDH), lactate dehydrogenase isoenzyme 1 (LDH-1), creatine kinase (CK), and creatine kinase polypeptide subunit MB (CK-MB) after a 12-wk cardiac rehabilitation exercise program.85

2.6 Cardiac Rehabilitation: It’s Barriers & Alternatives

Since 1960s when cardiac rehabilitation had been conceived as a treatment for patients who had suffered from an MI till now, the benefits of exercise training as a part of cardiac rehabilitation have been documented in hundreds of published researches and studies.16

According to evidence, Comprehensive cardiac rehabilitation programs are associated with improvements in exercise capacity, lipid profiles, psychological well-being, stress and mortality.12 Cardiac rehabilitation with either exercise alone or as a part of comprehensive program in MI and revascularization patients considerably reduces all cause or total mortality by at least 26 to 31%. In addition it improves functional capacity, quality of life, lipid profile and blood pressure.86

Practice guidelines and policies for cardiac rehabilitation recommend that it can be offered to all cardiovascular disease patients. Despite this, researchers
in Australia, Canada and US have reported low rates of participation. In spite of all documented benefits of cardiac rehabilitation less than 30% of all eligible patients attend CR and fewer complete the program. In a survey, Thomas (1996) estimated only 10.3 to 23.4% of all patients enroll in out-patient cardiac rehabilitation (OCR) after major heart surgeries. They included some barriers like financial difficulties, inconvenient scheduling and lack of transportation. Evidence suggests only 25 to 30% of eligible patients are enrolled in institutional based rehabilitation after coronary artery bypass grafting (CABG). Other researches showed approximately 20 to 25% of eligible post-CABG patients are enrolled in hospital-based CR in US and according to King et al. 30.8% in Canada. Poor patient uptake is related to availability and accessibility of program, strength of physician recommendation, treatment by general physician rather than cardiologist, beliefs of patient about whether their illness amenable to cure or controlled, socio-demographic factors, level of education and spouse involvement. Oldrige (1982) has reported drop-out rates of 20% in first 3 months up to 50% in 6 months to one year of institutional based CR which could be due to high intensity of exercise, poor organization of program, smokers with more than one MI and women more than men. Brubaker (2000) and Oldrige (1991) mentioned that long-term center-based rehabilitation has some difficulties like travel distances, scheduling conflicts, cost and lack of reimbursement which lead to more than 50% of drop out within 6 to 12 months of center-based CR.

All these barriers and difficulties of center or hospital-based CR lead to design some alternatives for it. These alternative methods have the potential to increase participation rate by meeting the individual needs of patient especially in elderly and patients with concomitant illness. In the past decade several types of alternative CR have been introduced and studies have documented the safety and efficacy of these programs but still there are limited data on the patterns of participation and the protocols. Sparks, Shaw and Eddy (1993) studied the effectiveness of a home exercise program using trans-telephonic exercise monitoring (TEM) and they concluded
that TEM is an effective alternative for the rehabilitation of patients who are unable to return to hospital-based program.\textsuperscript{88}

Brennan, Caldwell and Moor (1998) in order to make effective use of existing computer technology to provide more efficient cardiac care they mentioned about a computerized cardiac care service in first 3 months post-CABG patients. They mentioned about resources such as World Wide Web (WWW) links, lessons from computerized link projects, TV cables and other options. \textsuperscript{89}

Higgins, Hayes and McKenna (2001) evaluated the effect of an individual comprehensive home-based cardiac rehabilitation program combining exercise training with risk factor modification and psychological counseling on risk factors, psychological well-being, functional capacity and work resumption in 99 post percutaneous coronary intervention (PCI) patients. They suggested that an individual comprehensive home-based program improves risk factor profiles and work resumption for patients following PCI.\textsuperscript{90}

Yates, Heeren and Keller (2007) compared the effect of two methods of traditional and home-based cardiac rehabilitation on risk factor modification after cardiac events and concluded that home-based cardiac rehabilitation was not as effective as traditional-CR in reducing the frequency of anger but was as effective as traditional-CR in reducing cardiac risk factors such as BMI, waist circumference, blood pressure and cholesterol level. \textsuperscript{91}

Taylor, Watt and Dalal (2006) studied cost-effectiveness of home-based cardiac rehabilitation versus hospital-based program after myocardial infarction. They concluded that the cost of their home-based program in their setting was similar to hospital-based program and they mentioned further economic evaluations of cardiac rehabilitation in different settings are needed.\textsuperscript{92}

Collines, Scuffham and Gargett (2001) performed a cost analysis of an existing gym-based program with a proposed home-based program for cardiac rehabilitation services in West Moreton; Australia. They concluded that relevance of home-based program for rural patients facing barriers accessing traditional hospital- or gym-based programs is significant.\textsuperscript{93}

Papadakis, Oldrige and Coyle (2005) performed a systematic review of economic evaluation of cardiac rehabilitation and they suggested further trials are required to support the cost-effectiveness of cardiac rehabilitation in
patients who have undergone revascularization. According to them, literature evaluating home-based and alternative delivery models of cardiac rehabilitation is insufficient to draw conclusions about their relative cost-effectiveness. They suggested the overall quality of published economic evaluations of cardiac rehabilitation is poor and further well-designed trials are needed.  

Wu, Lin, Chen and Tsai (2006) compared heart rate recovery (HRR) in a home-based cardiac exercise with a control group of post-CABG patients. They found no significant difference between two groups.  

Fujiwara, Asakuma and Iwasaki (2000) evaluated the long-term effects of a non-supervised home exercise on exercise tolerance and quality of life (QOL) in post-MI patients. They concluded that home-based exercise group resulted in improvement in exercise tolerance but QOL score decreased and they mentioned exercise prescription is not enough and more psychological support to patients is needed.  

Brosseau, Juneau and Sirard (1995) studied the safety and feasibility of a self-monitored home-based exercise program for high risk patients after cardiac surgery. They found no complications during the program but they didn’t find any significant difference in peak VO₂ and peak rate pressure product (RPP).  

Jolly, Taylore, Lip and Stevens (2006) performed a meta-analysis and systematic review to compare home-based cardiac rehabilitation with a center-based and usual care groups. They concluded that current evidence does not show home-based cardiac rehabilitation to be significantly inferior to center-based program for low risk cardiac patients.  

Studies on Home-versus Hospital-based CR after CABG have mixed results. Some investigators have found no significant difference in exercise performance and some others found greater improvement in hospital-based. A recent retrospective review reported improvements in peak VO₂, peak work rate and peak MET in both methods but it was an observational method with some limitations like small sample size and standard protocol.  

It is observed that patients exiting a center-based CR have difficulty retaining the positive effects which derived from a 12 weeks of center-based program. Weates (1983) found CABG patients who are active in a long-term supervised CR after center-based CR had significantly higher functional capacity, better
hemodynamics and less re-hospitalization than similar patients exiting after a short duration of only center-based CR.  

Hands (1987) found no significant difference between patient’s response to supervised versus unsupervised exercise training 2 weeks after CABG but other researchers like Froelicher, Stevens and Hanson found mixed results 6 weeks post-CABG.  

2.7. Importance of Ejection Fraction & MET level in Cardiac Rehabilitation  

Decreased left ventricular systolic function is a well-established predictor of mortality in acute myocardial infarction. Although exercise capacity may also serve as an independent predictor of mortality in coronary patients, few data are available regarding this particular issue.  

Dutcher, Kahn, Grines et al ad Franklin (2007) reported that exercise capacity and Left ventricular ejection fraction (LVEF) are predictors of long-term mortality in post-MI patients and the MET level is a stronger predictor than LVEF.  

Koch, Duard and Broustet (1992) in a randomized clinical trial studied the effect of graded physical exercise in chronic heart failure. They found that training did not modify the EF, but exercise tolerance improved significantly.  

Adachi, Koiket, Obayshi(1996) reported improvement in cardiac function(such as stroke volume), both at rest and during exercise only in high intensity exercise training.  

There is less body of evidence regarding the effect of cardiac rehabilitation on LVEF globally and in our population as well.  

2.8 Review on Randomized Clinical Trials on Home versus Hospital-based Cardiac Rehabilitation  

An electronic data base search on comparative randomized clinical trials on Hospital versus Home based cardiac rehabilitation programs in Pub Med, Cochrane Library, Pro-quest and Blackwell on line journals,
BiomedCentral, clinical trials.gov, Evidence Based Medicine Resources(EBM) including Center for Evidence Based Medicine(CEBM), NHS Center for Reviews and Disseminations(CRD), Center for Evidence Based Physiotherapy (CEBP), PEDro, Sum Search data base, as well as a hand search on published national studies in both countries was done from the earliest up to August, 2007.

In a recent randomized trial, Karapolat, Eyigor, Zoghi, Yagdi, Nalbangil and Durmaz (2007), studied the effect of hospital-supervised versus home-based exercise on functional capacity, quality of life and psychological symptoms in heart transplant patients. According to the results, they recommended that a well-organized exercise program performed in a rehabilitation unit to improve postoperative exercise capacity and quality of life among heart transplant patients. Limitation of their study was small sample size of only 38 subjects.

Jolly, Taylor, Lip and Stevens (2006) performed a systematic review and meta-analysis of randomized clinical trials to determine the effectiveness of home based cardiac rehabilitation compared to usual care and supervised center-based cardiac rehabilitation on mortality, HRQOL and modifiable risk factors. They identified 18 trials for home versus usual care and 6 trials of home versus supervised center-based studies. They postulated current evidence does not show home-based cardiac rehabilitation to be significantly inferior to center-based cardiac rehabilitation for low risk cardiac patients. They reported that the numbers of patients included in the meta-analysis were small and ongoing trials will contribute to the debate on the acceptability, effectiveness and cost-effectiveness of home-based cardiac rehabilitation.

Ashworth, Chad, Harrison, Reeder and Marshall (2005) performed a systematic review on Home versus center-based physical activity programs in older adults. They reported home-based programs appear to be superior to center-based programs in terms of the adherence to the program especially in long-term.

Marchionni, Fattirolli and Fumagalli 26 (2003) in a randomized controlled trial studied the effect of Cardiac rehabilitation on exercise tolerance and quality of life in older patients after myocardial infarction. Their outcomes were Total work capacity (TWC) and Sickness Impact Profile (SIP). They used American
College of Sports Medicine (ACSM) guidelines for exercise prescription. They stratified the subjects based on age and gender with 3 age groups of middle age (45 to 65), old (65 to 75) and very old (above 75). Within each age group, participants were randomly allocated to Hospital-CR, Home-CR and no CR. Hospital-CR included 40 sessions of exercise consisted of 24 sessions of endurance (3 times/week) and 16 sessions (twice/week) of stretching and flexibility exercise. Endurance exercise included of 5 min warm up, 20 min cycle ergometer, 5 min cool down followed by 5 min post-exercise monitoring and flexibility exercise included of 1 hour session of stretching and flexibility exercise. Intensity of exercise was 70-85% of HR max. Home-CR program included 4-8 instruction sessions in hospital, cardiovascular risk factor management, and exercise prescription with wristwatch and cycle ergometer for 2 months. Every week visit was done at home. NO-CR group only single structured management session was done. They concluded Post-MI Hospital-CR and Home-CR are similarly effective in the short term and improve TWC and HRQOL in each group. However, with lower costs and more prolonged positive effects, Home-CR may be the treatment of choice in low risk older patients.

Jolly23 (2003) in a randomized controlled trial (Birmingham Rehabilitation Uptake Maximization Study) studied the cost effectiveness of Home versus Hospital-based CR in a multi-ethnic post-myocardial infarction and revascularization population. Their outcomes were cardiac risk factors including serum cholesterol, smoking cessation, blood pressure, and adherence measures with self-reported behavior, quality of life and death or other cardiac events, and Distance walked on Shuttle Walk Test at 6, 12, and 24 months. They stratified the subjects based on original disease, age and sex, ethnicity and hospital which they have recruited. Hospital-based group included National Service Framework (NSF), relaxation and exercise training for 6 to 12 weeks on a once or twice weekly base. Home-based program include HEART MANUAL for first 6 weeks post-MI or revascularization. Home visits were at 6 and 12 weeks and telephone contacts 3 times/week.

Arthur, Smith, Kodis and Mckelvie 24 (2002) in a randomized clinical trial studied a Home-based versus Hospital-based protocol in cardiac patients. Their primary outcome measure was Peak VO₂ or MET based on Graded Exercise
Test (GXT) on cycle ergometer and they studied HRQL based on SF-36 as a secondary outcome measure. In Hospital-based group subjects went on 3 session of exercise per week for 6 months. Exercise included 10-15 min of warm up by walking and stretching followed by 40 min of aerobic exercise consisting of cycle ergometer, treadmill walking, track walking and stair climbing which followed by 10-15 min of cool down by walking and stretching. In Home-based program subjects attended 1 hour individual exercise consultation at base line and after 3 months of exercise training. Subjects went on 5 sessions of exercise for 6 months. Each exercise training session included a 10-15 min warm up, 40 min of aerobic exercise with self-paced walking followed by 10-15 min cool down. Throughout the study, patients were asked to keep an exercise log of their activity, length of time involved in each exercise session, and heart rate during exercise. Home patients were telephoned every 2 weeks to monitor progress, assess and document adherence, revise the exercise prescription if necessary and provide support and education. Intensity of exercise after baseline GXT was based on target of 60% of peak VO₂. After 3 months it was increased to 70% of peak VO₂. They concluded that low-risk CABG patients may be served as well or better with a monitored, home-based exercise program than with a hospital-based program. They mentioned that limitations of their study were it was a single-center study, and some patients had taken psychological consult or nutritional consult from a dietician.

2.9 Research Gap

Review of literature shows that there are still controversies on overall effectiveness of cardiac rehabilitation generally because of many uncontrolled observations, small trials, and patient’s age of less than 65 in spite of 40% of patients over 65 years old and many trials included only men in spite of 30% of patients are women. Many of these studies have weaknesses like small sample size and lack of prescription of standard protocol. All these heterogeneity of trials impair their external validity and generalization of their conclusions beyond the groups they have been studied is not possible.
There is paucity of studies on effectiveness of cardiac rehabilitation on left ventricular ejection fraction (LVEF) as an important clinical outcome in CAD patients. There is also limited evidence on effectiveness of Home-based Cardiac Rehabilitation programs in our population in India & Iran.

According to the existing research gap regarding the effect of both Hospital and Home-based cardiac rehabilitation between our population and developed countries and limitations in generalization of their results to our communities as mentioned in the review of literature, and limited evidence in our population the current study intended to evaluate the effect of a Hospital versus Home-based cardiac rehabilitation on Quality of Life, Ejection Fraction and Functional Capacity in low and moderate risk patients with coronary artery disease in two developing countries; India & Iran.